Paediatric Drug Development from a Labeling Perspective

A detailed view on the European Summary of Product Characteristics with an exemplary comparison to the US Prescribing Information

Wissenschaftliche Prüfungsarbeit

zur Erlangung des Titels
„Master of Drug Regulatory Affairs“

der Mathematisch-Naturwissenschaftlichen Fakultät
der Rheinischen Friedrich-Wilhelms-Universität Bonn

vorgelegt von

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Bonn 2016

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Abstract

Triggered by legislative initiatives in the European Union and the United States in the last decade, pharmaceutical companies had to increase their efforts to investigate medicinal products also in the paediatric population. Therefore today's drug development processes are accompanied with the assessment of possibilities for a therapeutic use in the paediatric population.

This Master thesis aims to systematically investigate how the considerations related to paediatric development are translated into European prescribing information documents, i.e. Summary of Product Characteristics (SmPC), and what information is finally communicated to health care professionals via this medium. In order to achieve this, qualitative and quantitative criteria were established to associate information from SmPC documents with aspects relevant for the paediatric population. These criteria were then applied to a robust sample of SmPCs to yield over 600 datasets that were the basis for further analyses. The results of these analyses revealed a very clear picture on what information is communicated to health care professionals via the SmPCs. Information related to the paediatric population was gained for instance regarding the availability of information, different types of information or age ranges. Furthermore, an exemplary comparison to US prescribing information documents was performed.

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Abbreviations

ATC	Anatomical Therapeutic Chemical Classification System
COPD	Chronic Obstructive Pulmonary Disease
EMA	European Medicines Agency
EPAR	European Public Assessment Report
EU	European Union
MA	Marketing Authorisation
MAA	Marketing Authorisation Application
MAH	Marketing Authorisation Holder
PDCO	Paediatric Committee within the European Medicines Agency
PIP	Paediatric Investigation Plan
SmPC	Summary of Product Characteristics
US	United States of America
PI	Prescribing Information

1 Introduction and Goal

Triggered by legislative initiatives in the European Union and the United States in the last decade, pharmaceutical companies had to increase their efforts to investigate medicinal products also in the paediatric population.

From a European perspective, applicants must consider paediatric development for every new Marketing Authorisation Application (MAA) for which the procedure started after July 25th, 2008. For this reason every applicant needs to evaluate within the medicinal product development process, whether there are possibilities for a use in the paediatric population. An outcome of this assessment may be that the disease for which the medicinal product intended occurs only in adults, rendering a paediatric development pointless. Another outcome could be that the conduct of a paediatric development program under the scope of Paediatric Investigation Plan (PIP) would lead to an indication in the paediatric population. According to the Paediatric Regulation[1] and the Guideline on Summary of Product Characteristics (SmPC)[2], these outcomes need to be depicted in the corresponding SmPC documents.

This Master thesis aims to systematically investigate how the considerations related to paediatric development are translated into SmPCs and what information is finally communicated to health care professionals. In the first part of this thesis criteria will be established that allow a clustering of information related to the paediatric population in SmPCs. In the second part, these criteria will then be applied to a sample of registered SmPC documents in order to qualify and quantify what information related to paediatric development and its outcome is actually communicated to health care professionals. However, with thousands of medicinal products being registered in the European Union, it is necessary to restrict the sample to a reasonable amount of SmPCs. Finally, the criteria should be able to describe the information in the SmPCs in a way that they can be used for the assessment of other medicinal products registered in the European Union, but also for any other country in the world. In order to investigate this factor a comparison with a limited number of US prescribing information (PI) documents will be conducted.

A review of the available literature yielded a lot of publications related to clinical development in the paediatric population and also to off-label use, but only few publications addressed the topic of information on the paediatric population in prescribing information documents (e.g. SmPCs). These publications are then mostly focussed on subsets of information such as pre-clinical data[3] or specific

diseases[4,5]. The most significant literature reference is the “5-year report to the European Commission on the experience acquired as a result of the application of the Paediatric Regulation” (in the following referred to as “5-year report”)[6]. This document includes information with the closest proximity to the topic of this thesis and is discussed in greater detail in section 3.1.

2 Paediatric legislation and relevant regulatory guidance in the European Union

In the European Union, Regulation (EC) No 1901/2006 (= paediatric regulation) is the legal framework for the paediatric development of medicinal products and also governs the inclusion of information related to the paediatric population into the Summary of Product Characteristics (SmPC). Based on the paediatric regulation, the Guideline on Summary of Product Characteristics from 2009 clearly defines how this information should be reflected in the SmPC. As both documents are the key references from a European perspective, they are described in more detail in the following.[1,2]

2.1 Paediatric Regulation[1]

The paediatric regulation is a legislative initiative that aims to "facilitate the development and accessibility of medicinal products for use in the paediatric population" by introducing obligations and incentives/rewards for applicants or Marketing Authorisation Holders. One of the key obligations is the conduct of clinical studies in the paediatric population to ensure that all appropriate medicinal products have been investigated for their potential use in the paediatric population. The corresponding paediatric development program, as documented in the Paediatric Investigation Plan (PIP), must be approved by the Paediatric Committee (PDCO) within the European Medicines Agency (EMA). Only if the paediatric development has been conducted in compliance with the PIP and the respective results are included in the Marketing Authorisation Application (MAA), the medicinal product will be accepted for review by the competent authority (§ 7). However, Article 7 of the paediatric regulation also defines exceptions to this rule, as there are medicinal products or specific indications for which a paediatric development is not appropriate or there are scientific or technical grounds to delay the paediatric development. In order to comply with § 7 in these cases, the applicant must request a waiver or a deferral at the PDCO.

Once a Marketing Authorisation has been obtained for a medicinal product, the means of communicating "the results of studies in the paediatric population as well as the status of the paediatric investigation plans, waivers and deferrals" to health care providers and patients is the product information (§ 28).

As this thesis is focussing only on medicinal products where the MAA had to fulfil the requirements of § 7 (1) of the paediatric regulation, other obligations triggering the inclusion of information on the paediatric population (e.g. corresponding to § 8, § 45 or § 46) are not described in this document.

2.2 Guideline on Summary of Product Characteristics[2]

The most relevant guideline for the creation of prescribing information documents in the European Union is the SmPC guideline from 2009. As a general rule, this guideline states that information on specific populations (e.g. children and adolescents) should be given at the end of each section of the SmPC. Thus information on the paediatric population is distributed over the complete SmPC, topic by topic. For some sections the SmPC guideline gives specific provisions on how information on paediatric patients should be presented, which are summarised in the following.

Section 4.1: Therapeutic indications

A specific requirement for the indication section is the necessity to state the age limits of the indicated population. This attribution of an age group in the indication statement allows the differentiation between medicinal products with or without paediatric indication.

Section 4.2: Posology and method of administration

While the indications section is focussed only on those parts of the paediatric population where the benefit-risk ratio is positive, section 4.2 is the only section that provides information on all subsets of the paediatric population.

For subsets of the paediatric population covered in section 4.1, this translates into age-related recommendations for the dosage and administration of the medicinal product. For all other subsets of the paediatric population, section 4.2 aims at giving information about why the medicinal product is not indicated. As there may be several reasons for the latter aspect, the SmPC guideline defines several categories to classify medicinal products with regards to the absence of a paediatric indication. Within these classifications the two main drivers are insufficient data and data suggesting a negative benefit-balance in subsets of the paediatric population.

Reasons for insufficient data may be that

- there is no relevant use for the medicinal product in the paediatric population.

- no data are available, because a paediatric development is not required (e.g. medicinal product is likely to be ineffective or unsafe) and therefore waived.
- no data are available, because the outcome of studies in adults need to be awaited before commencing trials in the paediatric population, which are therefore deferred.
- there is limited data, but not enough to allow for an indication or dosage recommendations.

The reason for a negative benefit-risk balance may be data suggesting safety concerns, lack of efficacy or both. In particular cases where the medicinal product must not be given for safety reasons, a contraindication is warranted.

Section 4.3: Contraindications

With regards to contraindications, the SmPC guideline makes no difference between the paediatric population and other specific populations. In general, if a medicinal product must not be given for safety reasons in a specific patient population, this results in a contraindication for this group. The SmPC guideline further specifies that lack of data alone does not lead to a contraindication.

Section 4.4: Special warnings and precautions for use

The SmPC guideline clarifies that warnings and precautions specifically related to subsets of the indicated paediatric population should be included under the sub-heading “Paediatric population”. While the general definition for warnings and precautions also applies to paediatric patients, the SmPC guideline additionally gives examples for aspects that should be considered for the paediatric population such as long-term safety data on growth or impact on children’s daily activities.

Section 4.5: Interactions with other medicinal products and other forms of interaction

The sub-section on paediatric patients should draw a complete picture on the known and unknown interaction information related to the indicated parts of the paediatric population. The health care professional should be made aware of aspects that are specific to the paediatric population or where the magnitude of an interaction differs between adult and paediatric patients, but also if the interaction data are similar to those of adults, inconclusive or missing.

Section 4.8: Undesirable effects

Information on the safety profile in the paediatric population should always be given unless irrelevant for health care professionals. In all cases where safety data in the paediatric population is available, the size of the corresponding safety database and the respective age distribution should be described. The information may range from complete lists of adverse reactions in the investigated parts of the paediatric population over specific differences in the safety profile between adult and paediatric patients to standard language for medicinal products where the frequency, type and severity of adverse reactions in children are the same as in adults.

Section 4.9: Overdose

If applicable, this section should include specific considerations for the paediatric population including the risk of a fatal poisoning by ingestion of one dose unit.

Section 5.1: Pharmacodynamic properties

This section should include the results from all clinical efficacy studies as well as clinically relevant pharmacodynamics studies in the paediatric population. In addition, the outcome of clinical safety studies related to the paediatric population should be given. Besides the typically expected content such as study objectives or study duration, the description of paediatric studies should specifically provide details on age and dosing.

As opposed to the requirements for the description of studies in adults, information on clinical studies conducted in the paediatric population should also be given when the efficacy and safety cannot be established from the available data. In these cases a reference is made to section 4.2 and, if applicable, to section 4.3.

Another particularity for the paediatric population is the necessity to give information on granted waivers or deferrals related to the paediatric development. This is important information as it gives an explanation why certain data are not available or why the paediatric development program according to the paediatric investigation plan is still ongoing.

Section 5.2: Pharmacokinetic properties

The principal content of this section is the same as for adults. For the paediatric population differences between age groups or dosage forms as well as the comparability to adults may be of specific relevance.

Section 5.3: Preclinical safety data

Data from preclinical studies, e.g. in juvenile animals, may point towards clinically relevant effects in the paediatric population. These findings should be presented in this section with a discussion on the relevance and respective references to other sections such as special warnings and precautions.

3 Assessment of Product Information Documents

As laid out in the introduction, it is the aim of this Master thesis to assess information on the paediatric population in prescribing information documents under the scope of respective legislative initiatives with a focus on the European Union.

A meaningful assessment related to the described topic requires on the one hand a robust sample of prescribing information documents and on the other hand qualitative and quantitative criteria that correlate with the presentation of information on the paediatric population in general.

To clarify the exact scope of the assessment, “presentation of information on the paediatric population in general” has to be defined more clearly. The phrase refers to types of information relevant for medicinal products in conjunction with the paediatric population and where and how in the prescribing information these types of information are addressed. Not included in the assessment are product-specific particularities that cannot be generalised for the paediatric population. For instance, not every adverse reaction is taken into account, it is only considered if information on paediatric patients is included in section 4.8 of the SmPC or not.

The following approach was taken to achieve the defined goal of this thesis.

1. Discussion of basic considerations with reference to the 5-year report, which is one of the main references for this thesis.
2. Definition of a meaningful sample based on medicinal products registered in the European Union via the Centralised Procedure.
3. Creation of criteria (e.g. categories, scenarios) based on the EU legislation that allow a standardised assessment of prescribing information documents with the aim to qualify and to quantify information on the paediatric population presented to the health care professional in prescribing information documents. The criteria are designed to ensure the comparability between different countries for the same medicinal product as well as between different medicinal products for the same country.
4. Assessment of the EU SmPC documents included in the sample. To this end, the information was categorised, analysed and discussed, based on the defined criteria.
5. Comparison of defined criteria between the generated datasets from the analysis of the EU SmPC documents and the corresponding US PI documents, where available. As a comparison of all analysed EU SmPC

documents would go beyond the scope of this Master thesis, only the subset of orphan medicinal products is compared in regard to selected criteria.

3.1 5-year report to the European Commission on the experience acquired as a result of the application of the Paediatric Regulation

One of the key references for this thesis is the 5-year report, which captures the impact of the paediatric regulation on SmPC documents. In order to distinguish this thesis from the 5-year report and to clearly point out, which aspects from the 5-year report have been taken into account, corresponding considerations are presented in the following.[6]

The 5-year report investigates the progress related to all relevant aspects of the paediatric regulation, including paediatric development, availability of medicinal products for paediatric patients and increased information for medicinal products on the use in the paediatric population. One of the key measures to convey information on the paediatric population is the SmPC of a medicinal product. With regards to SmPCs, the 5-year report clusters the assessed medicinal products according to the following categories:

- Initial marketing authorisation (MA) including a paediatric indication
- Extension of therapeutic indication to include the paediatric population
- New route of administration or new pharmaceutical form for paediatric use
- Variation to include a statement on waiver or deferral in the SmPC
- Variation to include paediatric dosing information or recommendations (section 4.2 of SmPC)
- Variation with paediatric data linked to off-label use included in SmPC
- Variations under Article 36.1.2 – data of completed PIP failed to lead to a paediatric indication
- Paediatric regulation referral procedures (§ 29)

This categorisation and the associated assessment in the 5-year report shows a strong focus on the type of regulatory activity that lead to changes of the SmPC related to information on paediatric patients. In contrast to the 5-year report, this thesis is assessing all information on the paediatric population presented in the SmPCs, but does not take into account when and by which regulatory activity the different parts of this information have been included. The generated data are supposed to reflect the perspective of a customer (i.e. health care

professional), who is consulting the SmPC of a medicinal product to retrieve information about the paediatric population.

Although the perspective on the assessment of the SmPCs is different, some aspects have been taken into consideration for this thesis as they are independent from the regulatory procedural approach. The 5-year report, for instance, classifies information on paediatric patients presented in the SmPC into high level content units:

- Dosing information for children added to SmPC section 4.2
- Paediatric study results added to the SmPC section 5.1
- Paediatric safety information added to the SmPC section 4.8
- Statements on deferral or waiver included or added to SmPC section 5.1
- Other paediatric information added to other sections of the SmPC (e.g., section 5.2)
- PIP data failing to lead to paediatric indication (Annex II, sections 4.7 and 7.7)

This grouping is very relevant for the assessment of the SmPCs, as it informs about the types of information that the health care professional is going to find in the document. From the perspective of this thesis, the presented grouping requires additional levels of detail, which are presented in the following section 3.3.2

Another aspect considered for this thesis is the classification of section 4.1 (Therapeutic indications). The 5-year report differentiates between “paediatric only” or "mixed" (=adult and paediatric indication). As some products were not adequately represented by this classification, which is mainly related to the significant differences in the proportion of paediatric patients treated in clinical studies (e.g. 98% for Bexsero vs. 0,7% for Tivicay), a slightly different approach was used in this thesis, as described in section 3.3.1.1.

Compared to the sample assessed by the EMA in the 5-year report, the sample used in this thesis shows only a small degree of overlapping. This can be associated with the following three reasons:

- The evaluation in this thesis only includes medicinal products for which the start of procedure date for the MAA was after July 25th 2008. For this reason, SmPCs updated based on the provisions of § 8, § 45 and § 46 of the paediatric regulation, which play an important role in the 5-year report and contribute to a relevant number of the listed medicinal products, are out of scope.

- The 5-year report covers medicinal products registered between 2007 and 2011, while this thesis takes authorisation dates between 10/2009 and 07/2015 into account.
- This thesis considers only medicinal products registered via the Centralised Procedure. The 5-year report also reflects data from medicinal products authorised through National, Decentralised and Mutual Recognition Procedure

The medicinal products covered in the assessment in the 5-year report as well as in this thesis are listed in Table 1.

Table 1: Medicinal products covered in the assessment in the 5-year report as well as in this thesis

Medicine Name	Product Number	ATC code	Authorisation date
Chapter 4.1. Initial marketing authorisation (MA) including a paediatric indication			
Buccolam	EMEA/H/C/002267	N05CD08	05.09.2011
Cinryze	EMEA/H/C/001207	B06AC01	15.06.2011
Eurartesim	EMEA/H/C/001199	P01BF05	27.10.2011
Ilaris	EMEA/H/C/001109	L04AC08	23.10.2009
Menveo	EMEA/H/C/001095	J07AH08	15.03.2010
Prevenar 13	EMEA/H/C/001104	J07AL02	09.12.2009
Tobi Podhaler	EMEA/H/C/002155	J01GB01	20.07.2011
Votubia	EMEA/H/C/002311	L01XE10	02.09.2011
Vpriv	EMEA/H/C/001249	A16AB10	26.08.2010
Zoely	EMEA/H/C/001213	G03AA14	27.07.2011
Chapter 4.5. Variation to include paediatric dosing information or recommendations (section 4.2 of SmPC)			
Pandemic Influenza Vaccine H5N1 Baxter AG	EMEA/H/C/001200	J07BB01	16.10.2009

3.2 Sample Determination

The sample was determined based on several considerations that are described in the following.

As a starting point for the assessment, the European Union was picked for reasons of familiarity. Centrally authorised products were selected, as for these products the English versions of the SmPC are readily available on the website of the EMA together with a helpful set of metadata. Furthermore, the Centralised Procedure represents a consensus over all European Member States and therefore depicts a homogenous approach towards the assessment within MAAs and also towards the interpretation of the legal and regulatory framework. In contrast National, Mutual Recognition or Decentralised

Procedures may include a stronger bias on the investigated topic reflecting the individual opinion of single Member State. In addition, the number of registered products is vastly higher and the SmPCs are not always freely available in English language.

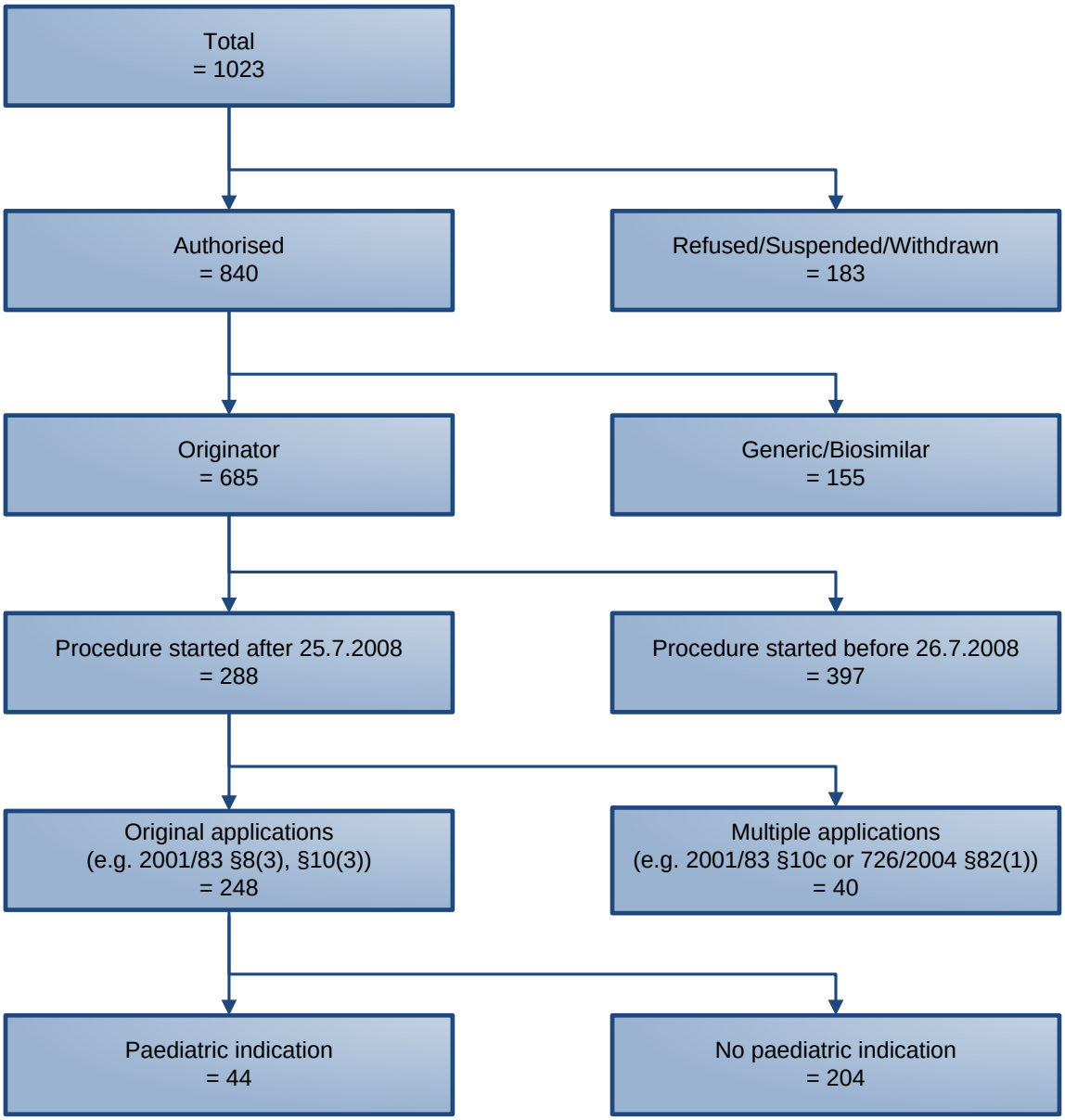
Technically, the registration information on medicinal products registered via the Centralised Procedure was retrieved on August 25th, 2015 from the webpage of the European Medicines Agency (http://www.ema.europa.eu/ema/) via the available site functionality to export certain information related to European Public Assessment Reports into an Excel spreadsheet for all listed applications (1023). The retrieved spreadsheet included the metadata depicted in Table 2.

Table 2: Data fields included in export of centrally registered products

Medicine Name	Authorisation Date
Product Number	Indication
Active Substance	Conditional Approval
Common Name	Exceptional Circumstance
ATC code	Is Orphan
Marketing Authorisation Holder	Is Generic
(Authorisation) Status	Biosimilar
Revision Number	

Based on the information available from the EMA via this spreadsheet, several filtering steps were applied to the data to yield the sample of medicinal products. The first two filtering steps could be directly executed without additional processing of the data: The following three filtering steps afforded additional data collection/processing and resulted in three new data fields: Start of Procedure Date, Multiple Application and Paediatric Indication. A detailed description of the individual filtering steps is presented in the following sub-sections. In addition, the results of the sample determination are presented in Figure 1 below.

Figure 1: Sample determination



3.2.1 Field “Authorisation Status”

All rejected, suspended or withdrawn applications or registration were excluded from the sample. The respective medicinal products are not marketed in the EU and therefore irrelevant to the prescriber.

3.2.2 Fields “Is Generic” and “Biosimilar”

Generic and Biosimilar medicinal products were excluded from the sample, as the relevant parts of the SmPCs of these products are copies of the originator SmPCs and don’t add much value for this thesis.

3.2.3 Field “Start of Procedure Date”

As mentioned in the introduction, this thesis only considers registrations that fall within the scope of § 7 of the paediatric regulation. § 57 of the paediatric regulation defines the entry into force of § 7 as July 26th 2008. This means that all Marketing Authorisation Applications submitted after July 25th 2008 must include results from the PIP or information on waivers and/or deferrals in the corresponding SmPCs.

In order to filter for this subset of registrations it is necessary to know the MAA procedures that started after July 25th 2008. With the authorisation date being a part of the spreadsheet from the EMA, a substantial part of registrations can be excluded or included based on the following considerations. Every medicinal product with an Authorisation Date older than July 26th 2008 was excluded as the start of procedure date must also be before that date. All medicinal products with an authorisation date after 01.01.2010 were included, because the maximum duration of an MAA in the Centralised Procedure is 523 days (a maximum of 277 days according to procedural timetable[7] and a maximum of 246 days of clock-stop time corresponding to 6+2 months[8]). For all other registrations (authorised between 26.07.2008 and 01.01.2010) the Start of Procedure Date was retrieved from the initial European Public Assessment Reports (EPAR) available on the website of the EMA.

3.2.4 Field “Multiple Application”

Marketing Authorisation Applications according to § 10 c of Directive 2001/83/EC (informed consent application) and § 82 (1) of Regulation (EC) No 726/2004 are regulatory pathways to obtain multiple registration for the same medicinal product. In these cases the relevant information in the SmPCs is identical to the “original” application. For these kinds of registrations the same applies as for Generics and Biosimilars, therefore they are excluded from the sample. The approach to identify the respective medicinal products was to search for duplicates in the data field “Active Substance”. If, within these duplicate entries, more than one entry was available for which the “Is Generic” field indicated “no” (i.e. no Generic medicinal product), there was high likelihood that these entries included § 10 c or § 82 (1) applications. For verification of the actual multiple registrations, the initial EPARs of the identified medicinal products were consulted. In some cases the active substance was worded in a slightly different way (e.g. mentioning of the salt or not), therefore the respective registrations were not identified within the initial filtering step. However, the corresponding products were excluded within the actual assessment.

3.2.5 Field “Paediatric indication”

The paediatric indication field is a “yes/no” qualifier that determines if a medicinal product is indicated in subsets of the paediatric population. It divides the sample into two parts that are connected to different questions in the assessment. In case of a paediatric indication, the prescriber knows that the medicinal product can be used in the paediatric population and the question is “What do I need to know regarding the safe and effective use of the medicinal product?”. In contrast to this, if there is no paediatric indication, the prescriber will ask “Why is there no paediatric indication and what information on the paediatric population is or will be available?”. In order to fill in the Paediatric Indication field, the “Indication” field in the spreadsheet from the EMA was assessed for the appearance of the word “adult” and missing classifiers for the paediatric population. This approach is related to the requirement given in the SmPC guideline that “it should be stated in which age groups the product is indicated, specifying the age limits, e.g. ‘X is indicated in <adults> <neonates> <infants> <children> <adolescents> <aged x to y <years,months>>”. Consequentially, every medicinal product only indicated in adults, is not indicated in the paediatric population. The field “Paediatric Indication” field was verified in the assessment of the SmPC documents, especially as there were some cases where the indication statement did not mention the age group.

3.2.6 Sample

The sample includes 248 medicinal products, which are listed in Table 12 (Annex I). The fields used for this list of medicinal products are presented together with a short explanation in Table 3 below:

Table 3: Data fields included in Table 12 (Annex I)

Field	Explanation
Medicine Name	Information required to clearly identify the medicinal product
Active Substance	Carries information on the type and class of the medicinal product (e.g. Biological, ending “gliptin” for inhibitors of dipeptidyl-peptidase-4 (DPP-4)
Product Number	Information required to clearly identify the medicinal product
ATC Code	Relevant for the assessment in association with therapeutic areas
Is Orphan	Basis for the sample of US PI documents
Start of Procedure Date	See 3.2.3
Authorisation Date	Important information on the timing of the MAA procedure
SmPC Date	Information required to clearly identify the SmPC version used for the assessment. The SmPC Date field is derived from the date listed in the field “Last updated” on the EMA website related to the Annex I-III on the Product Information tab of the EPAR. For products where the Annex I-III from the MAA is still valid (i.e. the field “Last updated” is empty) the field “First published” was used as SmPC Date.
Paediatric Indication	See 3.2.5

3.3 Criteria for SmPC assessment

The criteria for SmPC assessment were established based on the three questions the health care professional would ask when consulting the SmPC for information on paediatric patients:

- Is information related to the use of the medicinal product in the paediatric population available?
- What information is available?
- What age groups are affected by the provided information?

Based on these questions, the criteria are described in the following sections.

3.3.1 Availability of information with relation to the use in the paediatric population

The criteria for the availability of information were based on the SmPC guideline. As explained in section 2.2, the SmPC sections 4.1 (Therapeutic indications) and 4.2 (Posology and method of administration) provide a standardised approach to communicate different scenarios related to the use of a medicinal product in the paediatric population. The scenarios given in the SmPC guideline can be grouped according to the benefit-risk ratio of the medicinal product in the paediatric population: positive (scenario 1), negative (scenario 3), cannot be established (scenario 2), not relevant (scenario 4).

3.3.1.1 Scenario 1

Scenario 1 addresses the case of a paediatric indication, where the medicinal product can be used in subsets of the paediatric population. This must be stated in section 4.1 with a respective dosing statement in section 4.2. However, depending on the amount of paediatric patients the indication is based upon, the presentation of information is fundamentally different and requires additional differentiation into the following sub-scenarios:

Scenario 1a - Adult focussed indication

The indication section is covering adult as well as paediatric patients. A posology recommendation for the paediatric patients can be made. In this scenario, the paediatric population is considered a subgroup within the complete age range covered in the indication. The SmPC is focussed on adult patients and only the particularities for the paediatric population are described according to the SmPC guideline.

Scenario 1b – Paediatric + Adult indication

As in scenario 1a, the indication section is covering adult as well as paediatric patients and a posology recommendation for the paediatric patients can be made. The difference to scenario 1a is a similar amount of paediatric patients treated in clinical trials compared to the corresponding amount of adult patients. Medicinal products, for which the ratio between studied paediatric and adult patients could not be determined based on the information presented in the SmPC, were attributed with scenario “1a or 1b”.

Scenario 1c - Paediatric focussed indication

The medicinal product has been developed mainly for the paediatric population, but subsets of the adult population have also been studied and are included in the indication. The complete SmPC is written for the paediatric population and the adult population is addressed as subgroup for which particularities are described.

Scenario 1d - Paediatric only indication

The medicinal product has been developed only for the paediatric population. The complete SmPC is written for the paediatric population. Adult patients are not considered.

3.3.1.2 Scenario 2

Scenario 2 captures products for which no conclusion on the benefit-risk ratio can be drawn and sub-divides into:

Scenario 2a – No data

No data are available. Thus, safety and efficacy in paediatric patients has not been established. The interesting question for this scenario is, if the availability of data is pending or if it is unlikely that data for the paediatric population will be generated.

Scenario 2b – Limited data

Limited data in the paediatric population are available, but the safety and efficacy in paediatric patients cannot be established and no recommendation on a posology can be made. In this case the data are most likely insufficient or inconclusive and the benefit-risk ratio is neither positive nor negative. Ideally, more data will be generated to close the gap and give a clear recommendation for the paediatric population. Scenario 2b was also attributed when only pre-clinical data in juvenile animals were available.

3.3.1.3 Scenario 3

Scenario 3 covers all cases where the available clinical, non-clinical or literature data suggest a negative benefit-risk ratio. Depending on the severity, the SmPC guideline provides two options for this scenario:

Scenario 3a – Should not be used

In this scenario, the use of the medicinal product in the paediatric population is not completely excluded. There may be cases in which the treating physician anticipates a positive benefit-risk ratio for an individual paediatric patient, even though the data from the overall studied paediatric patients speak against it.

Scenario 3b – Contraindicated

The available data suggest a serious safety risk for the subsets of the paediatric population that outweighs any potential benefit and the medicinal product must not be used.

3.3.1.4 Scenario 4

Scenario 4 captures medicinal products with no relevant use in subsets of the paediatric population. This scenario is in principle a special case of scenario 2a where a justified reason for the absence of data is given.

3.3.2 Types of information on paediatric patients in the SmPC

While the 5-year report is clustering data according to “dosing information”, “paediatric study results”, “paediatric safety information”, “statements on deferral or waiver” and “other paediatric information”, the approach for this thesis is to use the full granularity given by the SmPC sections. Each section conveys information about a specific topic that can be derived from the respective section heading. This still allows an association with the categories mentioned in the 5-year report, but there is also the possibility to differentiate, e.g. between types of safety information. However, in section 5.1 two aspects related to paediatric patients are depicted: paediatric study results as well as waivers and deferrals. In order to clearly differentiate this, waivers and deferrals are captured via an additional data field in the assessment procedure. In summary, this criterion is a list of SmPC sections containing information about paediatric patients, which is attributed to each medicinal product in the investigated sample.

For some medicinal products multiple statements related to waivers and deferrals were available. For these cases the category for section 5.1 was further split up to differentiate between: “5.1 Pharmacodynamic properties – Studies”, “5.1 Pharmacodynamic properties – Waiver/Deferral” and “5.1 Pharmacodynamic properties - Studies + Waiver/Deferral”. However, the category “5.1 Pharmacodynamic properties – Waiver/Deferral” was only applied, if waivers and deferrals could not be adequately depicted via the Waiver/Deferral field. Furthermore, SmPC sections other than section 4.2 were not included in the assessment if they only included a statement on the absence of information.

3.3.3 Attribution of age ranges to different pieces of information

The SmPC guideline defines a set of age groups in the provisions for the indication section (i.e. neonates, infants, children, adolescents) and opens up to a specific declaration of the age range with the text block “aged x to y <years, months>”. This gives the possibility to closely align the indication to the actually studied population, which gives a more accurate picture than a categorisation according to age groups only.

The approach for this thesis was to capture the age ranges given in the investigated SmPCs for the indication in section 4.1, for the standard statements in section 4.2, for the waivers/deferrals in section 5.1 and for the study information (sections 5.1 and 5.2) in scenario 2b (limited data).

3.3.4 Other criteria relevant for the SmPC assessment

Multiple indications:

For some medicinal products different scenarios apply depending on the indication. The criteria listed above apply to these products in the same way as for other products, but in addition the field “Multiple indication” is filled in with an identifier (e.g. Indication 1, Indication 2, …) to differentiate the datasets related to the individual indications. For products for which the differentiation between indications is not relevant for the assessment within this thesis, the field is filled with “NA”.

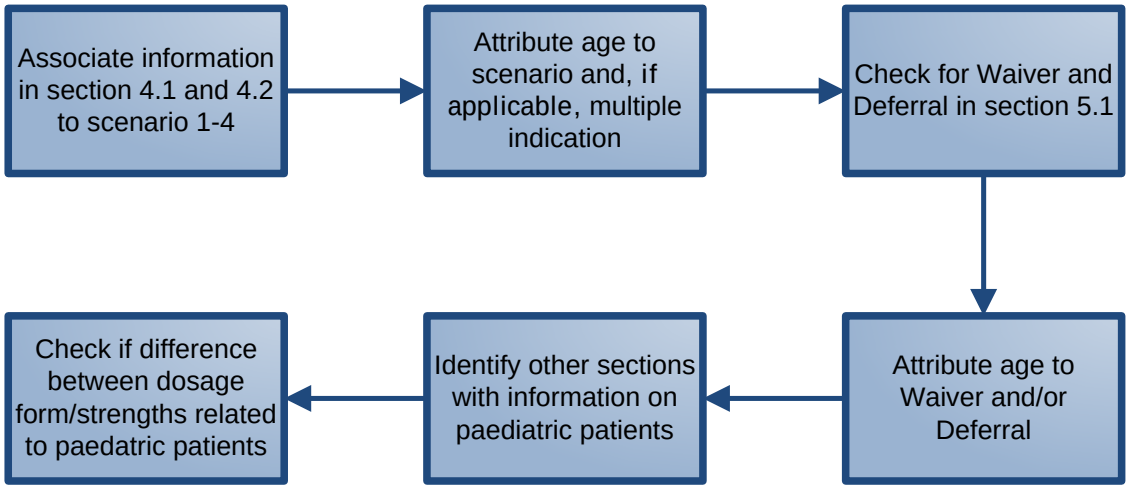
Dosage Forms/Strengths

The information provided on paediatric patients in the SmPC may vary depending on the dosage form and/or strength of the medicinal product. In order to reflect this criterion, the field “Dosage Forms/Strengths” was introduced. It is filled in similarly to the field “Multiple Indications”. The value is “NA”, if the dosage form or strength is not relevant for the assessment. Otherwise the respective dosage form and/or strength is included.

3.3.5 Application of the criteria on SmPC documents

For the assessment, the criteria established in this section were applied to the SmPCs of all medicinal products included in the sample according to the scheme shown in Figure 2 below. The respective documents are available on the website of the EMA.

Figure 2: Process for application of the criteria on SmPC documents



The data corresponding to the application of the criteria on the SmPC documents were captured in tables, which are shown in Annex II.

3.4 Results and Discussion of the SmPC assessment

The application of the criteria presented in section 3.3 to all SmPCs included in the sample resulted in 617 individual datasets describing the information communicated to health care professionals via this medium. In the following, the results are presented and discussed with a differentiation between medicinal products with and without paediatric indication. Aspects associated with both types of medicinal products are addressed in a separate subsection.

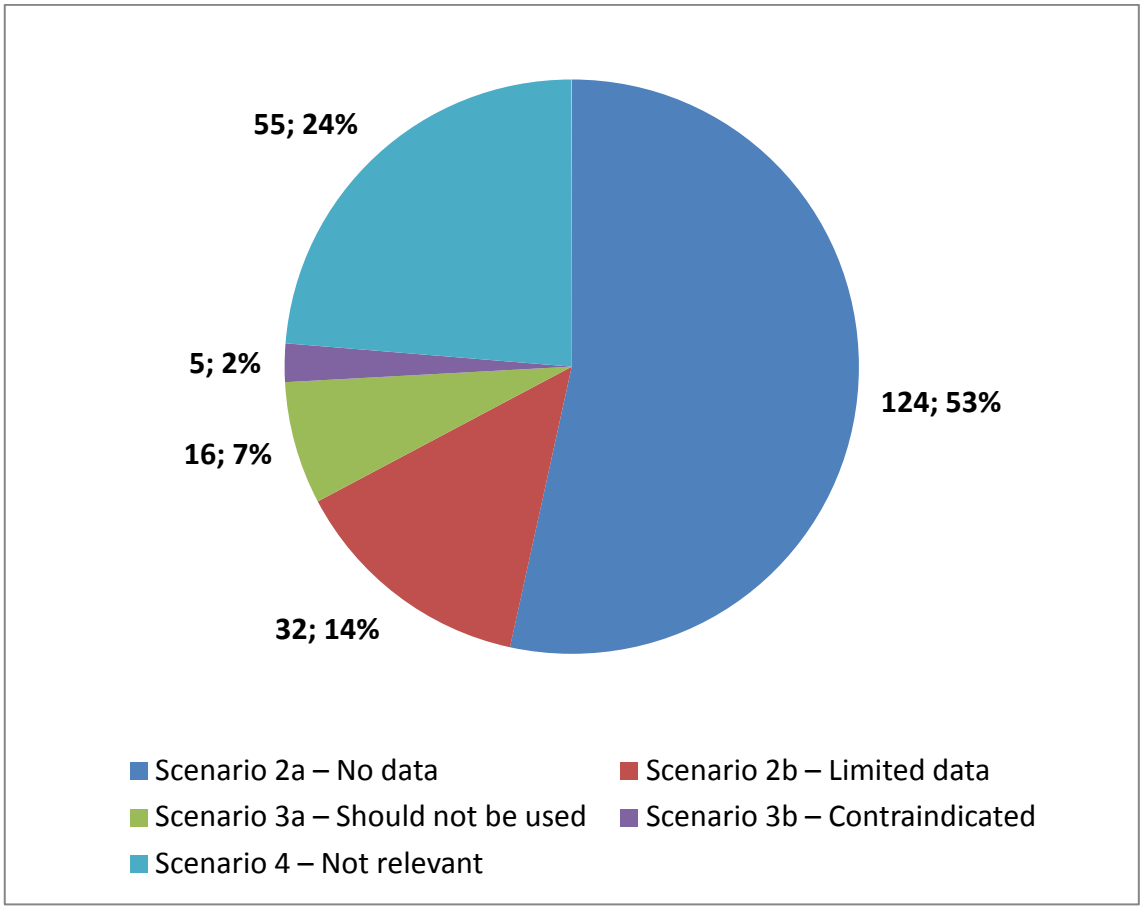
3.4.1 Medicinal products with no paediatric indication

A list of all datasets generated for medicinal products without a paediatric indication is presented in Annex II Table 13.

The starting point for the assessment of medicinal products with no paediatric indication is the distribution of the different scenarios defined in section 3.3.1 across the investigated SmPCs. The attribution of the scenarios yielded 232 datasets for section 4.2 of the investigated SmPCs. This number is higher than the number of investigated products, which can be mainly attributed to the fact that one product can include more than one scenario, e.g. related to different age groups or indications. For four products the associated scenario is applicable for two or three indications, resulting into two or three datasets.

As shown in Figure 3, about half of the medicinal products have not been investigated for the use in the paediatric population (scenario 2a). Another quarter is not relevant for the paediatric population (scenario 4). The medicinal products included in the remaining quarter belong to scenario 3a (should not be used), 3b (contraindicated) or 2b (limited data) with only a very small proportion of medicinal products being contraindicated in paediatric patients.

Figure 3: Scenarios associated with medicinal products with no paediatric indication



In the following, the reasons for multiple scenarios per medicinal product are further elucidated. Overall 182 products can be associated with one scenario, 19 products with two scenarios and two products with three scenarios, adding up to a total of 203 medicinal products. Interestingly, one product did not include a statement in section 4.2 of the SmPC, therefore it was not included in this part of the assessment. Figure 4 gives an overview of the different combinations together with their occurrence and Table 4 lists the corresponding reasons for the individual medicinal products. Overall the amount of medicinal products with an association to more than one scenario is very low (10%). The predominant combinations are “no data” (scenario 2a) together with “limited data” (scenario 2b) and “not relevant” (scenario 4). The main reason for multiple scenarios in one medicinal product is a different data basis for individual age groups. In four cases there is also a differentiation between multiple indications.

Figure 4: Frequency of different combinations of multiple scenarios per medicinal product

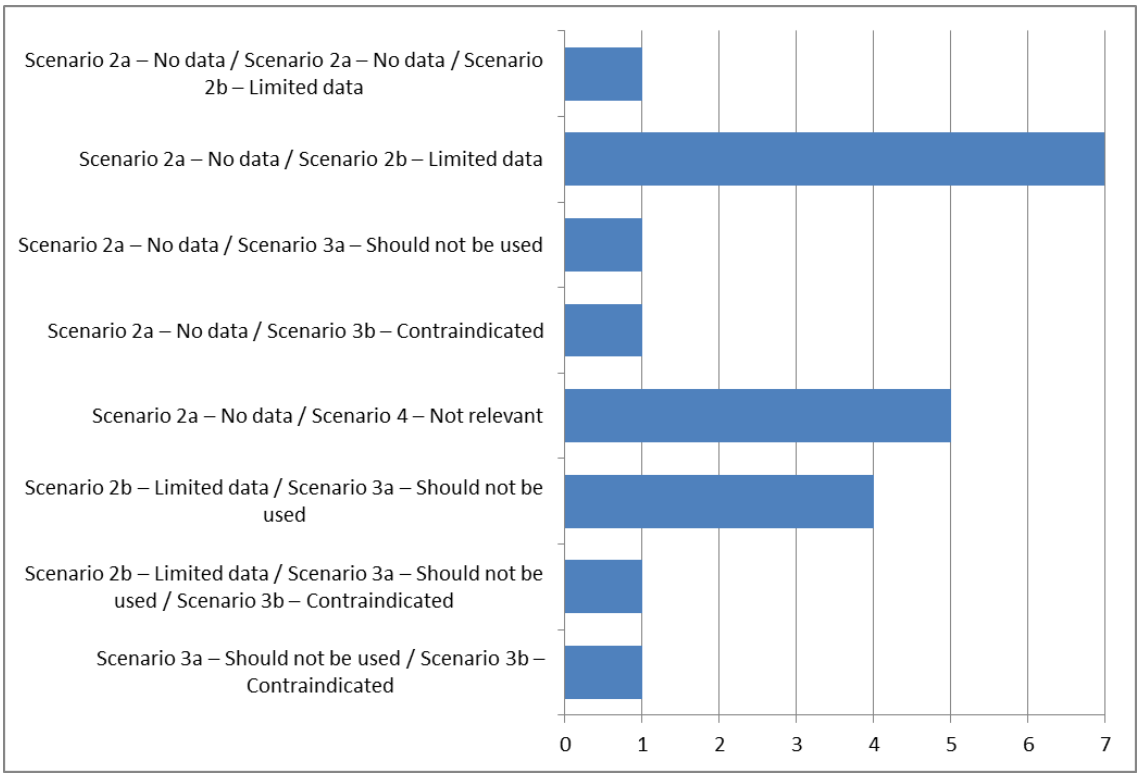


Table 4: Reasons for multiple scenarios per medicinal product

Medicine Name	Scenario combination	Reason (age or indication)
Adjupanrix	Scenario 2a – No data / Scenario 2a – No data / Scenario 2b – Limited data	0-3 / 9-18 / 3-9
Aflunov	Scenario 2a – No data / Scenario 2b – Limited data	0-0,5 / 0,5-18
Bronchitol	Scenario 2a – No data / Scenario 2b – Limited data	6-18 / 0-6
Foclivia	Scenario 2a – No data / Scenario 2b – Limited data	0-0,5 / 0,5-18
Lonquex	Scenario 2a – No data / Scenario 2b – Limited data	different indications
Prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) Novartis Vaccines and Diagnostics	Scenario 2a – No data / Scenario 2b – Limited data	0,5-18 / 0-0,5
Ruconest	Scenario 2a – No data / Scenario 2b – Limited data	0-12 / 13-18
Ryzodeg	Scenario 2a – No data / Scenario 2b – Limited data	different indications
Lenvima	Scenario 2a – No data / Scenario 3a – Should not be used	2-18 / 0-2
Simbrinza	Scenario 2a – No data / Scenario 3b – Contraindicated	0-2 / 2-18
Aubagio	Scenario 2a – No data / Scenario 4 – Not relevant	10-18 / 0-10
Lemtrada	Scenario 2a – No data / Scenario 4 – Not relevant	10-18 / 0-10

Medicine Name	Scenario combination	Reason (age or indication)
Ozurdex	Scenario 2a – No data / Scenario 4 – Not relevant	different indications
Stivarga	Scenario 2a – No data / Scenario 4 – Not relevant	different indications
Tecfidera	Scenario 2a – No data / Scenario 4 – Not relevant	0-10 / 10-18
Evotaz	Scenario 2b – Limited data / Scenario 3a – Should not be used	0-0,25 / 0,25-18
Rezolsta	Scenario 2b – Limited data / Scenario 3a – Should not be used	0-3 / 3-17
Stribild	Scenario 2b – Limited data / Scenario 3a – Should not be used	6-18 / 0-6
Votrient	Scenario 2b – Limited data / Scenario 3a – Should not be used	2-18 / 0-2
Rasilamlo	Scenario 2b – Limited data / Scenario 3a – Should not be used / Scenario 3b – Contraindicated	6-18 / 2-6 / 0-2
Mirvaso	Scenario 3a – Should not be used / Scenario 3b – Contraindicated	0-2 / 2-18

The further assessment of the medicinal products with no paediatric indication is divided into two parts. In the first part, the previously established 232 datasets, depicting the scenarios associated with section 4.2 of the SmPCs, are analysed from the perspective of different therapeutic areas as well as their authorisation date. The second part then looks at all datasets generated for medicinal products with no paediatric indication and investigates the particularities for the individual scenarios.

3.4.1.1 Therapeutic areas

Therapeutic areas are associated with the datasets for the medicinal products via the Anatomical Therapeutic Chemical (ATC) Classification System. The ATC code is part of the data retrieved from the EMA for every medicinal product (see 3.2) and includes five levels of information related to therapeutic and chemical characteristics of a medicinal product. For the assessment within this thesis, ATC level 1 (anatomical main group) and ATC level 2 (therapeutic main group) have been associated with each dataset. The results for all 232 datasets are shown in Table 5. Overall, the datasets can be attributed to 46 different therapeutic main groups and the distribution shows that most medicinal products can be found in the groups of L01 – Cytostatics (43), A10 - Drugs used in diabetes (20), J05 - Antivirals for systemic use (17), R03 - Anti-asthmatics (16) and L04 - Immunosuppressive agents (14). For one medicinal product, the ATC code was not yet available.

Table 5: Attribution of ATC levels 1 and 2 to all assessed medicinal products without paediatric indication

	Scenario 2a – No data	Scenario 2b – Limited data	Scenario 3a – Should not be used	Scenario 3b – Contra-indicated	Scenario 4 – Not relevant	Σ
A - Alimentary tract and metabolism	**25**	**2**	**2**		**2**	**31**
A02 - Drugs for acid related disorders					1	1
A04 - Antiemetics and antinauseants	2					2
A06 - Laxatives	1		1			2
A07 - Antidiarrheals, intestinal antiinflammatory/ antiinfective agents	1					1
A08 - Antiobesity preparations, excluding diet products			1			1
A10 - Drugs used in diabetes	17	2			1	20
A16 - Other alimentary tract and metabolism products	4					4
B - Blood and blood forming organs	**12**	**1**				**13**
B01 - Antithrombotic agents	8					8
B02 - Antihemorrhagics	3					3
B06 - Other hematological agents	1	1				2
C - Cardiovascular system	**6**	**1**	**2**	**3**	**2**	**14**
C01 - Cardiac therapy	1				1	2
C02 - Antihypertensives	1		1			2
C09 - Agents acting on the renin-angiotensin system	2	1	1	1	1	6
C10 - Lipid modifying agents	2			2		4
D - Dermatologicals	**2**		**2**	**1**	**1**	**6**
D02 - Emollients and protectives	1					1
D03 - Preparations for treatment of wounds & ulcers			1			1
D06 - Antibiotics and chemotherapeutics for dermatological use	1				1	2

	Scenario 2a – No data	Scenario 2b – Limited data	Scenario 3a – Should not be used	Scenario 3b – Contra-indicated	Scenario 4 – Not relevant	Σ
D11 - Other dermatological preparations			1	1		2
G - Genito urinary system and sex hormones	**1**				**7**	**8**
G03 - Sex hormones and modulators of the genital system					4	4
G04 - Urologicals	1				3	4
H - Systemic hormonal prep, excluding sex hormones	**2**					**2**
H01 - Pituitary and hypothalamic hormones	1					1
H02 - Corticosteroids for systemic use	1					1
J - General antiinfectives for systemic use	**21**	**12**	**3**		**1**	**37**
J01 - Antibacterials for systemic use	3	3				6
J04 - Antimycobacterials	2					2
J05 - Antivirals for systemic use	10	4	3			17
J06 - Immune sera and immunoglobulins		1			1	2
J07 - Vaccines	6	4				10
L - Antineoplastic and immunomodulating agents	**35**	**7**	**6**		**14**	**62**
L01 - Cytostatics	24	5	6		8	43
L02 - Endocrine therapy					2	2
L03 - Immunomodulating agents	2	1				3
L04 - Immunosuppressive agents	9	1			4	14
M - Musculo-skeletal system	**1**	**2**			**1**	**4**
M04 - Antigout preparations	1					1
M05 - Drugs for treatment of bone diseases		2				2
M09 - Other drugs for disorders of the musculo-skeletal system					1	1
N - Nervous system	**10**	**4**			**4**	**18**
N01 - Anesthetics					1	1

	Scenario 2a – No data	Scenario 2b – Limited data	Scenario 3a – Should not be used	Scenario 3b – Contra-indicated	Scenario 4 – Not relevant	Σ
N03 - Antiepileptics		1				1
N04 - Anti-parkinson drugs	1					1
N05 - Psycholeptics	5	3				8
N06 - Psychoanaleptics	1					1
N07 - Other nervous system drugs	3				3	6
R - Respiratory system	**1**	**2**			**15**	**18**
R03 - Anti-asthmatics		1			15	16
R05 - Cough and cold preparations	1	1				2
S - Sensory organs	**4**	**1**		**1**	**4**	**10**
S01 - Ophthalmologicals	4	1		1	4	10
V - Various	**4**				**4**	**8**
V03 - All other therapeutic products	2					2
V09 - Diagnostic radiopharmaceuticals	2				3	5
V10 - Therapeutic radiopharmaceuticals					1	1
Not yet assigned			**1**			**1**
Not yet assigned			1			1
Σ	**124**	**32**	**16**	**5**	**55**	**232**

Compared to the distribution of the different scenarios over all 232 datasets (see also Figure 3), there are significant differences for some therapeutic main groups. A large number of datasets corresponding to scenario 2a (no data) are found for “A10 - Drugs used in diabetes” and “B01 - Antithrombotic agents”. The therapeutic main groups with the most information on the use in paediatric patients (i.e. scenario 2b - limited data) are “J05 - Antivirals for systemic use”, “J07 – Vaccines” and “N05 – Psycholeptics”. Medicinal products that should not be used (i.e. scenario 3a) are found predominantly in the groups of “J05 - Antivirals for systemic use” and “L01 - Cytostatics”. An interesting observation can be made for the group of “R03 - Anti-asthmatics”, in which 94% of the datasets are considered not relevant for the paediatric population. This finding can be associated with indications for Chronic Obstructive Pulmonary Disease (COPD), which is not relevant for the paediatric population. Another main therapeutic group with a higher rate of scenario 4 (not relevant) is “S01 – Ophthalmologicals”. The results are summarised in Table 6 with the above mentioned aspects highlighted.

Table 6: Selected ATC main therapeutic groups in relation to scenarios

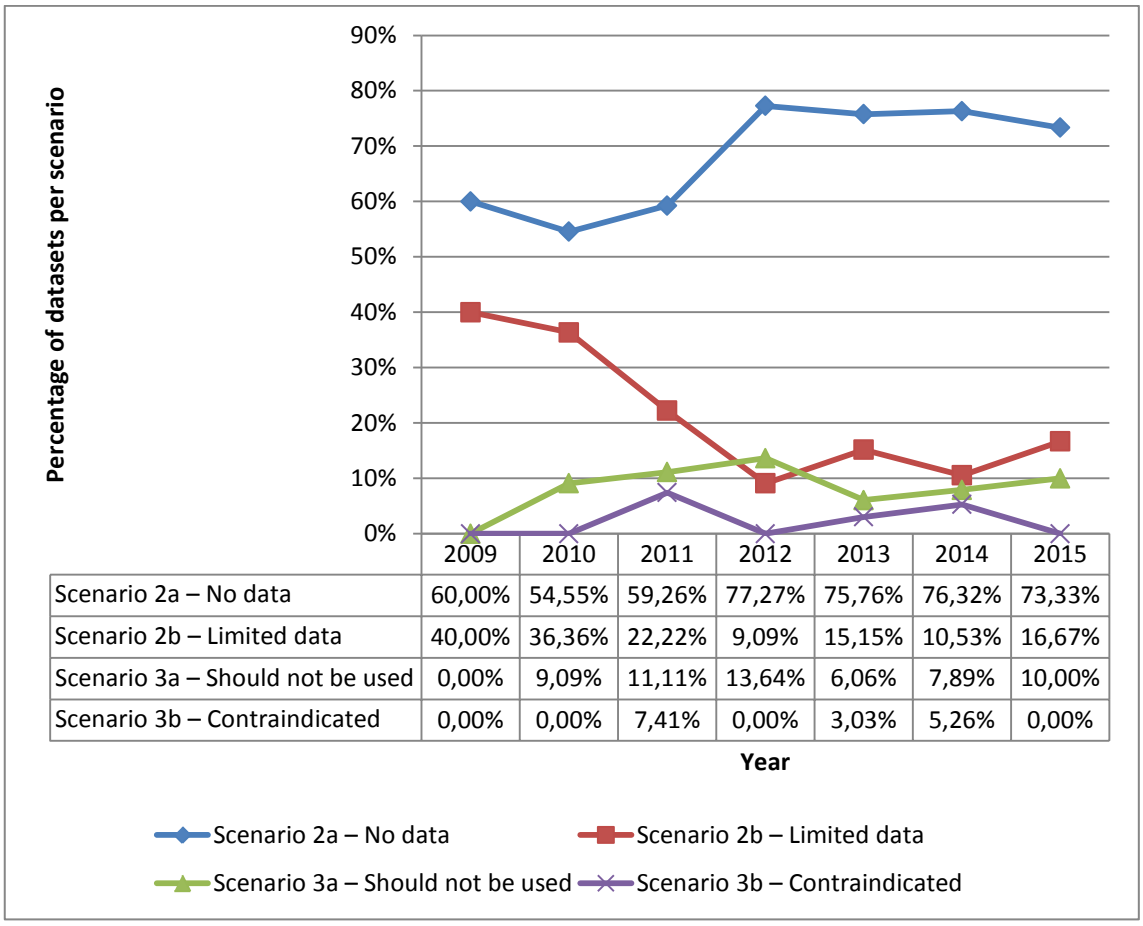
ATC code level 2 (# of datasets)	Scenario				
	2a	2b	3a	3b	4
A10 - Drugs used in diabetes (20)	85%	10%	0%	0%	5%
B01 - Antithrombotic agents (8)	100%	0%	0%	0%	0%
J05 - Antivirals for systemic use (17)	59%	24%	18%	0%	0%
J07 - Vaccines (10)	60%	40%	0%	0%	0%
L01 - Cytostatics (43)	56%	12%	14%	0%	19%
N05 – Psycholeptics (8)	63%	38%	0%	0%	0%
R03 - Anti-asthmatics (16)	0%	6%	0%	0%	94%
S01 – Ophthalmologicals (10)	40%	10%	0%	10%	40%
All datasets (232)	**53%**	**14%**	**7%**	**2%**	**24%**

3.4.1.2 Authorisation Date

The correlation of the distribution of scenarios to the authorisation date was performed to investigate the impact of time from approval on the availability of data. Especially when taking into account the concept of the deferral according to the paediatric regulation, it is anticipated that the proportion of datasets with

limited data increases over time, while the proportion of medicinal product with no data decreases. As shown in Figure 5, this assumption holds in principle true for the investigated medicinal products. However, the gradient is not continuous for all products. It appears that there is a plateau for medicinal products registered in last four years (2012 - 2015). An increase in the availability of data is only seen for products registered before 2012. From the available data there seems to be no impact by the authorisation date on scenario 3a (Should not be used) and 3b (Contraindicated).

Figure 5: Proportion of scenarios in relation to the year of authorisation



	2009	2010	2011	2012	2013	2014	2015
Scenario 2a – No data	60,00%	54,55%	59,26%	77,27%	75,76%	76,32%	73,33%
Scenario 2b – Limited data	40,00%	36,36%	22,22%	9,09%	15,15%	10,53%	16,67%
Scenario 3a – Should not be used	0,00%	9,09%	11,11%	13,64%	6,06%	7,89%	10,00%
Scenario 3b – Contraindicated	0,00%	0,00%	7,41%	0,00%	3,03%	5,26%	0,00%

In the following the individual scenarios are investigated, taking into account the different criteria established in section 3.3.1

3.4.1.3 Scenario 2a – No data

As already demonstrated in section 2.2, there are two apparent reasons, why no data for the paediatric population would be available:

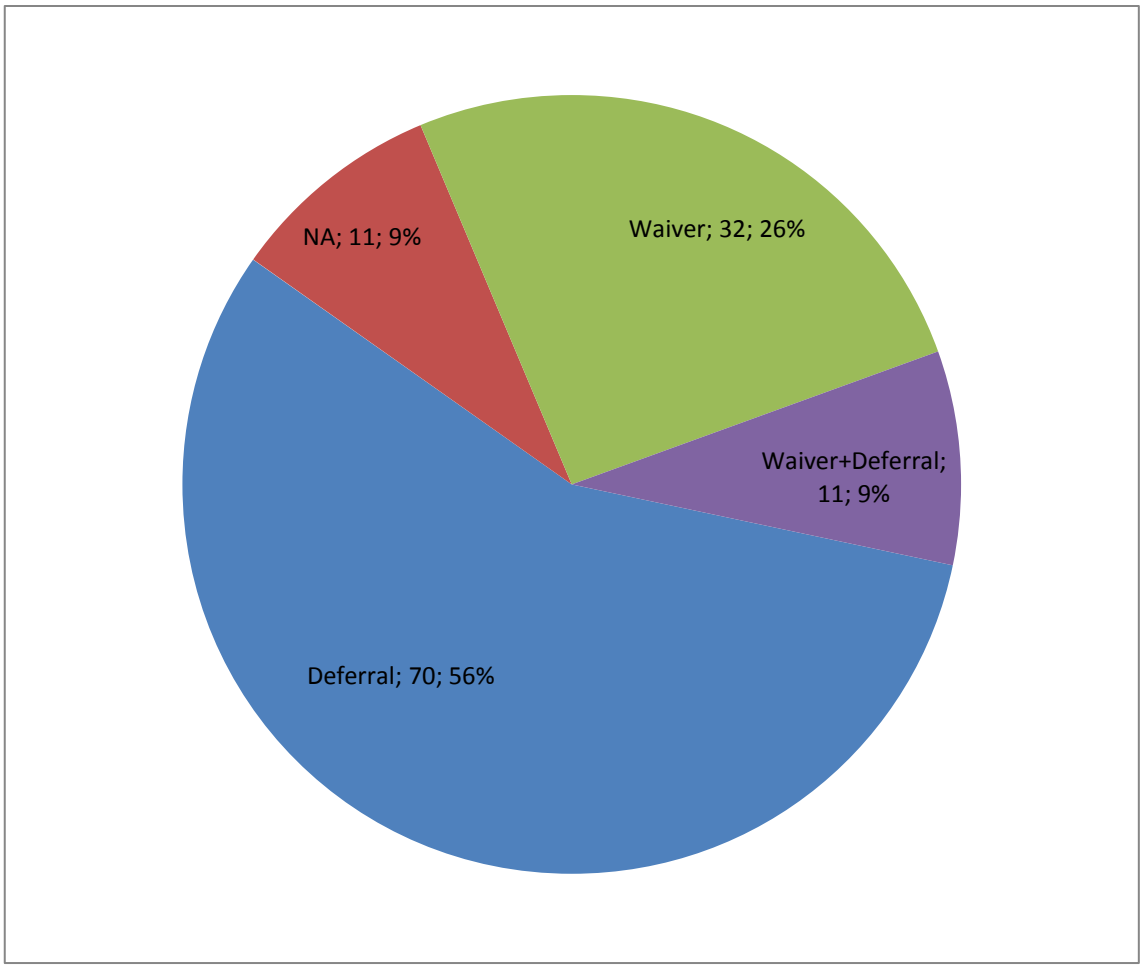
- a paediatric development is not required (e.g. medicinal product is likely to be ineffective or unsafe) and therefore waived

- the outcome of studies in adults need to be awaited before commencing trials in the paediatric population, which are therefore deferred.

Figure 6 shows all datasets for scenario 2a in correlation with the information in the Waiver/Deferral field. As anticipated, most datasets can be associated with waivers and deferrals with about twice as much deferrals than waivers. This means that more than half of the medicinal products that are currently in scenario 2a will most probably transfer into another scenario within the next years. Whenever new paediatric study data are available the benefit-risk ratio has to be newly evaluated and will trigger this scenario transition. If after the availability of new clinical data, no association to scenario 1 or 3 can be made, at least the now available limited data can be presented in the SmPC. Medicinal products with a waiver covering the complete paediatric population will most likely remain in scenario 2a.

There are also 11 medicinal products with no information on waivers and deferrals in the SmPC. This is surprising, as a reason is expected for the absence of data. Further investigation in the corresponding PIPs and EPARs, which are publicly available on the website of the EMA, showed that 7 of these products actually have waivers or deferrals (5 related to PIPs and 2 class waivers). For three of these medicinal products the EPAR stated under “Information on paediatric requirements”: “Not applicable”. For one product the reason for the absence of a waiver or deferral remained unclear.

Figure 6: Distribution of waivers and deferrals in scenario 2a – no data



Regarding the types of information on paediatric patients in the SmPC, scenario 2a only includes information in section 4.2 (standard statements according to the SmPC guideline) together with the corresponding information on waivers and deferrals in section 5.1. However, 9 medicinal products (12 datasets) also included information related to other sections of the SmPC. In most cases statements on the non-recommendation of the medicinal product were provided in section 4.4 (6 times) and section 4.8 (2 times). In three SmPCs this non-recommendation was further substantiated with clear reasons, i.e. clinical experience with other medicinal products of the class, size of an implant and potential side effects. The other five SmPCs only referred to lack of data in this regard. The remaining four datasets are related to information in section 4.9 (inadvertent ingestion by paediatric subjects), section 5.2 (information that a pharmacokinetic study in paediatric subjects is ongoing) and section 5.1 (information that the indication is not relevant for the paediatric population).

It is remarkable that the above mentioned non-recommendations in scenario 2a are not restricted to the sections 4.4 and 4.8 of the SmPC, but can also be found in section 4.2, in which six medicinal products contain non-

recommendations for the use in the paediatric population without further specifying the reasons for this. Even though this kind of non-recommendations concern only small amount of datasets, it is an interesting aspect to highlight, as it shows insecurity about the communication of scenario 2a and the location of this information in the SmPC. Reasons may be that some MAHs perceive a non-indication in combination with information about the absence of data as not explicit enough or they may consider it rather as part of the safety information than of the SmPC sections 4.1 and 4.2.

As to the criterion age, the SmPC standard statement in section 4.2 is mostly directed to all paediatric patients (0-18). For 11 medicinal products, scenario 2a only applies to a subset of paediatric patients, which is related to the combination of different scenarios as described in Table 4.

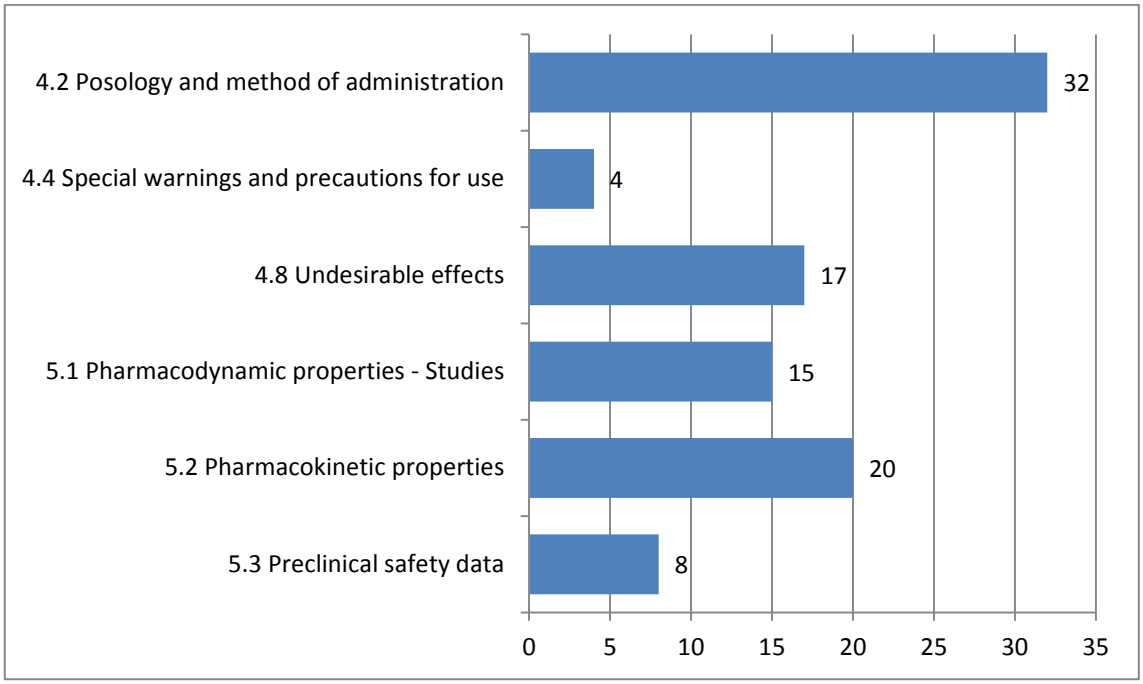
3.4.1.4 Scenario 2b – Limited data

For products associated with scenario 2b mostly data from clinical studies in the paediatric population are available, but they are neither sufficient to support a paediatric indication with respective dosage recommendations nor to suggest a negative benefit-risk balance.

In the following, two main aspects are addressed with regards to scenario 2b: the types of information on paediatric patients available in the respective SmPCs and the question if further clinical data will be generated in the future that may lead to a paediatric indication.

Scenario 2b (limited data) comprises of 33 medicinal products with a total of 101 datasets. The distribution of types of information related to the paediatric population within these datasets is shown in Figure 7. Of the 33 medicinal products only 31 were associated with scenario 2b in section 4.2 of the SmPC. For one product scenario 4 (not relevant) was associated and the presented data were related to a different disease than the indicated one. It remained unclear why the other product did not include a standard statement in section 4.2. The total number of 32 datasets for section 4.2 is related to one product with two datasets. Besides section 4.2, information is presented mostly related to undesirable effects (section 4.8), clinical efficacy/safety studies (section 5.1) and pharmacokinetic studies (section 5.2).

Figure 7: Types of information provided on the paediatric population for scenario 2b – limited data



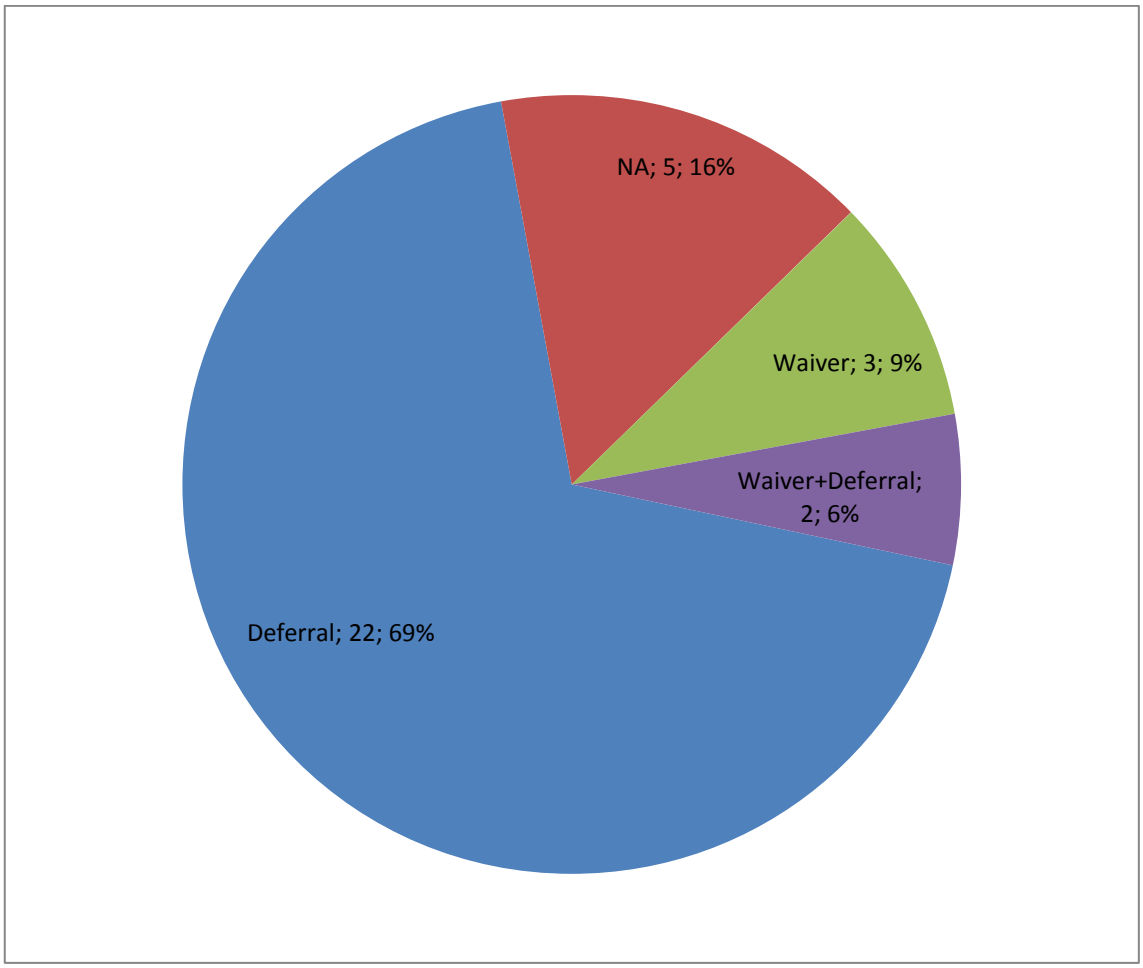
Almost all medicinal products from scenario 2b include data from clinical efficacy/safety, pharmacokinetic or pre-clinical studies (30 of 33). Interestingly, most medicinal products only contain study data from one type of study (24 of 33). Further 8 products contain information on different types of studies mainly in the combination of clinical efficacy/safety with pharmacokinetic studies. One medicinal product contains no study data, even though limited data on the paediatric population is given, which is related to the data being a reference to data from a “mono” product for a medicinal product with two active ingredients. The detailed numbers are presented in Table 7.

Table 7: Combinations of clinical efficacy/safety, pharmacokinetic or pre-clinical studies in SmPCs

5.1 Pharmacodynamic properties - Studies	5.2 Pharmacokinetic properties	5.3 Preclinical safety data	Number of medicinal products
	X		11
X			8
X	X		6
		X	5
	X	X	1
X	X	X	1
			1

Related to waivers and deferrals, Figure 8 shows that the majority of datasets are associated with deferrals, meaning that more clinical data are being generated. Consequentially, medicinal products included in this part of the datasets are likely to transition into scenario 1 or 3 in the next years. An exception would be medicinal products for which the complete clinical data generated via the PIP are not sufficient to support scenario 1 or 3. As in scenario 2a, there are also datasets with no waiver or deferral statement included in section 5.1 of the SmPC. In contrast to scenario 2a, a reason for the absence of this information could also be related to the finalisation of a PIP. Of the 5 medicinal products not including a statement on waivers or deferrals the EPAR states for two products under “Information on paediatric requirements”: “Not applicable” and makes reference to a PIP for one product, which also includes information on a deferral. From the remaining two products, the PIP seems to be finalised for one product and no reason could be identified for the other product.

Figure 8: Distribution of waivers and deferrals in scenario 2b – limited data



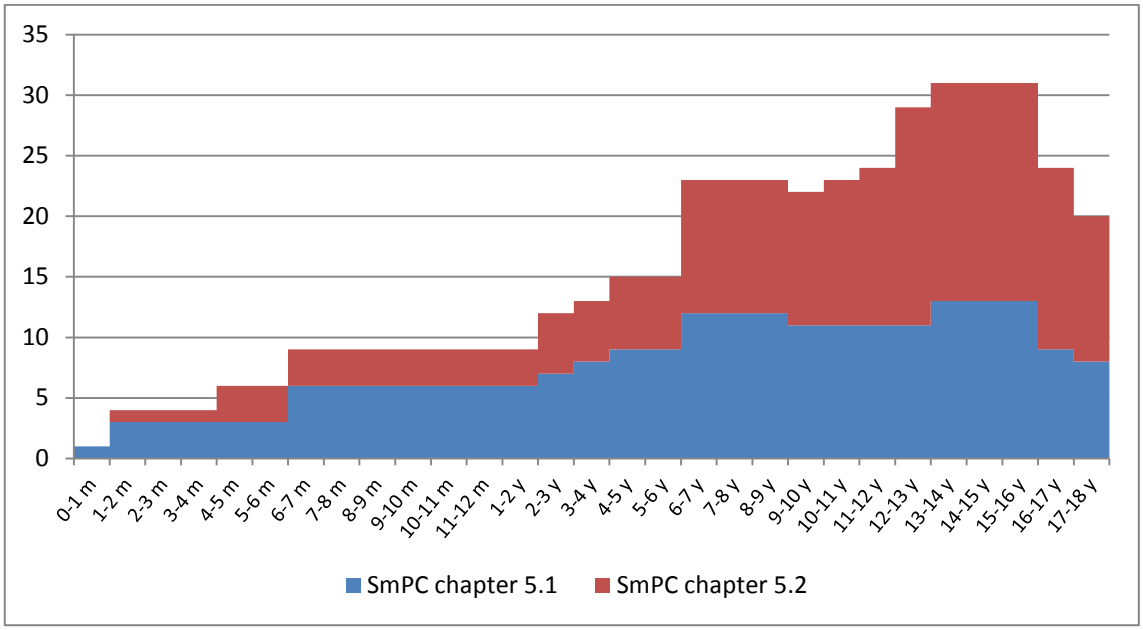
From the perspective of the criterion age, the information in section 4.2 is mostly covering the complete paediatric population, which is similar to scenario 2a. For medicinal products for which this is not the case, there is most likely a combination with another scenario capturing the remaining subset of the paediatric population.

As discussed above, most products (27) contain information on clinical efficacy/safety studies and/or pharmacokinetic studies. For 25 of these medicinal products, 32 datasets are available that include an age range in the description. Figure 9 visualises the age distribution of those datasets in the form of a histogram, in which the age ranges derived the SmPCs are transferred into monthly intervals for age values below 1 year and yearly intervals for age values above 1 year. The histogram reveals two facts:

The amount of data increases with the age of the paediatric patients, which makes sense, as it is probably easier to recruit older children and adolescents for paediatric studies than neonates, infants and young children. There is a slight decline for the age range of 16-18, but this can be explained with the proximity to the age of adults and with this the scientific gain is lower than in younger paediatric patients.

The amount of clinical efficacy/safety studies in relation to pharmacokinetic studies seems to be influenced by the age. While in adolescents (12-18) the ratio between those types of studies favours the pharmacokinetic studies, it is on the side of clinical efficacy/safety studies for paediatric patients in the age from 0 to 6 years. For children between 6 and 12 years of age distribution is about the same.

Figure 9: Histogram with age distribution related to information from clinical efficacy/safety and pharmacokinetic studies



3.4.1.5 Scenario 3a – Should not be used / Scenario 3b – Contraindicated

In total, 18 medicinal products have been associated with the scenarios 3a (15) and 3b (5) with two products being associated with both scenarios in different age ranges, which is a very small proportion of all investigated medicinal products, especially for products with a contraindication in the paediatric population. This can be interpreted as a success of the Paediatric Regulation, in relation to which the EMA highlighted in the 5-year report that “in the past, the lack of information had led to systematic but unjustified contra-indications in children”.

For medicinal products that should not be used or are contraindicated, several interesting questions come to mind:

- Why is the use in the paediatric population restricted?
- In what age groups is the use restricted?
- Is there a possibility that the scenario changes?

The reasons for the restrictions have been summarised according to the reasons listed in Table 8, in which also the respective frequencies are shown. In scenario 3a mostly findings in non-clinical studies are the reason for the restriction. However, five of the six medicinal products in this category include deferrals in section 5.1 of the SmPC opening the possibility that the clinical data may override the non-clinical data. In scenario 3b no contraindications are based on non-clinical data. Another observation is the relatively high amount of medicinal products giving no apparent reason for the restrictions for use, which

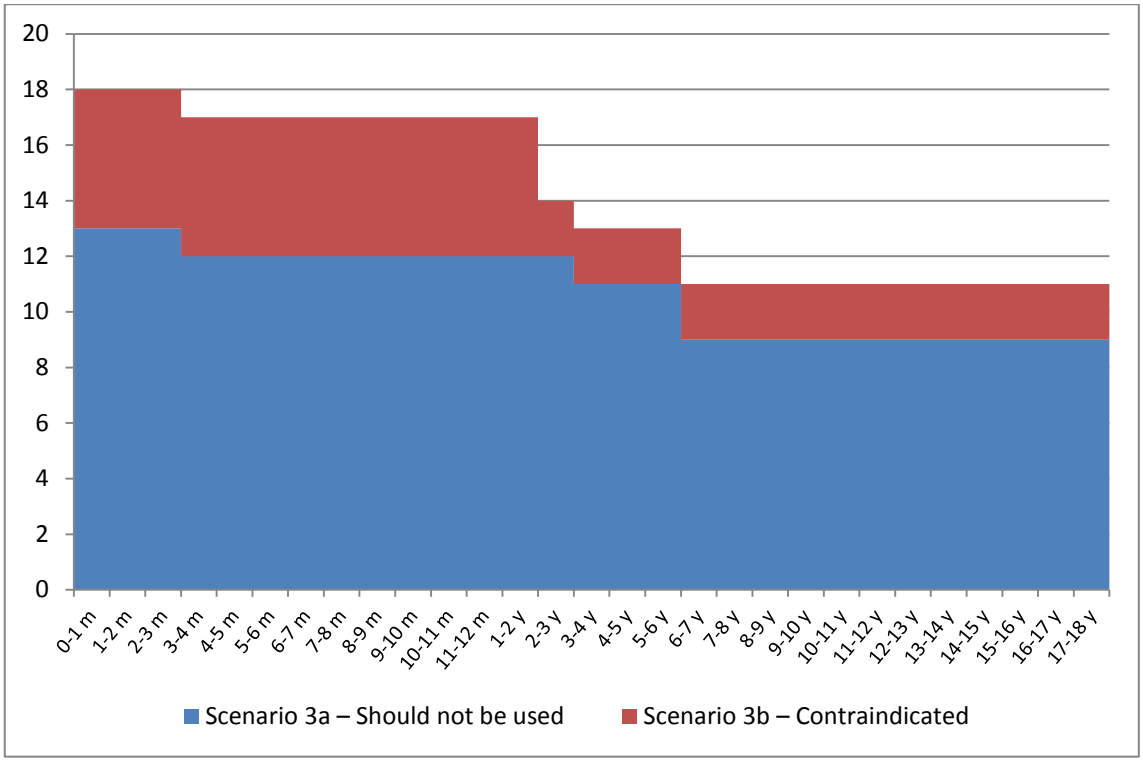
is somewhat unsatisfactory for the reader and makes the differentiation to scenario 2 more complicated. Reasons related to clinical studies included two interesting cases where the clinical experience was related to inadvertently ingested tablets by children. In general, the reason was not in all cases clearly stated in sections 4.2 and 4.3 making it more complicated for the reader to locate the information.

Table 8: Reasons for the restrictions of use in Scenario 3a (Should not be used) and Scenario 3b (Contraindicated)

Reason	Scenario 3a – Should not be used	Scenario 3b – Contraindicated
non-clinical	**6**	
no specific reason given	**4**	**1**
clinical	**3**	**2**
in vitro and pharmacokinetics	**1**	**1**
theoretical	**1**	
no relevant use		**1**

Figure 10 visualises the age groups in which the use restrictions apply. The histogram shows a slightly higher amount for neonates and infants, but most medicinal products are restricted for use in the complete paediatric population.

Figure 10: Histogram with age distribution for restrictions of use



Finally, with regards to waivers and deferrals, there are only waivers for datasets associated with scenario 3b. Therefore, this scenario is likely to remain

the same. As already mentioned above, for medicinal products that should not be used in a certain age range, the probability of a change of the scenario is probable. Of these medicinal products, 10 (67%) products include deferral statements.

3.4.1.6 Scenario 4 – Not relevant

Scenario 4 is in principle a subset of scenario 2a (no data) with a strong justification for not conducting studies in the paediatric population. The respective standard statement in section 4.2 of the SmPC gives a very clear message to the reader in this regard. This is also confirmed by the high amount of 51 waivers associated with 55 medicinal products. From the four remaining products one product included a deferral for an additional indication, one product was exempted from the requirements of the paediatric legislation and for two products the waiver statement related to a “not relevant” subset of the paediatric population was missing in section 5.1 of the SmPC, which was verified in the respective PIPs.

3.4.2 Medicinal products with paediatric indication

3.4.2.1 Availability of information with relation to the use in the paediatric population

The information provided in the SmPCs of the medicinal products with paediatric indication was associated with scenario 1, as explained in section 3.3.1. The determining factors were the information included in section 4.1 of the SmPC as well as information on the proportion of paediatric patients investigated in clinical trials, which is typically provided in the sections 4.8 Undesirable effects, 5.1 Pharmacodynamic properties or 5.2 Pharmacokinetic properties. Besides the medicinal products with paediatric only indications it was possible to determine the percentage of paediatric patients in clinical studies for 26 products, which are listed in Table 9 together with the respective scenarios. An exemption for the allocation of the scenario was the product Prevenar 13, which was not classified as adult focussed indication (scenario 1a), even though the proportion of paediatric patients is only 6%. However, because of the high amount of paediatric patients (n=5375) the information in the SmPC was considered more fitting to scenario 1b. Medicinal products for which the proportion of paediatric patients could not be determined were allocated to scenario “1a or 1b”.

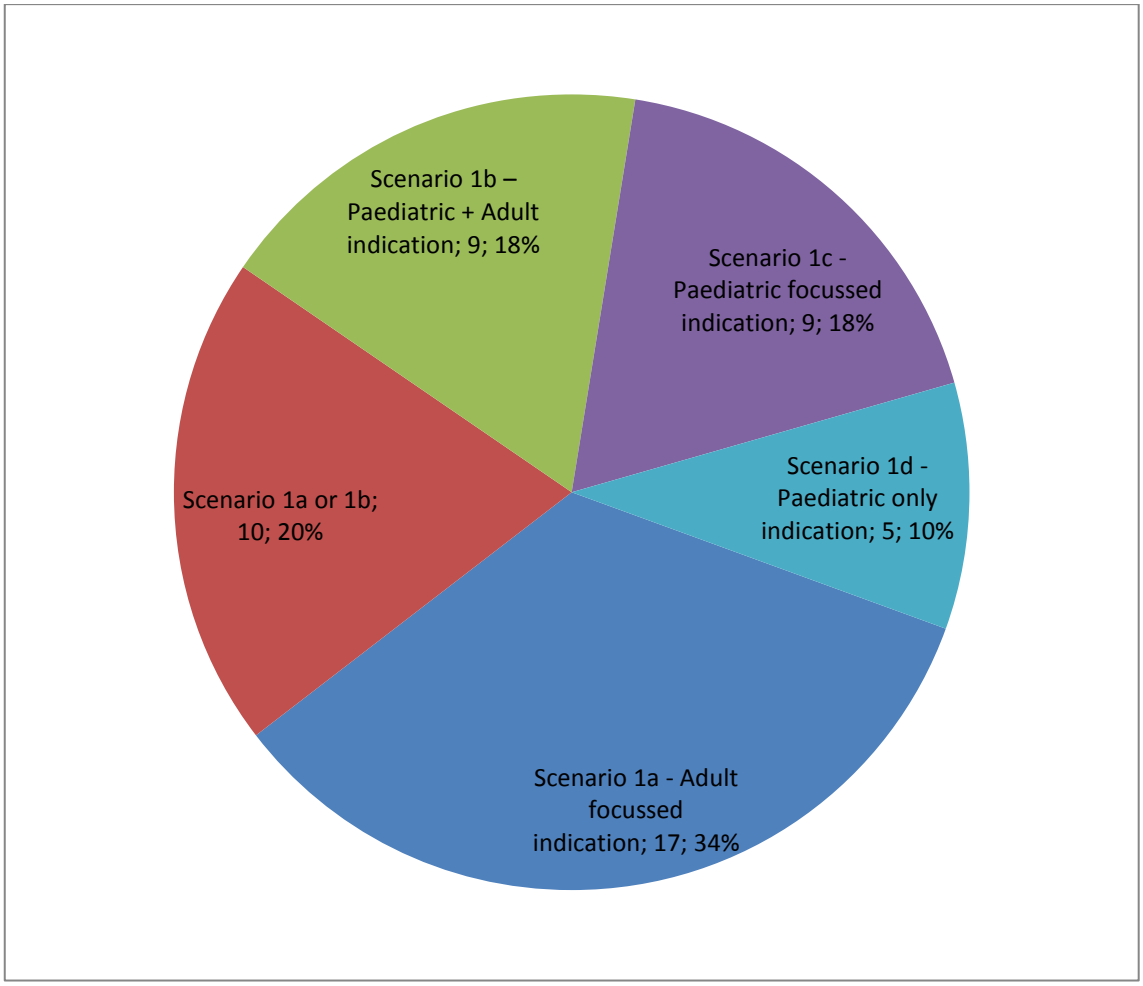
Table 9: Proportion of paediatric patients investigated in clinical trials per medicinal product

Medicine Name	Paediatric Patients	Scenario
Bexsero	98%	Scenario 1c - Paediatric focussed indication
Cinryze	12%	Scenario 1a - Adult focussed indication
Colobreathe	39%	Scenario 1b – Paediatric + Adult indication
Defitelio	50%	Scenario 1b – Paediatric + Adult indication
Dutrebis	13%	Scenario 1a - Adult focussed indication
Eurartesim	50%	Scenario 1b – Paediatric + Adult indication
Fycompa	10%	Scenario 1a - Adult focussed indication
Gardasil 9	50%	Scenario 1b – Paediatric + Adult indication
Kalydeco	16%	Scenario 1a - Adult focussed indication
Ketoconazole HRA	3%	Scenario 1a - Adult focussed indication
Menveo	73%	Scenario 1c - Paediatric focussed indication
Nimenrix	76%	Scenario 1c - Paediatric focussed indication
NovoEight	41%	Scenario 1b – Paediatric + Adult indication
NovoThirteen	38%	Scenario 1b – Paediatric + Adult indication
Nuwiq	45%	Scenario 1b – Paediatric + Adult indication
Pandemic Influenza Vaccine H5N1 Baxter AG	11%	Scenario 1a - Adult focussed indication
Prevenar 13	6% (n = 5375)	Scenario 1b – Paediatric + Adult indication
Procysbi	98%	Scenario 1c - Paediatric focussed indication
Repatha	10%	Scenario 1a - Adult focussed indication
Tivicay	0,7%	Scenario 1a - Adult focussed indication
Tobi Podhaler	45%	Scenario 1b – Paediatric + Adult indication
Tresiba	8%	Scenario 1a - Adult focussed indication
Triumeq	1%	Scenario 1a - Adult focussed indication
Vepacel	13%	Scenario 1a - Adult focussed indication
Votubia	85%	Scenario 1c - Paediatric focussed indication
Vpriv	21%	Scenario 1a - Adult focussed indication

Overall, the sample includes 44 medicinal products with paediatric indication (18% of all investigated products) corresponding to 50 datasets for section 4.1. For five of these products two datasets have been allocated due to multiple indications and for one product due to different dosage forms. The respective scenarios were the same in these medicinal products, besides one product for which scenario 1b as well as 1c were allocated. The distribution of the scenarios over these datasets is shown in Figure 11. It reveals that about half of

the SmPCs are either completely covering the paediatric population (scenarios 1c and 1d) or equally considering paediatric and adult patients (scenario 1b). In only one third of the datasets the paediatric population was clearly considered a smaller subgroup. For 10 datasets an unambiguous allocation to scenario 1a or 1b was not possible, based on the information provided in the SmPC.

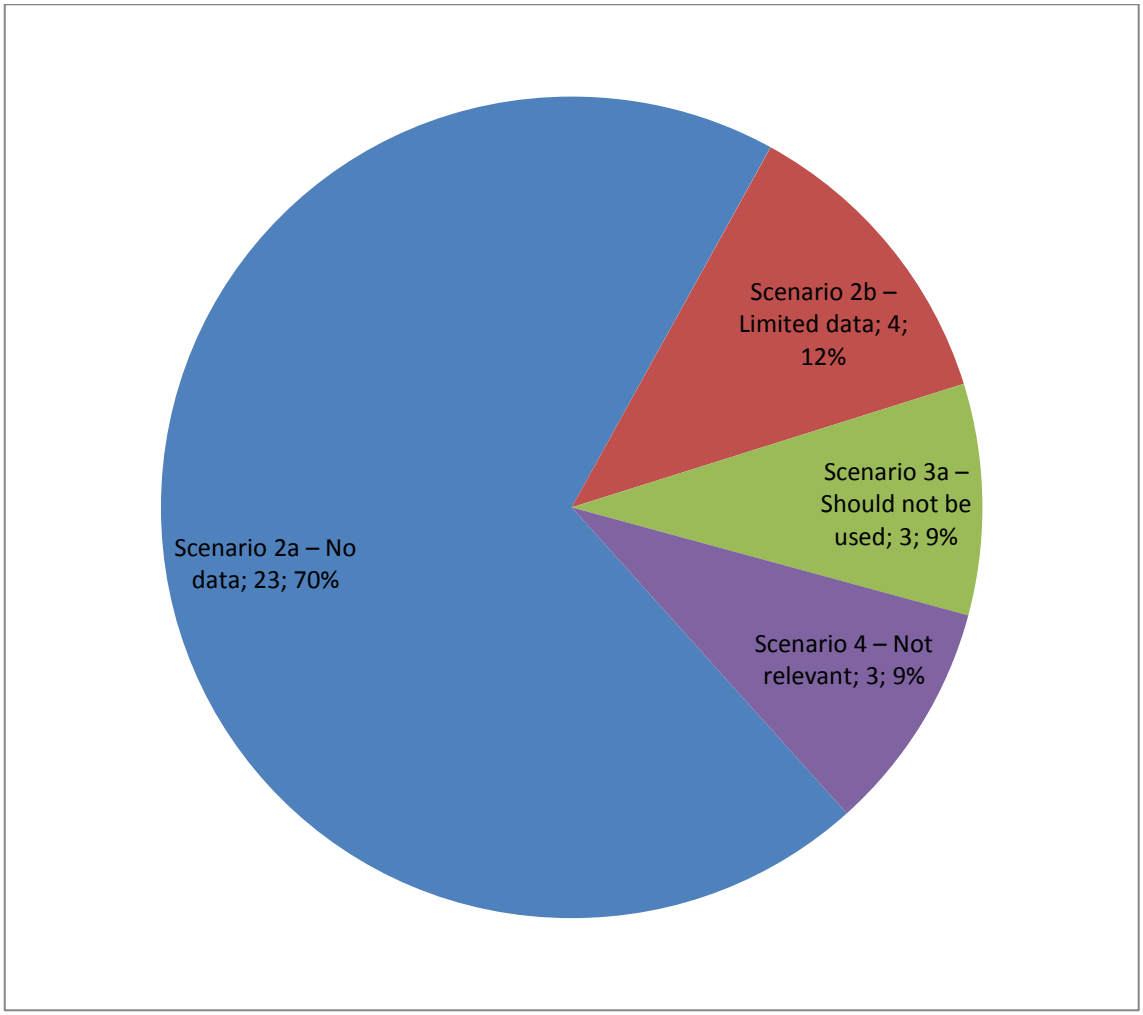
Figure 11: Scenarios associated to section 4.1 of the SmPC for medicinal products with paediatric indication



In addition to section 4.1 of the SmPC, in which the indication statements were associated with the scenarios 1a to 1d, also section 4.2 was evaluated for the presence of statements corresponding to scenarios 2 to 4. Of the 44 medicinal products with paediatric indication 24 could be associated with scenarios 2-4 resulting in 33 datasets. The main reason for this is that the indication does not cover the complete paediatric population, but only a subset. Consequentially, there must be one or more scenarios relevant for the non-indicated part of the paediatric population. Respective age distributions are further discussed below. Another factor that influences the availability of scenarios 2-4 in medicinal products with paediatric indication are different scenarios applying to different

indications or potential indications. The results related to the assessment of section 4.2 are presented in Figure 12. While the vast majority of datasets indicate the absence of data (scenario 2a), some age groups and/or indications are also associated with the scenarios 2b, 3a or 4.

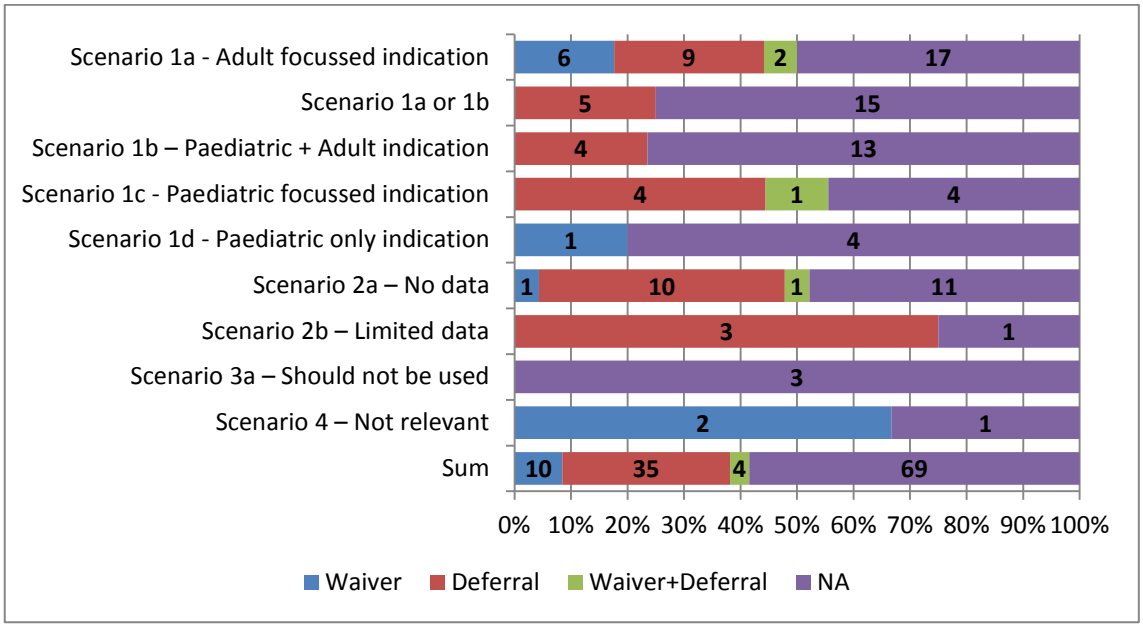
Figure 12: Scenarios associated to section 4.2 of the SmPC for medicinal products with paediatric indication



The final part of the assessment related to the availability of information is a look at waivers and deferrals. Even if a paediatric indication is available, this does not mean that all paediatric studies are concluded. Furthermore, as explained in the previous paragraph, there is a significant amount of datasets associated with the scenarios 2a and 2b, which are likely to contain deferrals according to the assessment of medicinal products with no paediatric indication in section 3.4.1 On the other hand, absence of a waiver or deferral statement in products with a paediatric indication can mean that the PIP is finalised and all obligations of the MAH towards paediatric development have been fulfilled. Figure 13 summarises the generated data with regards to waivers and deferrals.

In about 60% of the datasets there are no waiver or deferral statements, suggesting that the obligations from the PIP are fulfilled in most cases. A proportion of approximately 30% deferrals shows that still a relevant amount of paediatric data is under way. Waivers are only present in a small number of datasets. In comparison, the scenarios show differences related to the proportion of datasets without a deferral or waiver statement, which is ~75% in datasets classified as scenario "1a or 1b", 1b and 1d and ~50% in datasets corresponding to scenario 1a, 1c and 2a. Waivers are mainly found in conjunction with scenario 1a and 4.

Figure 13: Distribution of waivers and deferrals associated to section 4.1 and 4.2 of the SmPC for medicinal products with paediatric indication

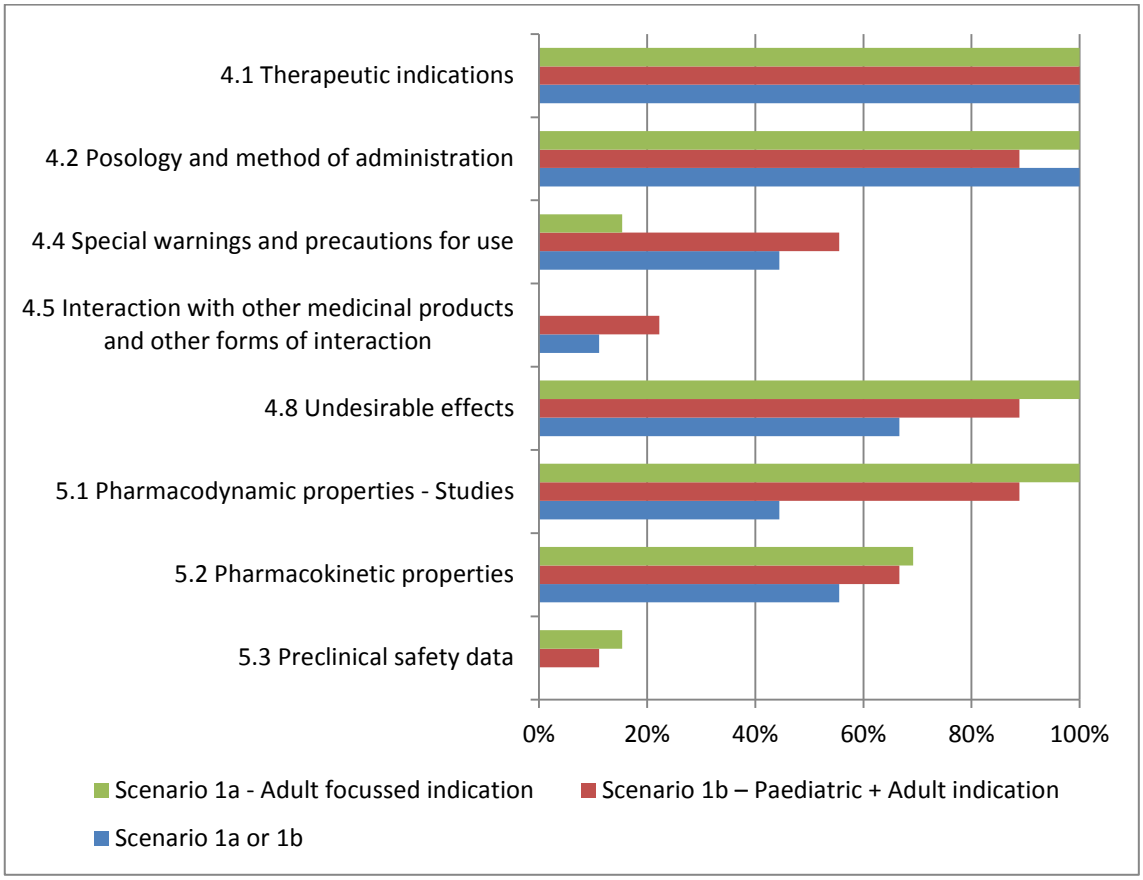


3.4.2.2 Types of information on paediatric patients in the SmPC

Regarding the types of information on paediatric patients in the SmPC, only scenario 1a, 1b and "1a or 1b" are more closely analysed, because for scenario 1c and 1d the SmPC can be considered as completely written for the paediatric population. In scenario 1c the adult population would be the actual subpopulation. Another important aspect for this type of analysis is the reference for the quantification. In the assessment performed for scenario 2b, the number of datasets was used as reference. Due to the fact that 5 out of 13 medicinal products in scenario 1a include two datasets each, this makes the comparison to the other scenarios less meaningful. However, as all medicinal products with two datasets contain the information on paediatric patients in the exact same sections of the SmPC, the analysis just considers for each product, if information on paediatric patients is included in an SmPC section or not. The

resulting distribution of types of information in scenario 1a and/or 1b are shown in Figure 14.

Figure 14: Types of information provided on the paediatric population for medicinal products with paediatric indication

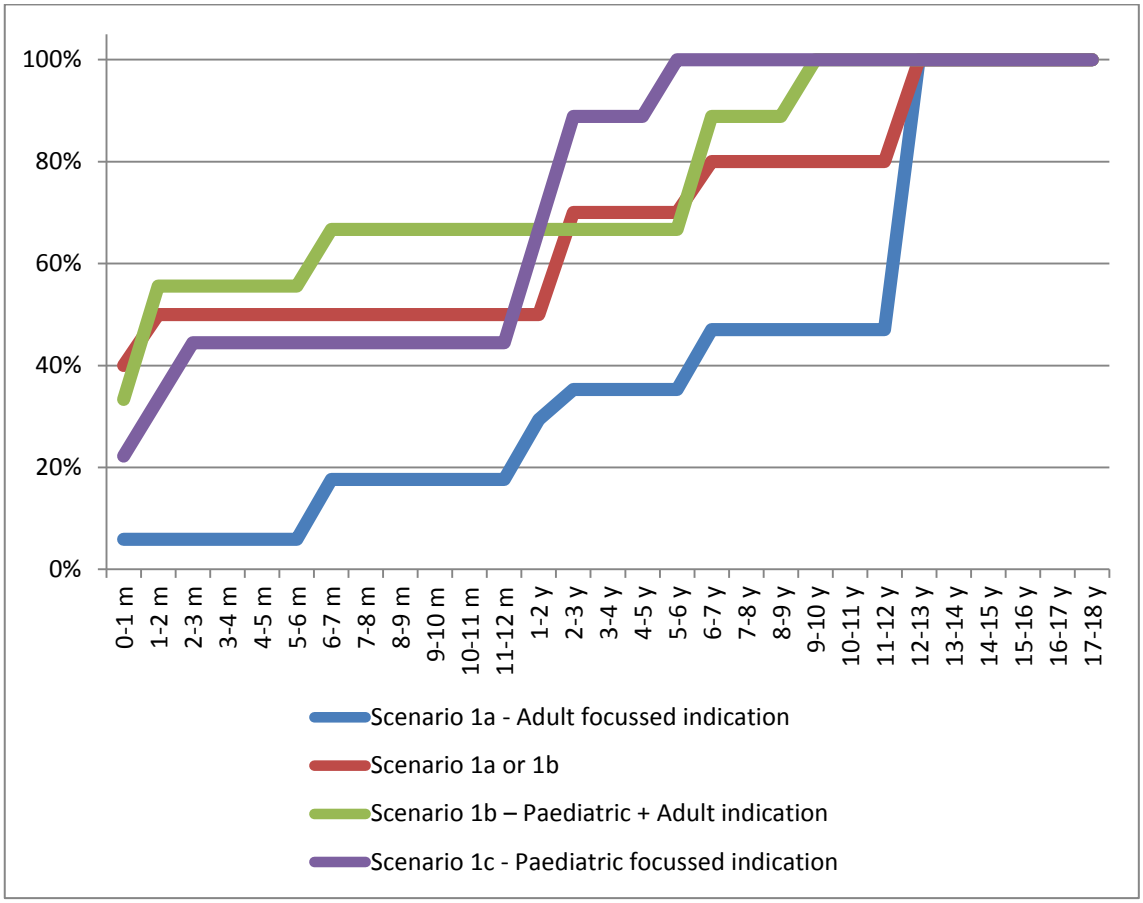


The presented data show that all medicinal products in the depicted scenarios include information on paediatric patients regarding the indication and dosage and administration. The reason why one medicinal product in scenario 1b is not including a dataset for section 4.2 is that this SmPC does not differentiate between adults and paediatric patients, which also affects the data for the other sections. With regards to information on undesirable effects (section 4.8), information on clinical efficacy/safety studies (section 5.1) and pharmacokinetic studies (section 5.2) the scenarios 1a and 1b can be considered similar. Nearly all SmPCs are providing information in sections 4.8 and 5.1 and about 70% of the SmPCs are providing information in section 5.2. Compared to this, information specific to paediatric patients in the sections 4.8 and 5.1 is provided less often in scenario “1a or 1b”. Information on interactions (section 4.5) and pre-clinical safety (section 5.3) is very rare in all scenarios shown. A major difference between scenario 1a and 1b/”1a or 1b” is the occurrence of warnings and precautions related to the paediatric population (section 4.4), which is significantly higher in the scenarios 1b and ”1a or 1b”.

3.4.2.3 Attribution of age ranges

The age range is one of the key factors related to the use of a medicinal product in the paediatric population. Figure 15 depicts the attribution of age ranges to the different subgroups of scenario 1, which are all associated with section 4.1 (Therapeutic indications). In order to allow for a comparison between the scenarios, it was necessary to normalise the respective distributions by calculating the proportion of datasets that can be associated with the individual age groups. Example: 100% in the age group 17-18 years means that the indications in all datasets apply to this age group; 0% means that no indication is included in the datasets that cover this age group.

Figure 15: Histogram with age distribution for scenarios 1a to 1c



The histogram shows that all indications, independent form the listed scenarios, are applicable to adolescents (12-18 years of age). Below the age of 12 years the proportion of indications applicable for the individual age groups decreases with age. Related to the different scenarios, there is a steep decrease for datasets corresponding to scenario 1a. This is a significant difference to the other scenarios, which include a greater proportion of the paediatric population.

An interesting difference can also be seen for scenario 1b and 1c. While the datasets from scenario 1c capture a bigger proportion of the paediatric patients between 2 and 12 years of age, the datasets corresponding to scenario 1b do so for the age range of 0 to 12 months. Not displayed in Figure 15 are the values related to scenario 1d. This group only includes 5 medicinal products, which have very particular age ranges (3 months to 18 years, 2 years to 18 years (2x), 5 weeks to 5 months, 2 months to 2 years).

3.4.2.4 Therapeutic areas

Also the medicinal products with paediatric indication were assessed with regards to their distribution of therapeutic areas, which is depicted in Table 10. In general, a broad range of therapeutic main groups are covered with the paediatric indications. The only therapeutic main group with a comparably high number of medicinal products (9; 20%) is “J07 – Vaccines” with 5 products allocated to the scenarios 1c and 1d. However, a certain accumulation was anticipated for this class of medicines.

Table 10: Attribution of ATC levels 1 and 2 to all assessed medicinal products with paediatric indication

A - Alimentary tract and metabolism	**6**
A05 - Bile and liver therapy	1
A10 - Drugs used in diabetes	1
A16 - Other alimentary tract and metabolism products	4
B - Blood and blood forming organs	**7**
B01 - Antithrombotic agents	1
B02 - Antihemorrhagics	5
B06 - Other hematological agents	1
C - Cardiovascular system	**2**
C07 - Beta blocking agents	1
C10 - Lipid modifying agents	1
H - Systemic hormonal prep, excluding sex hormones	**1**
H01 - Pituitary and hypothalamic hormones	1
J - General antiinfectives for systemic use	**17**
J01 - Antibacterials for systemic use	2
J02 - Antimycotics for systemic use	1
J04 - Antimycobacterials	1
J05 - Antivirals for systemic use	3
J06 - Immune sera and immunoglobulins	1
J07 - Vaccines	9
L - Antineoplastic and immunomodulating agents	**3**
L01 - Cytostatics	2
L04 - Immunosuppressive agents	1

M - Musculo-skeletal system	**1**
M05 - Drugs for treatment of bone diseases	1
N - Nervous system	**2**
N03 - Antiepileptics	1
N05 - Psycholeptics	1
P - Antiparasitic products	**1**
P01 - Antiprotozoals	1
R - Respiratory system	**3**
R03 - Anti-asthmatics	1
R07 - Other respiratory system products	2
Not yet assigned	**1**
Not yet assigned	1
Σ	**44**

3.4.3 Dosage forms/strengths, Multiple indications and Age Ranges for Waivers/Deferrals

The criteria dosage forms, multiple indications and age ranges for waivers/deferrals have already been discussed in conjunction with the assessment of other criteria presented for the subsets of medicinal products with and without paediatric indication. In the following these criteria are analysed from the perspective of all datasets.

3.4.3.1 Dosage forms/strengths

Within the assessment of the SmPCs it was only assessed, for which medicinal products there was a differentiation of dosage forms/strengths between adult and paediatric patients. This means it was not captured if a dosage form was eligible for paediatric patients or not, as this was seen as a given in case of paediatric indications. For example a solution for infusion that can be used for adult as well as paediatric patients was captured with the value “NA”. On the other hand, if the information regarding paediatric patients is different between, e.g. 150 mg film-coated tablets and 50 mg granules in sachet, the information related to the respective dosage forms were captured in different datasets.

The results show that dosage forms and strengths are of surprisingly small significance in relation to the qualification and quantification of information on the paediatric population presented to the health care professional in prescribing information documents. Overall, for only 3 medicinal products a differentiation between dosage forms/strengths could be found, which is presented in Table 11.

Table 11: Medicinal products with a relevant differentiation between dosage forms/strengths for the paediatric population

Medicine Name	Dosage Forms/Strengths	Differentiation
Kalydeco	• 150 mg film-coated tablets • 50/75 mg granules in sachet	Different age range in indication (6-18 years vs. 2-18 years). Different posology for children < 25 kg body weight
Somatropin Biopartners	• 2, 4, 7 mg powder and solvent for prolonged-release suspension for injection • 10, 20 mg powder and solvent for prolonged-release suspension for injection	The 2, 4, 7 mg strengths are only relevant for adult patients. Reference is made in section 4.2 of the respective SmPC that "for the treatment of children and adolescents aged 2 to 18 years the 10 mg and 20 mg vials of this medicinal product should be used."
Votubia	2.5/5/10 mg tablets 2/3/5 mg dispersible tablets	The 2/3/5 mg dispersible tablets are medicinal products with a paediatric focussed indication. Thus they are the preferred option for paediatric patients. The 2.5/5/10 mg tablets include an additional adult indication associated with a waiver for the complete paediatric population. However, it is mentioned in the SmPC that these tablets can also be used in the paediatric population.

3.4.3.2 Multiple indications

Of all assessed medicinal products, 22 were associated with multiple indications (in most cases two indications). For 10 of these products there was no differentiation between the indications on the level of section 4.1 and 4.2 of the SmPC. The differences between the indications in section 4.1 and 4.2 in the other 12 medicinal products were mostly related to the association of different scenarios according to section 3.3.1. Within the other sections of the SmPC, the proportion of two different datasets for the same product was similar for sections 4.4, 4.8, 5.1 (only study data) and 5.2. The highest diversity was found in section 5.1 of the SmPC related to waivers and deferrals.

3.4.3.3 Age Ranges for Waivers/Deferrals

Overall, 439 of the 623 datasets (71%) include information on waivers and deferrals. Thereof, 253 (58%) are allocated to deferrals, 158 (36%) to waivers

and 28 (6%) to waivers and deferrals. Looking at the information related to the age ranges, a very clear picture is drawn.

- Deferrals: 87% of all datasets have been associated with the statement defined in the SmPC guideline according to which the deferral extends to “one or more subsets of the paediatric population”. This information is somewhat unsatisfactory, as the reader gets no information on the deferred age ranges. In the remaining 13% of the datasets there is an age range available, which extends mostly to the complete paediatric population or significant parts of it.
- Waivers: About 78% of all datasets that are allocated to waivers cover the age range of 0-18 years. About half of the remaining datasets are related to medicinal products with paediatric indication and complement the non-indicated parts of the paediatric population.

With regards to the interpretation of these data, it has to be taken into account that the waiver/deferral criterion has been applied to all datasets corresponding to a medicinal product. Therefore, products with multiple datasets (e.g. related to multiple sections of the SmPC including information on paediatric patients) are overrepresented, which mainly affects datasets corresponding to scenario 1a, 1b and 2b. However, this has no relevant impact on the overall message of this subsection.

3.5 Comparison of defined criteria between datasets for orphan medicinal products from the EU SmPC assessment and the corresponding US PI documents

For the exemplary comparison of EU SmPCs with US PIs, orphan medicinal products were chosen, as they address various therapeutic areas and include a meaningful amount of paediatric indications. Furthermore, the criteria were narrowed down to the availability of information with relation to the use in the paediatric population and age ranges attributed to these scenarios.

3.5.1 Sample

In total, 115 datasets for 42 orphan medicinal products are available. The sample used for the comparison is composed of two subgroups:

- datasets capturing section 4.1 of the SmPC for medicinal products with paediatric indication (13 datasets corresponding to 12 medicinal products)

- datasets related to section 4.2 of the SmPC for medicinal products without paediatric indication (32 datasets corresponding to 30 medicinal products)

3.5.2 Comparison

The US PIs required for the comparison were retrieved from DailyMed (http://dailymed.nlm.nih.gov/dailymed/index.cfm) on February 04, 2016. For datasets corresponding to medicinal products with paediatric indication, the necessary information needed for the comparison could be retrieved from the sections 1 (Indications and Usage), 8.4 (Pediatric Use) and 14 (Clinical Studies). For products without paediatric indication, the relevant information could be located in section 8.4 (Pediatric Use).

Of the 44 medicinal products:

- 11 (26%) are not registered in the US (3 products with paediatric indication, 8 without paediatric indication).
- 18 (43%) were associated with the same scenarios and the same age ranges (2 products with paediatric indication, 16 without paediatric indication). Most cases are datasets with scenario 2a (no data), for which a consistency is anticipated.
- 7 (17%) resulted in a different scenario (3 products with paediatric indication, 4 without paediatric indication).
    - Within the products with a paediatric indication, there was one product that is not indicated in the US, which poses a major difference. Another product included information on an additional study, which influenced the proportion of investigated paediatric patients (45% in the EU SmPC and 17% in the US PI) and thus the selected scenario (1b in the EU and 1a in the US). The third medicinal product included four additional adult indications, which explains scenario 1a (Adult focussed indication) in the US and scenario 1c (Paediatric focussed indication) in the EU.
    - From the medicinal products without paediatric indication, it was surprising that scenario 3a (should not be used) and scenario 4 (not relevant) in the EU was not reflected in the US PIs. All products included a statement that the safety and effectiveness has not been established in paediatric patients, which corresponds to scenario 2a (no data). In one case non-clinical data were provided in section 8.4 leading to scenario 2b (limited data) as compared to scenario 4 (not relevant) in the EU.

- 5 (12%) had a different age range associated to the respective scenario (only products with paediatric indication). In all cases the difference was related to the lower limit of the age range. In two medicinal products the difference was only one month and one week, respectively. In the other three products the indications were more restrictive than in the EU. The age range in the EU was 0 to 18 years for all three medicinal products, the indicated age ranges in the US started at 2, 4 and 5 years of age.
- One product was assessed to be different in scenario and age range. According to the US PI only one scenario (limited data) was associated, even though the medicinal product was divided into two scenarios in the EU for different age groups (scenario 3a (should not be used) and scenario 2a (no data)), the basis being underlying non-clinical data in both cases. This is a major difference, as in the EU there is a restriction for the use of the medicinal product and in the US the prescriber has to draw own conclusions. Both judgements are based on the non-clincial data.

The results of the comparison for each investigated dataset are presented in Annex III in Table 15.

4 Conclusion and Outlook

This thesis achieved to systematically investigate how the considerations related to paediatric development are translated into SmPCs and what information is finally communicated to health care professionals.

Based on the considerations of the Paediatric Regulation, the Guideline on Summary of Product Characteristics (SmPC) and the 5-year report to the European Commission on the experience acquired as a result of the application of the Paediatric Regulation, qualitative and quantitative criteria were established to associate information from SmPC documents to major aspects such as the availability of information with relation to the use in the paediatric population as well as types of information related to paediatric patients. Furthermore, age ranges were investigated for indications, waivers/deferrals as well as for other fields. Additional factors like dosage forms or multiple indications were also taken into account.

Using a robust sample of 244 medicinal products, which is capturing a huge variety of characteristics, the criteria were applied to the corresponding SmPC documents yielding over 600 datasets that were the basis for further analyses. The results of these analyses revealed a very clear picture on what information is communicated to health care professionals via the SmPCs. In the following some of the key findings are summarised.

- Even though only 18% of the investigated products contained a paediatric indication, there is a huge amount of deferrals mentioned in the SmPCs, giving rise to the anticipation of future paediatric indications.
- The age distribution for medicinal products with paediatric indication shows that adolescents are mostly included in the paediatric indications and that paediatric patients below 2 year age have the worst coverage. For paediatric patients below 12 years of age there is a big difference between adult focussed indications and more paediatric focussed indications.
- Dosage forms and strengths were only in very few cases relevant for the qualification and to quantification of information presented in the SmPCs.
- The amount of medicinal products with a contraindication in the paediatric population is very low.
- The availability of data seems to increase with a delay of about 4 years after granting of the marketing authorisation.

In addition to the aspects mentioned above, some areas were identified with a certain room for improvement. On the one hand, age ranges were mostly absent in deferral statements making it complicated for the health care professional to get an overview on the age groups covered in the deferred studies. On the other hand, the proportion of treated paediatric patients was missing in several SmPC documents, which would be helpful to set the data into perspective.

The final exemplary comparison to the US PIs of orphan medicinal products showed that the established criteria can also be successfully used on other types of prescribing information documents.

Looking into the future, the results from this thesis not only provide a comprehensive overview on the distribution of information on paediatric development and the use in the paediatric population in SmPC documents, but they can also be used as a basis for further investigations as well as to support regulatory affairs professionals in their day-to-day work.

Further investigations can be for instance conducted for a broader range of US PIs, but also for other countries. Additionally, the criteria can be used as a standardised filter to systematically investigate subsets of prescribing information documents. Furthermore, the generated datasets for the EU will always provide a robust historical reference with regards to the evaluated criteria.

An immediate benefit is created for regulatory affairs professionals, who are involved in the creation of prescribing information documents. The generated data provide a clear reference on all aspects that should be considered in the creation process of these documents and provide numerous examples for different scenarios, therapeutic areas, age ranges and other topics.

Annex I: Sample of Medicinal Products

Table 12: List of medicinal products included in sample according to section 3.2

Medicine Name	Active Substance	Product Number	ATC Code	Is Orphan	Start of Procedure Date	Authorisation Date	SmPC Date	Paediatric Indication
Aubagio	teriflunomide	EMEA/H/C/002514	L04AA31	no	> 25.07.2008	26.08.2013	30.07.2015	No
Abilify Maintena	aripiprazole	EMEA/H/C/002755	N05AX12	no	> 25.07.2008	15.11.2013	07.07.2015	No
Adasuve	loxapine	EMEA/H/C/002400	N05AH01	no	> 25.07.2008	20.02.2013	05.10.2015	No
Adcetris	brentuximab vedotin	EMEA/H/C/002455	L01XC12	yes	> 25.07.2008	25.10.2012	05.05.2015	No
Adempas	riociguat	EMEA/H/C/002737	C02KX05	yes	> 25.07.2008	27.03.2014	09.09.2015	No
Adjupanrix (previously Pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) GlaxoSmithKline Biologicals)	split influenza virus, inactivated, containing antigen: A/VietNam/1194/2004 (H5N1) like strain used (NIBRG-14)	EMEA/H/C/001206	J07BB02	no	15.07.2009	10.10.2009	04.08.2014	No
Aflunov	influenza virus surface antigens (haemagglutinin and neuraminidase) of strain: A/turkey/Turkey/1/05 (H5N1)-like strain (NIBRG-23)	EMEA/H/C/002094	J07BB02	no	> 25.07.2008	29.11.2010	14.08.2015	No
Akynzeo	netupitant / palonosetron hydrochloride	EMEA/H/C/003728	A04AA	no	> 25.07.2008	27.05.2015	23.06.2015	No
Ameluz	5-aminolevulinic acid hydrochloride	EMEA/H/C/002204	L01XD04	no	> 25.07.2008	14.12.2011	12.03.2015	No
Amyvid	florbetapir (18F)	EMEA/H/C/002422	V09AX05	no	> 25.07.2008	14.01.2013	22.09.2015	No
Anoro	umeclidinium bromide /	EMEA/H/C/002751	R03AL03	no	> 25.07.2008	08.05.2014	13.05.2015	No

Medicine Name	Active Substance	Product Number	ATC Code	Is Orphan	Start of Procedure Date	Authorisation Date	SmPC Date	Paediatric Indication
	vilanterol trifenatate							
Arzerra	ofatumumab	EMEA/H/C/001131	L01XC10	yes	> 25.07.2008	19.04.2010	29.09.2015	No
Benlysta	belimumab	EMEA/H/C/002015	L04AA26	no	> 25.07.2008	13.07.2011	07.11.2014	No
Betmiga	mirabegron	EMEA/H/C/002388	G04BD12	no	> 25.07.2008	20.12.2012	15.10.2015	No
Bexsero	recombinant Neisseria meningitidis group-B NHBA fusion protein /recombinant Neisseria meningitidis group-B NadA protein /recombinant Neisseria meningitidis group B fHbp fusion protein /outer mem-brane vesiclesfrom Neis-seria meningitidis group-B strain NZ98	EMEA/H/C/002333	J07AH09	no	> 25.07.2008	14.01.2013	05.11.2015	Yes
Bosulif	bosutinib (as monohydrate)	EMEA/H/C/002373	L01XE14	yes	> 25.07.2008	27.03.2013	07.09.2015	No
Brilique	ticagrelor	EMEA/H/C/001241	B01AC24	no	> 25.07.2008	03.12.2010	11.08.2015	No
Brimica Genuair	aclidinium / formoterol fumarate dihydrate	EMEA/H/C/003969	R03AL05	no	> 25.07.2008	19.11.2014	08.06.2015	No
Brinavess	vernakalant hydrochloride	EMEA/H/C/001215	C01BG11	no	> 25.07.2008	01.09.2010	29.09.2015	No
Brintellix	vortioxetine	EMEA/H/C/002717	N06AX26	no	> 25.07.2008	18.12.2013	22.07.2015	No
Bronchitol	mannitol	EMEA/H/C/001252	R05CB16	yes	> 25.07.2008	13.04.2012	25.09.2015	No
Buccolam	midazolam	EMEA/H/C/002267	N05CD08	no	> 25.07.2008	05.09.2011	27.03.2014	Yes
Bydureon	exenatide	EMEA/H/C/002020	A10BX04	no	> 25.07.2008	17.06.2011	06.02.2015	No
Caprelsa	vandetanib	EMEA/H/C/002315	L01XE	no	> 25.07.2008	17.02.2012	05.12.2014	No
Cerdelga	eliglustat	EMEA/H/C/003724	A16AX10	yes	> 25.07.2008	19.01.2015	21.04.2015	No
Cholib	fenofibrate / simvastatin	EMEA/H/C/002559	C10BA04	no	> 25.07.2008	26.08.2013	09.09.2015	No
Cinryze	C1 inhibitor (human)	EMEA/H/C/001207	B06AC01	no	> 25.07.2008	15.06.2011	25.09.2015	Yes
Clopidogrel/Acetylsalicylic acid Teva	clopidogrel / acetylsalicylic acid	EMEA/H/C/002272	B01AC30	no	> 25.07.2008	01.09.2014	26.09.2014	No
Colobreathe	colistimethate sodium	EMEA/H/C/001225	R07AX	no	> 25.07.2008	13.02.2012	30.06.2015	Yes

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Cometriq	cabozantinib	EMEA/H/C/002640	L01XE	yes	> 25.07.2008	21.03.2014	08.10.2015	No
Constella	linaclotide	EMEA/H/C/002490	A06AX04	no	> 25.07.2008	26.11.2012	26.08.2015	No
Cosentyx	secukinumab	EMEA/H/C/003729	L04AC10	no	> 25.07.2008	15.01.2015	11.05.2015	No
Cuprymina	copper (64Cu) chloride	EMEA/H/C/002136	V	no	> 25.07.2008	23.08.2012	06.11.2015	No
Cyramza	ramucirumab	EMEA/H/C/002829	L01XC	yes	> 25.07.2008	19.12.2014	07.10.2015	No
Dacogen	decitabine	EMEA/H/C/002221	L01BC08	yes	> 25.07.2008	20.09.2012	26.05.2015	No
Daklinza	daclatasvir dihydrochloride	EMEA/H/C/003768	J05AX14	no	> 25.07.2008	22.08.2014	05.11.2015	No
Daxas	roflumilast	EMEA/H/C/001179	R03DX07	no	> 25.07.2008	05.07.2010	04.06.2015	No
Defitelio	defibrotide	EMEA/H/C/002393	B01AX01	yes	> 25.07.2008	18.10.2013	13.03.2015	Yes
Deltyba	delamanid	EMEA/H/C/002552	J04AK06	yes	> 25.07.2008	28.04.2014	12.08.2015	No
Dexdor	dexmedetomidine hydro-chloride	EMEA/H/C/002268	N05CM18	no	> 25.07.2008	16.09.2011	20.08.2015	No
Dificlir	fidaxomicin	EMEA/H/C/002087	A07AA12	no	> 25.07.2008	05.12.2011	11.08.2014	No
Duaklir Genuair	aclidinium bromide / for-moterol fumarate dihydrate	EMEA/H/C/003745	R03AL	no	> 25.07.2008	19.11.2014	28.05.2015	No
Duavive	oestrogens conjugated / bazedoxifene	EMEA/H/C/002314	G03CX	no	> 25.07.2008	16.12.2014	23.10.2015	No
DuoCover	clopidogrel / acetylsalicylic acid	EMEA/H/C/001144	B01AC30	no	> 25.07.2008	15.03.2010	24.07.2015	No
DuoPlavin	clopidogrel / acetylsalicylic acid	EMEA/H/C/001143	B01AC30	no	> 25.07.2008	15.03.2010	13.07.2015	No
DuoResp Spiromax	budesonide / formoterol fumarate dihydrate	EMEA/H/C/002348	R03AK07	no	> 25.07.2008	28.04.2014	07.10.2015	No
Dutrebis	lamivudine / raltegravir potassium	EMEA/H/C/003823	J05AR16	no	> 25.07.2008	26.03.2015	21.04.2015	Yes
Edarbi	azilsartan medoxomil	EMEA/H/C/002293	C09CA09	no	> 25.07.2008	07.12.2011	01.10.2014	No
Edurant	rilpivirine hydrochloride	EMEA/H/C/002264	J05AG05	no	> 25.07.2008	28.11.2011	13.05.2014	No
Eklira Genuair	aclidinium bromide, mi-cronised	EMEA/H/C/002211	R03BB	no	> 25.07.2008	20.07.2012	03.06.2015	No
Eliquis	apixaban	EMEA/H/C/002148	B01AF02	no	> 25.07.2008	18.05.2011	25.08.2015	No
Elonva	corifollitropin alfa	EMEA/H/C/001106	G03GA09	no	> 25.07.2008	25.01.2010	12.11.2015	No

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Entyvio	vedolizumab	EMEA/H/C/002782	L04AA	no	> 25.07.2008	22.05.2014	25.09.2015	No
Enurev Breezhaler	glycopyrronium bromide	EMEA/H/C/002691	R03BB06	no	> 25.07.2008	28.09.2012	28.09.2015	No
Envarsus	tacrolimus	EMEA/H/C/002655	L04AD02	no	> 25.07.2008	18.07.2014	06.10.2015	No
Eperzan	albiglutide	EMEA/H/C/002735	A10BX13	no	> 25.07.2008	21.03.2014	04.02.2015	No
Erivedge	vismodegib	EMEA/H/C/002602	L01XX43	no	> 25.07.2008	12.07.2013	04.06.2015	No
Esbriet	pirfenidone	EMEA/H/C/002154	L04AX05	yes	> 25.07.2008	28.02.2011	07.10.2015	No
Esmya	ulipristal acetate	EMEA/H/C/002041	G03XB02	no	> 25.07.2008	23.02.2012	07.07.2015	No
Eurartesim	piperaquine tetraphosphate / dihydroartemisinin	EMEA/H/C/001199	P01BF05	no	> 25.07.2008	27.10.2011	18.08.2015	Yes
Evarrest	human fibrinogen / human thrombin	EMEA/H/C/002515	B02BC30	no	> 25.07.2008	25.09.2013	23.12.2014	No
Eviplera	emtricitabine / rilpivirine hydrochloride /tenofovir disoproxil fumarate	EMEA/H/C/002312	J05AR08	no	> 25.07.2008	28.11.2011	29.06.2015	No
Evotaz	atazanavir sulfate / cobi-cistat	EMEA/H/C/003904	J05AR	no	> 25.07.2008	13.07.2015	10.08.2015	No
Exforge HCT	amlodipine besylate / valsartan / hydrochlorothi-azide	EMEA/H/C/001068	C09DX01	no	24.09.2008	16.10.2009	08.06.2015	No
Exviera	dasabuvir sodium	EMEA/H/C/003837	J05	no	> 25.07.2008	15.01.2015	30.09.2015	No
Eylea	aflibercept	EMEA/H/C/002392	S01LA05	no	> 25.07.2008	22.11.2012	20.04.2015	No
Fampyra	fampridine	EMEA/H/C/002097	N07XX07	no	> 25.07.2008	20.07.2011	14.08.2015	No
Fluenz Tetra	influenza virus type A, H1N1 / influenza virus type A, H3N2 / influenza virus type B (Victoria lineage) / influenza virus, type B (Yamagata lineage)	EMEA/H/C/002617	J07BB03	no	> 25.07.2008	04.12.2013	08.10.2015	Yes
Foclivia	influenza virus surface antigens, inactivated: A/Viet Nam/1194/2004 (H5N1)	EMEA/H/C/001208	J07BB02	no	15.07.2009	19.10.2009	08.07.2015	No
Fortacin	lidocaine / prilocaine	EMEA/H/C/002693	N01BB20	no	> 25.07.2008	15.11.2013	08.12.2014	No

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Forxiga	dapagliflozin propanediol monohydrate	EMEA/H/C/002322	A10BX09	no	> 25.07.2008	12.11.2012	08.05.2015	No
Fycompa	perampanel	EMEA/H/C/002434	N03AX22	no	> 25.07.2008	23.07.2012	03.08.2015	Yes
Gardasil 9	human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed)	EMEA/H/C/003852	J07BM	no	> 25.07.2008	10.06.2015	03.07.2015	Yes
Gazyvaro	obinutuzumab	EMEA/H/C/002799	L01XC15	yes	> 25.07.2008	23.07.2014	17.08.2015	No
Gilenya	fingolimod hydrochloride	EMEA/H/C/002202	L04AA27	no	> 25.07.2008	17.03.2011	14.07.2015	No
Giotrif	afatinib	EMEA/H/C/002280	L01XE13	no	> 25.07.2008	25.09.2013	23.10.2015	No
Glybera	alipogene tiparvovec	EMEA/H/C/002145	C10 AX10	yes	> 25.07.2008	25.10.2012	26.06.2015	No
Granupas (previously Para-aminosalicylic acid Lucane)	para-aminosalicylic acid	EMEA/H/C/002709	J04AA01	yes	> 25.07.2008	07.04.2014	23.07.2014	Yes
Halaven	eribulin	EMEA/H/C/002084	L01XX41	no	> 25.07.2008	17.03.2011	27.10.2015	No
Harvoni	sofosbuvir / ledipasvir	EMEA/H/C/003850	J05	no	> 25.07.2008	17.11.2014	24.07.2015	No
Hemangiol	propranolol hydrochloride	EMEA/H/C/002621	C07AA05	no	> 25.07.2008	23.04.2014	19.11.2014	Yes
Hetlioz	tasimelteon	EMEA/H/C/003870	N05CH	yes	> 25.07.2008	03.07.2015	22.07.2015	No
Hexacima	diphtheria toxoid /tetanus toxoid / two-component acellular pertus-sis(pertussis toxoidand filamentous haemagglu-tinin) /inactivated poliomye-litis virus types 1,2 and 3 /Haemophilus influenzae type-b polysaccharide (polyribosylribitol phos-phate) conjugated	EMEA/H/C/002702	J07CA09	no	> 25.07.2008	17.04.2013	15.09.2015	Yes
Hirobriz Breezhaler	indacaterol maleate	EMEA/H/C/001211	R03AC18	no	26.07.2009	30.11.2009	11.11.2014	No
Hizentra	human normal immuno-globulin (SCIg)	EMEA/H/C/002127	J06BA01	no	> 25.07.2008	14.04.2011	09.01.2015	Yes
Holoclar	ex vivo expanded autolo-gous human corneal epi-	EMEA/H/C/002450	S01XA19	yes	> 25.07.2008	17.02.2015	02.03.2015	No

Medicine Name	Active Substance	Product Number	ATC Code	Is Orphan	Start of Procedure Date	Authorisation Date	SmPC Date	Paediatric Indication
	thelial cells containing stem cells							
HyQvia	human normal immuno-globulin	EMEA/H/C/002491	J06BA	no	> 25.07.2008	16.05.2013	13.08.2015	No
Iclusig	ponatinib	EMEA/H/C/002695	L01XE24	yes	> 25.07.2008	01.07.2013	05.10.2015	No
Ikervis	ciclosporin	EMEA/H/C/002066	S01XA18	no	> 25.07.2008	19.03.2015	23.07.2015	No
Ilaris	canakinumab	EMEA/H/C/001109	L04AC08	no	24.12.2008	23.10.2009	14.04.2015	Yes
Imbruvica	ibrutinib	EMEA/H/C/003791	L01XE27	yes	> 25.07.2008	21.10.2014	14.09.2015	No
Imnovid (previously Pomalidomide Celgene)	pomalidomide	EMEA/H/C/002682	L04AX06	yes	> 25.07.2008	05.08.2013	21.07.2015	No
Imvanex	modified vaccinia Ankara - Bavarian Nordic (MVA-BN) virus	EMEA/H/C/002596	J07BX	no	> 25.07.2008	31.07.2013	30.01.2015	No
Incivo	telaprevir	EMEA/H/C/002313	J05AE	no	> 25.07.2008	19.09.2011	13.08.2015	No
Incresync	alogliptin / pioglitazone	EMEA/H/C/002178	A10BD09	no	> 25.07.2008	19.09.2013	05.02.2015	No
Incruse	umeclidinium bromide	EMEA/H/C/002809	R03BB07	no	> 25.07.2008	28.04.2014	03.06.2015	No
Inlyta	axitinib	EMEA/H/C/002406	L01XE17	no	> 25.07.2008	03.09.2012	13.07.2015	No
Invokana	canagliflozin	EMEA/H/C/002649	A10BX11	no	> 25.07.2008	15.11.2013	28.09.2015	No
Izba	travoprost	EMEA/H/C/002738	S01EE04	no	> 25.07.2008	20.02.2014	17.03.2014	No
Jakavi	ruxolitinib (as phosphate)	EMEA/H/C/002464	L01XE18	no	> 25.07.2008	23.08.2012	02.06.2015	No
Jardiance	empagliflozin	EMEA/H/C/002677	A10BX12	no	> 25.07.2008	22.05.2014	04.02.2015	No
Jentadueto	linagliptin / metformin	EMEA/H/C/002279	A10BD11	no	> 25.07.2008	20.07.2012	22.01.2015	No
Jetrea	ocriplasmin	EMEA/H/C/002381	S01XA22	no	> 25.07.2008	13.03.2013	27.08.2015	No
Jevtana	cabazitaxel	EMEA/H/C/002018	L01CD	no	> 25.07.2008	17.03.2011	24.07.2015	No
Kadcyla	trastuzumab emtansine	EMEA/H/C/002389	L01XC14	no	> 25.07.2008	15.11.2013	03.12.2014	No
Kalydeco	ivacaftor	EMEA/H/C/002494	R07AX02	yes	> 25.07.2008	23.07.2012	15.12.2015	Yes
Kengrexal	cangrelor	EMEA/H/C/003773	B01	no	> 25.07.2008	23.03.2015	12.06.2015	No
Ketoconazole HRA	ketoconazole	EMEA/H/C/003906	J02AB02	yes	> 25.07.2008	19.11.2014	22.04.2015	Yes
Keytruda	pembrolizumab	EMEA/H/C/003820	L01	no	> 25.07.2008	17.07.2015	30.07.2015	No

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Komboglyze	metformin hydrochloride /saxagliptin hydrochloride	EMEA/H/C/002059	A10BD10	no	> 25.07.2008	24.11.2011	10.09.2015	No
Krystexxa	pegloticase	EMEA/H/C/002208	M04AX02	no	> 25.07.2008	08.01.2013	01.12.2014	No
Latuda	lurasidone	EMEA/H/C/002713	N05AE05	no	> 25.07.2008	21.03.2014	12.10.2015	No
Laventair	umeclidinium bromide / vilanterol	EMEA/H/C/003754	R03AL03	no	> 25.07.2008	08.05.2014	19.11.2015	No
Lemtrada	alemtuzumab	EMEA/H/C/003718	L04AA34	no	> 25.07.2008	12.09.2013	26.03.2014	No
Lenvima	lenvatinib mesylate	EMEA/H/C/003727	L01XE	yes	> 25.07.2008	28.05.2015	25.06.2015	No
Vantobra	tobramycin	EMEA/H/C/002633	J01GB01	no	> 25.07.2008	18.03.2015	19.03.2015	Yes
Vargatef	nintedanib	EMEA/H/C/002569	L01XE3	no	> 25.07.2008	21.11.2014	27.05.2015	No
Velphoro	mixture of polynuclear iron(III)-oxyhydroxide, sucrose and starches	EMEA/H/C/002705	V03AE05	no	> 25.07.2008	26.08.2014	26.10.2015	No
Vepacel	Influenza virus (whole virion, inactivated), contain-ing antigen of: A/Vietnam/1203/2004 (H5N1)	EMEA/H/C/002089	J07BBOI	no	> 25.07.2008	17.02.2012	20.07.2015	Yes
Lixiana	edoxaban tosylate	EMEA/H/C/002629	B01	no	> 25.07.2008	19.06.2015	03.07.2015	No
Lojuxta	lomitapide	EMEA/H/C/002578	C10AX12	no	> 25.07.2008	31.07.2013	18.08.2015	No
Lonquex	lipegfilgrastim	EMEA/H/C/002556	L03AA14	no	> 25.07.2008	25.07.2013	28.07.2015	No
Lymphoseek	tilmanocept	EMEA/H/C/002085	V09IA09	no	> 25.07.2008	19.11.2014	08.01.2015	No
Lynparza	olaparib	EMEA/H/C/003726	L01	yes	> 25.07.2008	16.12.2014	09.01.2015	No
Lyxumia	lixisenatide	EMEA/H/C/002445	A10BX10	no	> 25.07.2008	01.02.2013	23.12.2014	No
Mekinist	trametinib	EMEA/H/C/002643	L01XE25	no	> 25.07.2008	30.06.2014	04.11.2015	No
Menveo	meningococcal group A, C, W-135 and Y conjugate vaccine	EMEA/H/C/001095	J07AH08	no	> 25.07.2008	15.03.2010	07.10.2015	Yes
Mirvaso	brimonidine tartrate	EMEA/H/C/002642	D11AX21	no	> 25.07.2008	21.02.2014	08.07.2015	No
Moventig	naloxegol oxalate	EMEA/H/C/002810	A06AH03	no	> 25.07.2008	08.12.2014	07.12.2014	No
Mysimba	bupropion hydrochloride / naltrexone hydrochloride	EMEA/H/C/003687	A08AA62	no	> 25.07.2008	26.03.2015	15.04.2015	No

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Neuraceq	florbetaben (18F)	EMEA/H/C/002553	V09AX06	no	> 25.07.2008	20.02.2014	12.10.2015	No
Nexium Control	esomeprazole	EMEA/H/C/002618	A02BC05	no	> 25.07.2008	26.08.2013	17.08.2015	No
NexoBrid	concentrate of proteolytic enzymes enriched in bromelain	EMEA/H/C/002246	D03BA03	yes	> 25.07.2008	18.12.2012	21.10.2014	No
Nimenrix	Neisseria meningitidis serogroup A polysaccharide conjugated to tetanus toxoid / Neisseria meningitidis serogroup C polysaccharide conjugated to tetanus toxoid /Neisseria meningitidis serogroup W-135 polysaccharide conjugated to tetanus toxoid / Neisseria	EMEA/H/C/002226	J07AH08	no	> 25.07.2008	20.04.2012	28.05.2015	Yes
NovoEight	turoctocog alfa	EMEA/H/C/002719	B02BD02	no	> 25.07.2008	13.11.2013	03.08.2015	Yes
NovoThirteen	catridecacog	EMEA/H/C/002284	B02BD11	no	> 25.07.2008	03.09.2012	25.03.2014	Yes
Nuedexta	dextromethorphan / quinidine	EMEA/H/C/002560	N07XX59	no	> 25.07.2008	24.06.2013	26.11.2014	No
Nulojix	belatacept	EMEA/H/C/002098	L04AA28	no	> 25.07.2008	17.06.2011	24.02.2015	No
Nuwiq	simoctocog alfa	EMEA/H/C/002813	B02BD02	no	> 25.07.2008	24.07.2014	26.11.2015	Yes
Ofev	nintedanib	EMEA/H/C/003821	L01XE	yes	> 25.07.2008	15.01.2015	13.02.2015	No
Olysio	simeprevir	EMEA/H/C/002777	J05AE14	no	> 25.07.2008	14.05.2014	25.09.2015	No
Onbrez Breezhaler	indacaterol maleate	EMEA/H/C/001114	R03AC18	no	28.01.2009	30.11.2009	21.11.2014	No
Opdivo	nivolumab	EMEA/H/C/003985	L01XC	no	> 25.07.2008	19.06.2015	16.07.2015	No
Opsumit	macitentan	EMEA/H/C/002697	C02KX04	yes	> 25.07.2008	20.12.2013	17.09.2015	No
Orbactiv	oritavancin diphosphate	EMEA/H/C/003785	J01XA05	no	> 25.07.2008	19.03.2015	04.05.2015	No
Orphacol	cholic acid	EMEA/H/C/001250	A05AA03	yes	> 25.07.2008	12.09.2013	21.04.2015	Yes
Oslif Breezhaler	indacaterol maleate	EMEA/H/C/001210	R03AC18	no	26.07.2009	30.11.2009	26.10.2014	No
Otezla	apremilast	EMEA/H/C/003746	L04AA32	no	> 25.07.2008	15.01.2015	16.02.2015	No

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Ozurdex	dexamethasone	EMEA/H/C/001140	S01BA01	no	> 25.07.2008	27.07.2010	07.05.2015	No
Pandemic Influenza Vaccine H5N1 Baxter AG	influenza vaccine (whole virion, inactivated) containing antigen of: A/Vietnam/1203/2004(H5N1V)	EMEA/H/C/001200	J07BB01	no	10.07.2009	16.10.2009	06.02.2014	Yes
Perjeta	pertuzumab	EMEA/H/C/002547	L01XC13	no	> 25.07.2008	04.03.2013	08.10.2015	No
Pheburane	sodium phenylbutyrate	EMEA/H/C/002500	A16AX03	no	> 25.07.2008	31.07.2013	06.10.2014	Yes
Picato	ingenol mebutate	EMEA/H/C/002275	D06BX02	no	> 25.07.2008	15.11.2012	23.09.2015	No
Pixuvri	pixantrone dimaleate	EMEA/H/C/002055	L01DB11	no	> 25.07.2008	10.05.2012	02.06.2015	No
Plegridy	peginterferon beta-1a	EMEA/H/C/002827	L03AB13	no	> 25.07.2008	18.07.2014	25.10.2015	No
Plenadren	hydrocortisone	EMEA/H/C/002185	H02AB09	yes	> 25.07.2008	03.11.2011	25.10.2013	No
Pravafenix	fenofibrate / pravastatin	EMEA/H/C/001243	C10BA03	no	> 25.07.2008	14.04.2011	12.05.2015	No
Prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) Novartis Vaccines and Diagnostics	influenza virus surface antigens (haemagglutinin and neuraminidase) of strain A/Viet Nam/1194/2004 (H5N1)	EMEA/H/C/002269	J07BB02	no	> 25.07.2008	29.11.2010	11.09.2015	No
Prevenar 13	pneumococcal polysaccharide serotype 1 /pneumococcal polysaccharide serotype 14 /pneumococcal polysaccharide serotype 18C /pneumococcal polysaccharide serotype 19A / pneumococcal polysaccharide serotype 19F /pneumococcal polysaccharide serotype 23F /pneum	EMEA/H/C/001104	J07AL02	no	24.12.2008	09.12.2009	21.12.2015	Yes
Procysbi	mercaptamine bitartrate	EMEA/H/C/002465	A16AA04	yes	> 25.07.2008	06.09.2013	20.11.2014	Yes
Prolia	denosumab	EMEA/H/C/001120	M05BX04	no	> 25.07.2008	26.05.2010	13.08.2015	No

Medicine Name	Active Substance	Product Number	ATC Code	Is Orphan	Start of Procedure Date	Authorisation Date	SmPC Date	Paediatric Indication
Xeplion	paliperidone palmitate	EMEA/H/C/002105	N05AX13	no	> 25.07.2008	04.03.2011	22.09.2015	No
Xgeva	denosumab	EMEA/H/C/002173	M05BX04	no	> 25.07.2008	13.07.2011	19.08.2015	Yes
Xiapex	collagenase Clostridium histolyticum	EMEA/H/C/002048	M09AB02	no	> 25.07.2008	28.02.2011	26.06.2015	No
Xigduo	metformin hydrochloride / dapagliflozin propanediol monohydrate	EMEA/H/C/002672	A10BD15	no	> 25.07.2008	16.01.2014	10.03.2015	No
Xofigo	radium Ra223 dichloride	EMEA/H/C/002653	V10XX03	no	> 25.07.2008	13.11.2013	16.10.2015	No
Quinsair	levofloxacin	EMEA/H/C/002789	J01MA12	no	> 25.07.2008	26.03.2015	13.10.2015	No
Rapiscan	regadenoson	EMEA/H/C/001176	C01EB21	no	> 25.07.2008	06.09.2010	27.08.2015	No
Raplixa	human fibrinogen / human thrombin	EMEA/H/C/002807	B02BC30	no	> 25.07.2008	19.03.2015	04.05.2015	No
Rasilamlo	aliskiren / amlodipine	EMEA/H/C/002073	C09XA53	no	> 25.07.2008	14.04.2011	14.07.2015	No
Relvar Ellipta	fluticasone furoate / vilanterol	EMEA/H/C/002673	R03AK10	no	> 25.07.2008	13.11.2013	21.12.2015	Yes
Repatha	evolocumab	EMEA/H/C/003766	C10	no	> 25.07.2008	17.07.2015	03.08.2015	Yes
Revestive	teduglutide	EMEA/H/C/002345	A16AX08	yes	> 25.07.2008	30.08.2012	10.09.2015	No
Revolade	eltrombopag olamine	EMEA/H/C/001110	B02BX05	no	> 25.07.2008	11.03.2010	11.08.2015	No
Rezolsta	darunavir / cobicistat	EMEA/H/C/002819	J05	no	> 25.07.2008	19.11.2014	12.12.2014	No
Rixubis	nonacog gamma	EMEA/H/C/003771	B02BD04	no	> 25.07.2008	19.12.2014	08.07.2015	Yes
Ruconest	conestat alfa	EMEA/H/C/001223	B06AC04	no	> 25.07.2008	28.10.2010	10.10.2013	No
Ryzodeg	insulin degludec / insulin aspart	EMEA/H/C/002499	A10AD06	no	> 25.07.2008	21.01.2013	26.08.2015	No
Sancuso	granisetron	EMEA/H/C/002296	A04AA02	no	> 25.07.2008	20.04.2012	26.08.2015	No
Saxenda	liraglutide	EMEA/H/C/003780	A10BX07	no	> 25.07.2008	23.03.2015	16.04.2015	No
Scenesse	afamelanotide	EMEA/H/C/002548	D02BB02	yes	> 25.07.2008	22.12.2014	12.02.2015	No
Scintimun	besilesomab	EMEA/H/C/001045	V09HA03	no	> 25.07.2008	11.01.2010	30.09.2014	No
Seebri Breezhaler	glycopyrronium bromide	EMEA/H/C/002430	R03BB06	no	> 25.07.2008	28.09.2012	05.10.2015	No
Selincro	nalmefene hydrochloride dihydrate	EMEA/H/C/002583	N07BB05	no	> 25.07.2008	25.02.2013	08.07.2015	No
Senshio	ospemifene	EMEA/H/C/002780	G03XC05	no	> 25.07.2008	15.01.2015	17.02.2015	No

Medicine Name	Active Substance	Product Number	ATC Code	Is Orphan	Start of Procedure Date	Authorisation Date	SmPC Date	Paediatric Indication
Signifor	pasireotide	EMEA/H/C/002052	H01CB05	yes	> 25.07.2008	24.04.2012	19.08.2015	No
Silodyx	silodosin	EMEA/H/C/001209	G04CA04	no	> 25.07.2008	29.01.2010	20.04.2015	No
Simbrinza	brinzolamide / brimonidine tartrate	EMEA/H/C/003698	S01EC54	no	> 25.07.2008	18.07.2014	03.08.2015	No
Sirturo	bedaquiline fumarate	EMEA/H/C/002614	J04A	yes	> 25.07.2008	05.03.2014	10.06.2015	No
Sivextro	tedizolid phosphate	EMEA/H/C/002846	J01	no	> 25.07.2008	23.03.2015	12.11.2015	No
Somatropin Biopart-ners	somatropin	EMEA/H/C/002196	H01AC01	no	> 25.07.2008	05.08.2013	30.07.2014	Yes
Sovaldi	sofosbuvir	EMEA/H/C/002798	J05AX15	no	> 25.07.2008	16.01.2014	21.09.2015	No
Spedra	avanafil	EMEA/H/C/002581	G04BE10	no	> 25.07.2008	21.06.2013	26.10.2015	No
Stivarga	regorafenib	EMEA/H/C/002573	L01XE21	no	> 25.07.2008	26.08.2013	23.06.2015	No
Stribild	elvitegravir / cobicistat / emtricitabine / tenofovir disoproxil fumarate	EMEA/H/C/002574	J05AR09	no	> 25.07.2008	24.05.2013	05.08.2015	No
Sycrest	asenapine maleate	EMEA/H/C/001177	N05AH05	no	> 25.07.2008	01.09.2010	28.10.2015	No
Sylvant	siltuximab	EMEA/H/C/003708	L04AC11	yes	> 25.07.2008	22.05.2014	23.07.2015	No
Synjardy	empagliflozin / metformin	EMEA/H/C/003770	A10BD20	no	> 25.07.2008	27.05.2015	12.06.2015	No
Tafinlar	dabrafenib	EMEA/H/C/002604	L01XE23	no	> 25.07.2008	26.08.2013	20.11.2015	No
Tecfidera	dimethyl fumarate	EMEA/H/C/002601	N07XX09	no	> 25.07.2008	30.01.2014	21.08.2015	No
Teysuno	tegafur / gimeracil / oteracil	EMEA/H/C/001242	L01BC53	no	> 25.07.2008	14.03.2011	27.08.2015	No
Tivicay	dolutegravir	EMEA/H/C/002753	J05AX12	no	> 25.07.2008	16.01.2014	05.11.2015	Yes
Tobi Podhaler	tobramycin	EMEA/H/C/002155	J01GB01	yes	> 25.07.2008	20.07.2011	23.01.2015	Yes
Topotecan Hospira	topotecan	EMEA/H/C/001192	L01XX17	no	> 25.07.2008	10.06.2010	11.08.2015	No
Tovanor Breezhaler	glycopyrronium bromide	EMEA/H/C/002690	R03BB06	no	> 25.07.2008	28.09.2012	21.09.2015	No
Trajenta	linagliptin	EMEA/H/C/002110	A10BH05	no	> 25.07.2008	24.08.2011	11.08.2015	No
Translarna	ataluren	EMEA/H/C/002720	00 -not yet assigned	yes	> 25.07.2008	31.07.2014	16.04.2015	Yes
Tresiba	insulin degludec	EMEA/H/C/002498	A10AE06	no	> 25.07.2008	21.01.2013	24.08.2015	Yes
Triumeq	abacavir sulfate / dolute-gravir sodium / lamivudine	EMEA/H/C/002754	J05AR13	no	> 25.07.2008	01.09.2014	09.11.2015	Yes

Medicine Name	Active Substance	Product Number	ATC Code	Is Orphan	Start of Procedure Date	Authorisation Date	SmPC Date	Paediatric Indication
Trobalt	retigabine	EMEA/H/C/001245	N03AX21	no	> 25.07.2008	28.03.2011	12.05.2015	No
Trulicity	dulaglutide	EMEA/H/C/002825	A10	no	> 25.07.2008	21.11.2014	08.09.2015	No
Twynsta	telmisartan / amlodipine	EMEA/H/C/001224	C09DB04	no	> 25.07.2008	07.10.2010	08.10.2015	No
Tybost	cobicistat on silicon dioxide	EMEA/H/C/002572	V03AX03	no	> 25.07.2008	19.09.2013	04.06.2015	No
Ultibro Breezhaler	indacaterol / glycopyrroni-um bromide	EMEA/H/C/002679	R03AL04	no	> 25.07.2008	19.09.2013	10.11.2015	No
Ulunar Breezhaler	glycopyrronium bromide / indacaterol maleate	EMEA/H/C/003875	R03	no	> 25.07.2008	23.04.2014	05.11.2015	No
Urorec	silodosin	EMEA/H/C/001092	G04CA04	no	> 25.07.2008	29.01.2010	08.05.2015	No
Vibativ	telavancin	EMEA/H/C/001240	J01XA03	no	> 25.07.2008	02.09.2011	01.12.2014	No
Victrelis	boceprevir	EMEA/H/C/002332	J05AE	no	> 25.07.2008	18.07.2011	09.03.2015	No
Viekirax	ombitasvir / paritaprevir / ritonavir	EMEA/H/C/003839	J05	no	> 25.07.2008	15.01.2015	30.11.2015	No
Vimizim	recombinant human n-acetylgalactosamine-6-sulfatase (rhgalns)	EMEA/H/C/002779	A16AB12	yes	> 25.07.2008	28.04.2014	20.05.2015	Yes
Vipdomet	alogliptin benzoate / met-formin hydrochloride	EMEA/H/C/002654	A10BD13	no	> 25.07.2008	19.09.2013	28.01.2015	No
Vipidia	alogliptin	EMEA/H/C/002182	A10BH04	no	> 25.07.2008	19.09.2013	29.09.2014	No
Vitekta	elvitegravir	EMEA/H/C/002577	J05AX11	no	> 25.07.2008	13.11.2013	24.04.2015	No
Vizamyl	flutemetamol (18F)	EMEA/H/C/002557	V09AX04	no	> 25.07.2008	22.08.2014	10.11.2015	No
Vokanamet	canagliflozin / metformin hydrochloride	EMEA/H/C/002656	A10BD16	no	> 25.07.2008	23.04.2014	29.09.2015	No
Voncento	human coagulation factor VIII / von Willebrand factor	EMEA/H/C/002493	B02BD06	no	> 25.07.2008	12.08.2013	23.09.2015	Yes
Votrient	pazopanib	EMEA/H/C/001141	L01XE11	no	> 25.07.2008	14.06.2010	27.10.2015	No
Votubia	everolimus	EMEA/H/C/002311	L01XE10	yes	> 25.07.2008	02.09.2011	06.05.2015	Yes
Vpriv	velaglucerase alfa	EMEA/H/C/001249	A16AB10	yes	> 25.07.2008	26.08.2010	06.11.2015	Yes
Vyndaqel	tafamidis	EMEA/H/C/002294	N07XX08	yes	> 25.07.2008	16.11.2011	21.10.2015	No
Xadago	safinamide methanesul-fonate	EMEA/H/C/002396	N04B	no	> 25.07.2008	24.02.2015	06.11.2015	No
Xalkori	crizotinib	EMEA/H/C/002489	L01XE16	no	> 25.07.2008	23.10.2012	08.06.2015	No

Medicine Name	Active Substance	Product Number	ATC Code	Is Orphan	Start of Procedure Date	Authorisation Date	SmPC Date	Paediatric Indication
Xaluprine (previously Mercaptopurine Nova Laboratories)	6-mercaptopurine mono-hydrate	EMEA/H/C/002022	L01BB02	yes	> 25.07.2008	09.03.2012	09.12.2014	Yes
Xtandi	enzalutamide	EMEA/H/C/002639	L02BB04	no	> 25.07.2008	21.06.2013	29.10.2015	No
Xultophy	insulin degludec / lirag-lutide	EMEA/H/C/002647	A10	no	> 25.07.2008	18.09.2014	20.08.2015	No
Xydalba	dalbavancin hcl	EMEA/H/C/002840	J01XA04	no	> 25.07.2008	19.02.2015	13.05.2015	No
Yellox	bromfenac sodium sesqui-hydrate	EMEA/H/C/001198	S01BC11	no	> 25.07.2008	18.05.2011	13.03.2015	No
Yervoy	ipilimumab	EMEA/H/C/002213	L01XC11	no	> 25.07.2008	13.07.2011	26.08.2015	No
Zaltrap	aflibercept	EMEA/H/C/002532	L01XX44	no	> 25.07.2008	01.02.2013	07.10.2015	No
Zelboraf	vemurafenib	EMEA/H/C/002409	L01XE15	no	> 25.07.2008	17.02.2012	03.06.2015	No
Zinforo	ceftaroline fosamil	EMEA/H/C/002252	J01DI02	no	> 25.07.2008	23.08.2012	05.11.2015	No
Zoely	nomegestrol acetate / estradiol	EMEA/H/C/001213	G03AA14	no	> 25.07.2008	27.07.2011	29.07.2015	No
Zontivity	vorapaxar sulfate	EMEA/H/C/002814	B01	no	> 25.07.2008	19.01.2015	02.03.2015	No
Zutectra	human hepatitis-B immu-noglobulin	EMEA/H/C/001089	J06BB04	no	19.11.2008	30.11.2009	13.03.2015	No
Zyclara	imiquimod	EMEA/H/C/002387	D06BB10	no	> 25.07.2008	23.08.2012	14.10.2015	No
Zydelig	idelalisib	EMEA/H/C/003843	L01XX47	no	> 25.07.2008	18.09.2014	11.08.2015	No
Zykadia	ceritinib	EMEA/H/C/003819	L01XE	no	> 25.07.2008	06.05.2015	28.09.2015	No
Zytiga	abiraterone acetate	EMEA/H/C/002321	L02BX03	no	> 25.07.2008	05.09.2011	14.08.2015	No

Annex II: Detailed results of the EU SmPC assessment

Table 13: Datasets corresponding to the assessment of medicinal product without paediatric indication

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
Abilify Maintena	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Adasuve	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Deferral	12-18	Indication 1
Adasuve	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Deferral	10-18	Indication 2
Adasuve	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Waiver	0-10	Indication 2
Adasuve	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Waiver	0-12	Indication 1
Adasuve	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver+Deferral	see 5.1	Indication 1
Adasuve	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver+Deferral	see 5.1	Indication 2
Adcetris	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Adcetris	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Adcetris	NA	5.3 Preclinical safety data	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Adempas	NA	4.2 Posology and method of administration	Scenario 3a – Should not be used	0-18	Deferral	one or more subsets	NA
Adempas	NA	5.2 Pharmacokinetic properties	Scenario 3a – Should not be used	0-18	Deferral	one or more subsets	NA
Adempas	NA	5.3 Preclinical safety data	Scenario 3a – Should not be used	0-18	Deferral	one or more subsets	NA
Adempas	NA	4.4 Special warnings and precautions for use	Scenario 3a – Should not be used	0-18	Deferral	one or more subsets	NA
Adjupanrix	NA	5.1 Pharmacodynamic properties - Studies + W/D	Scenario 2b – Limited data	3-9	Deferral	one or more subsets	NA
Adjupanrix	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	3-9	Deferral	one or more subsets	NA
Adjupanrix	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-3	Deferral	one or more subsets	NA
Adjupanrix	NA	4.2 Posology and method of administration	Scenario 2a – No data	9-18	Deferral	one or more subsets	NA
Adjupanrix	NA	4.4 Special warnings and precautions for use	Scenario 2b – Limited data	3-9	Deferral	one or more subsets	NA
Adjupanrix	NA	4.8 Undesirable effects	Scenario 2b – Limited data	3-9	Deferral	one or more subsets	NA

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
Aflunov	NA	5.1 Pharmacodynamic properties - Studies + W/D	Scenario 2b – Limited data	0,5-18	Deferral	one or more subsets	NA
Aflunov	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-0,5	Deferral	one or more subsets	NA
Aflunov	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0,5-18	Deferral	one or more subsets	NA
Aflunov	NA	4.8 Undesirable effects	Scenario 2b – Limited data	0,5-18	Deferral	one or more subsets	NA
Akynzeo	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Ameluz	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Amyvid	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Anoro	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Arzerra	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Aubagio	NA	4.2 Posology and method of administration	Scenario 2a – No data	10-18	Deferral	10-18	NA
Aubagio	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-10	Waiver	0-10	NA
Benlysta	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Betmiga	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Bosulif	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Brilique	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Brimica Genuair	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Brinavess	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Brintellix	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Waiver	0-7	NA
Brintellix	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Deferral	7-18	NA
Brintellix	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver+Deferral	see 5.1	NA
Brintellix	NA	5.3 Preclinical safety data	Scenario 2a – No data	0-18	Waiver+Deferral	see 5.1	NA
Brintellix	NA	4.4 Special warnings and precautions for use	Scenario 2a – No data	0-18	Waiver+Deferral	see 5.1	NA
Bronchitol	NA	5.1 Pharmacodynamic properties - Studies	Scenario 2b – Limited data	6-18	NA		NA
Bronchitol	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	6-18	NA		NA
Bronchitol	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-6	NA		NA
Bronchitol	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	6-18	NA		NA
Bronchitol	NA	4.8 Undesirable effects	Scenario 2b – Limited data	6-18	NA		NA
Bydureon	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Bydureon	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	12-16	Deferral	one or more subsets	NA
Caprelsa	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Cerdelga	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Waiver	0-18	Indication 2
Cerdelga	NA	5.1 Pharmacodynamic properties -	Scenario 2a – No data	0-18	Deferral	2-18	Indication 1

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
		Waiver/Deferral					
Cerdelga	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Deferral	2-18	Indication 3
Cerdelga	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver+Deferral	see 5.1	Indication 3
Cerdelga	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver+Deferral	see 5.1	Indication 2
Cerdelga	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver+Deferral	see 5.1	Indication 1
Cholib	NA	4.2 Posology and method of administration	Scenario 3b – Contraindicated	0-18	Waiver	0-18	NA
Cholib	NA	4.3 Contraindications	Scenario 3b – Contraindicated	0-18	Waiver	0-18	NA
Clopidogrel/Acetyl salicylic acid Teva	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Cometriq	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Constella	NA	4.2 Posology and method of administration	Scenario 3a – Should not be used	0-18	Deferral	one or more subsets	NA
Constella	NA	4.4 Special warnings and precautions for use	Scenario 3a – Should not be used	0-18	Deferral	one or more subsets	NA
Cosentyx	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Waiver	0-6	NA
Cosentyx	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Deferral	6-18	NA
Cosentyx	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver+Deferral	see 5.1	NA
Cuprymina	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 3a – Should not be used	0-18	Waiver	0-18	NA
Cuprymina	NA	4.2 Posology and method of administration	Scenario 3a – Should not be used	0-18	Waiver	0-18	NA
Cyramza	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Dacogen	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Daklinza	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Daklinza	NA	4.4 Special warnings and precautions for use	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Daxas	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Deltyba	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Dexdor	NA	5.1 Pharmacodynamic properties - Studies	Scenario 2b – Limited data	0,083-18	NA		NA
Dexdor	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	NA		NA
Dexdor	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	0,083-18	NA		NA
Dexdor	NA	4.8 Undesirable effects	Scenario 2b – Limited data	0,083-18	NA		NA
Dificlir	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Duaklir Genuair	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Duavive	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
DuoCover	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
DuoPlavin	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
DuoResp Spiromax	NA	5.1 Pharmacodynamic properties - Studies	Scenario 2b – Limited data	6-17	NA		NA
DuoResp Spiromax	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	NA		NA
DuoResp Spiromax	NA	4.8 Undesirable effects	Scenario 2b – Limited data	0-18	NA		NA
Edarbi	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Edurant	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Edurant	NA	5.2 Pharmacokinetic properties	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Eklira Genuair	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Eliquis	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Elonva	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Deferral	one or more subsets	NA
Entyvio	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Enurev Breezhaler	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Envarsus	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	NA		NA
Eperzan	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Erivedge	NA	4.2 Posology and method of administration	Scenario 3a – Should not be used	0-18	Waiver	0-18	NA
Erivedge	NA	5.3 Preclinical safety data	Scenario 3a – Should not be used	0-18	Waiver	0-18	NA
Erivedge	NA	4.4 Special warnings and precautions for use	Scenario 3a – Should not be used	0-18	Waiver	0-18	NA
Esbriet	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Esmya	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Evarrest	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Eviplera	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Eviplera	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	0,33-18	Deferral	one or more subsets	NA
Eviplera	NA	4.8 Undesirable effects	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Evotaz	NA	4.2 Posology and method of administration	Scenario 3a – Should not be used	0-0,25	Deferral	0-18	NA
Evotaz	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0,25-18	Deferral	0-18	NA
Evotaz	NA	4.8 Undesirable effects	Scenario 2b – Limited data	0,25-18	Deferral	0-18	NA
Exforge HCT	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Exviera	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Eylea	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
Fampyra	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Foclivia	NA	5.1 Pharmacodynamic properties - Studies + W/D	Scenario 2b – Limited data	0,5-18	Deferral	one or more subsets	NA
Foclivia	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-0,5	Deferral	one or more subsets	NA
Foclivia	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0,5-18	Deferral	one or more subsets	NA
Foclivia	NA	4.8 Undesirable effects	Scenario 2b – Limited data	0,5-18	Deferral	one or more subsets	NA
Fortacin	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Forxiga	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Gazyvaro	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Gilenya	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Gilenya	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	11-18	Deferral	one or more subsets	NA
Giotrif	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Glybera	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Halaven	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Harvoni	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Harvoni	NA	4.4 Special warnings and precautions for use	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Hetlioz	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Hirobriz Breezhaler	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Holoclar	NA	5.1 Pharmacodynamic properties - Studies + W/D	Scenario 2b – Limited data	13-18	Deferral	one or more subsets	NA
Holoclar	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Holoclar	NA	4.8 Undesirable effects	Scenario 2b – Limited data	8-18	Deferral	one or more subsets	NA
HyQvia	NA	5.1 Pharmacodynamic properties - Studies + W/D	Scenario 2b – Limited data	4-16	Deferral	one or more subsets	NA
HyQvia	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
HyQvia	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	4-16	Deferral	one or more subsets	NA
HyQvia	NA	4.8 Undesirable effects	Scenario 2b – Limited data	4-16	Deferral	one or more subsets	NA
Iclusig	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Waiver	0-1	Indication 1
Iclusig	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Deferral	1-18	Indication 2
Iclusig	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Waiver	0-1	Indication 2
Iclusig	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Deferral	1-18	Indication 1
Iclusig	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver+Deferral	see 5.1	Indication 1

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
Iclusig	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver+Deferral	see 5.1	Indication 2
Ikervis	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Imbruvica	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Imnovid	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Imvanex	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	0-18	NA
Incivo	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Incresync	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Incruse	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Inlyta	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Invokana	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Izba	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	NA		NA
Jakavi	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Jardiance	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Jentadueto	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Jetrea	NA	5.1 Pharmacodynamic properties - Studies	Scenario 2b – Limited data	0-16	NA		Indication 2
Jetrea	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	Indication 1
Jevtana	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Kadcyla	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Kengrexal	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Keytruda	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Komboglyze	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Krystexxa	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Latuda	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Latuda	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	6-17	Deferral	one or more subsets	NA
Laventair	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Lemtrada	NA	4.2 Posology and method of administration	Scenario 2a – No data	10-18	Deferral	10-18	NA
Lemtrada	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-10	Waiver	0-10	NA
Lenvima	NA	4.2 Posology and method of administration	Scenario 2a – No data	2-18	Deferral	one or more subsets	NA
Lenvima	NA	4.2 Posology and method of administration	Scenario 3a – Should not be used	0-2	Deferral	one or more subsets	NA
Lenvima	NA	5.3 Preclinical safety data	Scenario 3a – Should not be used	0-2	Deferral	one or more subsets	NA
Lixiana	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Lojuxta	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Lonquex	NA	5.1 Pharmacodynamic properties - Studies	Scenario 2b – Limited data	2-16	NA		Indication 2

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
Lonquex	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Deferral	0-18	Indication 1
Lonquex	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	0-18	Indication 1
Lonquex	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	NA		Indication 2
Lonquex	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	2-18	NA		Indication 2
Lonquex	NA	4.8 Undesirable effects	Scenario 2b – Limited data	0-18	NA		Indication 2
Lymphoseek	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Lynparza	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Lyxumia	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Mekinist	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	Deferral	0-18	NA
Mekinist	NA	5.3 Preclinical safety data	Scenario 2b – Limited data	0-18	Deferral	0-18	NA
Mirvaso	NA	4.2 Posology and method of administration	Scenario 3b – Contraindicated	0-2	Waiver	0-18	NA
Mirvaso	NA	4.2 Posology and method of administration	Scenario 3a – Should not be used	2-18	Waiver	0-18	NA
Mirvaso	NA	4.3 Contraindications	Scenario 3b – Contraindicated	0-2	Waiver	0-18	NA
Mirvaso	NA	4.9 Overdose	Scenario 3b – Contraindicated	0-2	Waiver	0-18	NA
Mirvaso	NA	4.9 Overdose	Scenario 3a – Should not be used	2-18	Waiver	0-18	NA
Moventig	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	0,5-18	NA
Mysimba	NA	4.2 Posology and method of administration	Scenario 3a – Should not be used	0-18	Deferral	one or more subsets	NA
Neuraceq	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Nexium Control	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	NA		NA
NexoBrid	NA	5.1 Pharmacodynamic properties - Studies	Scenario 3a – Should not be used	4-18	Deferral	one or more subsets	NA
NexoBrid	NA	4.2 Posology and method of administration	Scenario 3a – Should not be used	0-18	Deferral	one or more subsets	NA
NexoBrid	NA	4.8 Undesirable effects	Scenario 3a – Should not be used	4-18	Deferral	one or more subsets	NA
Nuedexta	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Nulojix	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Ofev	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Olysio	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Deferral	3-18	NA
Olysio	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	3-18	NA
Onbrez Breezhaler	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Opdivo	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	0-18	NA

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
Opsumit	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Orbactiv	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Oslif Breezhaler	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Otezla	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	NA		NA
Ozurdex	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	Indication 1
Ozurdex	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	NA		Indication 2
Perjeta	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Picato	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Pixuvri	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Deferral	0,5-18	NA
Pixuvri	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Waiver	0-0,5	NA
Pixuvri	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver+Deferral	see 5.1	NA
Plegridy	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Plenadren	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	NA		NA
Pravafenix	NA	4.2 Posology and method of administration	Scenario 3b – Contraindicated	0-18	Waiver	0-18	NA
Pravafenix	NA	4.3 Contraindications	Scenario 3b – Contraindicated	0-18	Waiver	0-18	NA
Prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) Novartis Vaccines and Diagnostics	NA	5.1 Pharmacodynamic properties - Studies + W/D	Scenario 2b – Limited data	0,5-18	Deferral	one or more subsets	NA
Prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) Novartis Vaccines and Diagnostics	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0,5-18	Deferral	one or more subsets	NA
Prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted)	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-0,5	Deferral	one or more subsets	NA

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
Novartis Vaccines and Diagnostics							
Prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) Novartis Vaccines and Diagnostics	NA	4.8 Undesirable effects	Scenario 2b – Limited data	0,5-18	Deferral	one or more subsets	NA
Prolia	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2b – Limited data	0-18	Waiver	0-2	Indication 2
Prolia	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2b – Limited data	0-18	Waiver	0-18	Indication 1
Prolia	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	Waiver	see 5.1	Indication 1
Prolia	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	Waiver	see 5.1	Indication 2
Prolia	NA	5.3 Preclinical safety data	Scenario 2b – Limited data	0-18	Waiver	see 5.1	Indication 1
Prolia	NA	5.3 Preclinical safety data	Scenario 2b – Limited data	0-18	Waiver	see 5.1	Indication 2
Quinsair	NA	5.1 Pharmacodynamic properties - Studies + W/D	Scenario 2b – Limited data	6-18	Deferral	one or more subsets	NA
Quinsair	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Quinsair	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	6-17	Deferral	one or more subsets	NA
Quinsair	NA	5.3 Preclinical safety data	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Quinsair	NA	4.8 Undesirable effects	Scenario 2b – Limited data	6-18	Deferral	one or more subsets	NA
Rapiscan	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Raplixa	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Rasilamlo	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	6-18	Waiver	0-18	NA
Rasilamlo	NA	4.2 Posology and method of administration	Scenario 3a – Should not be used	2-6	Waiver	0-18	NA
Rasilamlo	NA	4.2 Posology and method of administration	Scenario 3b – Contraindicated	0-2	Waiver	0-18	NA
Rasilamlo	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	6-18	Waiver	0-18	NA
Rasilamlo	NA	5.2 Pharmacokinetic properties	Scenario 3b – Contraindicated	0-2	Waiver	0-18	NA
Rasilamlo	NA	5.2 Pharmacokinetic properties	Scenario 3a – Should not be used	2-6	Waiver	0-18	NA
Rasilamlo	NA	4.3 Contraindications	Scenario 3b – Contraindicated	0-2	Waiver	0-18	NA
Rasilamlo	NA	5.3 Preclinical safety data	Scenario 3b – Contraindicated	0-2	Waiver	0-18	NA
Rasilamlo	NA	5.3 Preclinical safety data	Scenario 3a – Should not be used	2-6	Waiver	0-18	NA
Rasilamlo	NA	4.4 Special warnings and precautions for use	Scenario 3b – Contraindicated	0-2	Waiver	0-18	NA

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
Rasilamlo	NA	4.4 Special warnings and precautions for use	Scenario 3a – Should not be used	0-2	Waiver	0-18	NA
Rasilamlo	NA	4.8 Undesirable effects	Scenario 2b – Limited data	6-18	Waiver	0-18	NA
Revestive	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Revolade	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Rezolsta	NA	4.2 Posology and method of administration	Scenario 3a – Should not be used	0-3	Deferral	one or more subsets	NA
Rezolsta	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	3-17	Deferral	one or more subsets	NA
Rezolsta	NA	5.3 Preclinical safety data	Scenario 2b – Limited data	3-17	Deferral	one or more subsets	NA
Rezolsta	NA	5.3 Preclinical safety data	Scenario 3a – Should not be used	0-3	Deferral	one or more subsets	NA
Rezolsta	NA	4.4 Special warnings and precautions for use	Scenario 2b – Limited data	3-17	Deferral	one or more subsets	NA
Rezolsta	NA	4.4 Special warnings and precautions for use	Scenario 3a – Should not be used	0-3	Deferral	one or more subsets	NA
Ruconest	NA	5.1 Pharmacodynamic properties - Studies + W/D	Scenario 2b – Limited data	13-18	Deferral	one or more subsets	NA
Ruconest	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-12	Deferral	one or more subsets	NA
Ruconest	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-12	Deferral	one or more subsets	NA
Ruconest	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	13-18	Deferral	one or more subsets	NA
Ryzodeg	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2b – Limited data	0-18	Deferral	1-18	Indication 1
Ryzodeg	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Waiver	0-1	Indication 1
Ryzodeg	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Waiver	0-18	Indication 2
Ryzodeg	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver+Deferral	see 5.1	Indication 2
Ryzodeg	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	Waiver+Deferral	see 5.1	Indication 1
Ryzodeg	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	6-18	Waiver+Deferral	see 5.1	Indication 1
Ryzodeg	NA	4.8 Undesirable effects	Scenario 2b – Limited data	6-18	Waiver+Deferral	see 5.1	Indication 1
Sancuso	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	NA		NA
Saxenda	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Scenesse	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Scenesse	NA	4.4 Special warnings and precautions for use	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Scintimun	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	NA		NA
Seebri Breezhaler	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Selincro	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Senshio	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
Signifor	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Silodyx	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Simbrinza	NA	4.2 Posology and method of administration	Scenario 3b – Contraindicated	0-2	Waiver	0-18	NA
Simbrinza	NA	4.2 Posology and method of administration	Scenario 2a – No data	2-18	Waiver	0-18	NA
Simbrinza	NA	4.3 Contraindications	Scenario 3b – Contraindicated	0-2	Waiver	0-18	NA
Simbrinza	NA	4.4 Special warnings and precautions for use	Scenario 3b – Contraindicated	0-2	Waiver	0-18	NA
Simbrinza	NA	4.4 Special warnings and precautions for use	Scenario 2a – No data	2-18	Waiver	0-18	NA
Simbrinza	NA	4.9 Overdose	Scenario 2a – No data	0-18	Waiver	0-18	NA
Sirturo	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Sivextro	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Sivextro	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	12-17	Deferral	one or more subsets	NA
Sovaldi	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Sovaldi	NA	4.4 Special warnings and precautions for use	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Spedra	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Stivarga	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	Indication 2
Stivarga	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	Indication 1
Stribild	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	6-18	Deferral	one or more subsets	NA
Stribild	NA	4.2 Posology and method of administration	Scenario 3a – Should not be used	0-6	Deferral	one or more subsets	NA
Stribild	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	12-18	Deferral	one or more subsets	NA
Stribild	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	0,33-18	Deferral	one or more subsets	NA
Stribild	NA	4.8 Undesirable effects	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Sycrest	NA	5.1 Pharmacodynamic properties - Studies + W/D	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Sycrest	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Sycrest	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	10-18	Deferral	one or more subsets	NA
Sycrest	NA	4.8 Undesirable effects	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Sylvant	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Synjardy	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Tafinlar	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Tafinlar	NA	5.3 Preclinical safety data	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Tecfidera	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-10	Deferral	one or more subsets	NA
Tecfidera	NA	4.2 Posology and method of administration	Scenario 2a – No data	10-18	Deferral	one or more subsets	NA
Teysuno	NA	4.2 Posology and method of administration	Scenario 3a – Should not be used	0-18	Waiver	0-18	NA

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
Topotecan Hospira	NA	5.1 Pharmacodynamic properties - Studies	Scenario 2b – Limited data	0,083-16	NA		NA
Topotecan Hospira	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	NA		NA
Topotecan Hospira	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	2-21	NA		NA
Tovanor Breezhaler	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Trajenta	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Trobalt	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2b – Limited data	0-18	Deferral	0-18	Indication 1
Trobalt	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Waiver	0-2	Indication 2
Trobalt	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Deferral	2-18	Indication 2
Trobalt	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	Deferral	0-18	Indication 1
Trobalt	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	12-18	Deferral	0-18	Indication 1
Trulicity	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Twynsta	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Tybost	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Tybost	NA	4.8 Undesirable effects	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Ultibro Breezhaler	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Ulunar Breezhaler	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Urorec	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Vargatef	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Velphoro	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Vibativ	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Victrelis	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Viekirax	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Vipdomet	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Vipidia	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Vitekta	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Vitekta	NA	4.8 Undesirable effects	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Vizamyl	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Vokanamet	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Votrient	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2b – Limited data	2-18	Deferral	one or more subsets	Indication 2
Votrient	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Waiver	0-18	Indication 1
Votrient	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	2-18	Waiver+Deferral	see 5.1	Indication 2

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
Votrient	NA	4.2 Posology and method of administration	Scenario 3a – Should not be used	0-2	Waiver+Deferral	see 5.1	Indication 2
Votrient	NA	5.3 Preclinical safety data	Scenario 3a – Should not be used	0-2	Waiver+Deferral	see 5.1	Indication 2
Votrient	NA	5.3 Preclinical safety data	Scenario 2b – Limited data	2-18	Waiver+Deferral	see 5.1	Indication 2
Votrient	NA	4.4 Special warnings and precautions for use	Scenario 3a – Should not be used	0-2	Waiver+Deferral	see 5.1	Indication 2
Votrient	NA	4.4 Special warnings and precautions for use	Scenario 2b – Limited data	2-18	Waiver+Deferral	see 5.1	Indication 2
Vyndaqel	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Xadago	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	NA		NA
Xalkori	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Xeplion	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Xiapex	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Xigduo	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Xofigo	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Xtandi	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Xultophy	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0,5-18	Waiver	0-18	NA
Xydalba	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	NA
Xydalba	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	12-16	Deferral	one or more subsets	NA
Yellox	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Yervoy	NA	4.2 Posology and method of administration	Scenario 3a – Should not be used	0-18	Deferral	one or more subsets	NA
Yervoy	NA	5.3 Preclinical safety data	Scenario 3a – Should not be used	0-18	Deferral	one or more subsets	NA
Zaltrap	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA
Zelboraf	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	NA		NA
Zinforo	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	0-18	NA
Zoely	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	0-18	NA		NA
Zoely	NA	4.4 Special warnings and precautions for use	Scenario 2b – Limited data	0-18	NA		NA
Zontivity	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Zutectra	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	NA		NA
Zyclara	NA	5.1 Pharmacodynamic properties	Scenario 2a – No data	0-18	NA		NA
Zyclara	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	NA		NA
Zydelig	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Deferral	one or more subsets	NA
Zykadia	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	NA
Zytiga	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	NA

Table 14: Datasets corresponding to the assessment of medicinal product with paediatric indication

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
Bexsero	NA	4.1 Therapeutic indications	Scenario 1c - Paediatric focussed indication	0,167-18	Deferral	one or more subsets	NA
Buccolam	NA	4.1 Therapeutic indications	Scenario 1d - Paediatric only indication	0,25-18	Waiver	0-0,25	NA
Cinryze	NA	4.1 Therapeutic indications	Scenario 1a - Adult focussed indication	12-18	Deferral	one or more subsets	Indication 1
Cinryze	NA	4.1 Therapeutic indications	Scenario 1a - Adult focussed indication	12-18	Deferral	one or more subsets	Indication 2
Cinryze	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-12	Deferral	one or more subsets	Indication 1
Cinryze	NA	4.2 Posology and method of administration	Scenario 1a - Adult focussed indication	12-18	Deferral	one or more subsets	Indication 1
Cinryze	NA	4.2 Posology and method of administration	Scenario 1a - Adult focussed indication	12-18	Deferral	one or more subsets	Indication 2
Cinryze	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-12	Deferral	one or more subsets	Indication 2
Cinryze	NA	4.4 Special warnings and precautions for use	Scenario 1a - Adult focussed indication	12-18	Deferral	one or more subsets	Indication 1
Cinryze	NA	4.4 Special warnings and precautions for use	Scenario 1a - Adult focussed indication	12-18	Deferral	one or more subsets	Indication 2
Cinryze	NA	4.8 Undesirable effects	Scenario 2b – Limited data	2-12	Deferral	one or more subsets	Indication 2
Cinryze	NA	4.8 Undesirable effects	Scenario 2b – Limited data	2-12	Deferral	one or more subsets	Indication 1
Cinryze	NA	4.8 Undesirable effects	Scenario 1a - Adult focussed indication	12-18	Deferral	one or more subsets	Indication 2
Cinryze	NA	4.8 Undesirable effects	Scenario 1a - Adult focussed indication	12-18	Deferral	one or more subsets	Indication 1
Cinryze	NA	5.1 Pharmacodynamic properties - Studies + W/D	Scenario 1a - Adult focussed indication	12-18	Deferral	one or more subsets	Indication 2
Cinryze	NA	5.1 Pharmacodynamic properties - Studies + W/D	Scenario 1a - Adult focussed indication	12-18	Deferral	one or more subsets	Indication 1
Cinryze	NA	5.1 Pharmacodynamic properties - Studies + W/D	Scenario 2b – Limited data	2-12	Deferral	one or more subsets	Indication 1
Cinryze	NA	5.1 Pharmacodynamic properties - Studies + W/D	Scenario 2b – Limited data	2-12	Deferral	one or more subsets	Indication 2
Cinryze	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Deferral	one or more subsets	Indication 3
Cinryze	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	2-12	Deferral	one or more subsets	Indication 1
Cinryze	NA	5.2 Pharmacokinetic properties	Scenario 2b – Limited data	2-12	Deferral	one or more subsets	Indication 2
Cinryze	NA	5.2 Pharmacokinetic properties	Scenario 1a - Adult focussed indication	12-18	Deferral	one or more subsets	Indication 2
Cinryze	NA	5.2 Pharmacokinetic properties	Scenario 1a - Adult focussed	12-18	Deferral	one or more subsets	Indication 1

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
			indication				
Colobreathe	NA	4.1 Therapeutic indications	Scenario 1b – Paediatric + Adult indication	6-18	Deferral	one or more subsets	NA
Colobreathe	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-6	Deferral	one or more subsets	NA
Colobreathe	NA	4.2 Posology and method of administration	Scenario 1b – Paediatric + Adult indication	6-18	Deferral	one or more subsets	NA
Colobreathe	NA	4.8 Undesirable effects	Scenario 1b – Paediatric + Adult indication	6-18	Deferral	one or more subsets	NA
Colobreathe	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1b – Paediatric + Adult indication	6-18	Deferral	one or more subsets	NA
Colobreathe	NA	5.2 Pharmacokinetic properties	Scenario 1b – Paediatric + Adult indication	6-18	Deferral	one or more subsets	NA
Defitelio	NA	4.1 Therapeutic indications	Scenario 1b – Paediatric + Adult indication	0,083-18	NA		NA
Defitelio	NA	4.2 Posology and method of administration	Scenario 1b – Paediatric + Adult indication	0,083-18	NA		NA
Defitelio	NA	4.4 Special warnings and precautions for use	Scenario 2a – No data	0-0,083	NA		NA
Defitelio	NA	4.8 Undesirable effects	Scenario 1b – Paediatric + Adult indication	0,083-18	NA		NA
Defitelio	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1b – Paediatric + Adult indication	0,083-18	NA		NA
Defitelio	NA	5.3 Preclinical safety data	Scenario 1b – Paediatric + Adult indication	0,083-18	NA		NA
Dutrebis	NA	4.1 Therapeutic indications	Scenario 1a - Adult focussed indication	6-18	NA		NA
Dutrebis	NA	4.2 Posology and method of administration	Scenario 3a – Should not be used	0-6	NA		NA
Dutrebis	NA	4.2 Posology and method of administration	Scenario 1a - Adult focussed indication	6-18	NA		NA
Dutrebis	NA	4.8 Undesirable effects	Scenario 1a - Adult focussed indication	6-18	NA		NA
Dutrebis	NA	5.1 Pharmacodynamic properties	Scenario 3a – Should not be used	0-6	NA		NA
Dutrebis	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1a - Adult focussed indication	6-18	NA		NA
Dutrebis	NA	5.2 Pharmacokinetic properties	Scenario 3a – Should not be used	0-6	NA		NA
Dutrebis	NA	5.2 Pharmacokinetic properties	Scenario 1a - Adult focussed indication	6-18	NA		NA
Dutrebis	NA	5.3 Preclinical safety data	Scenario 1a - Adult focussed indication	6-18	NA		NA
Eurartesim	NA	4.1 Therapeutic indications	Scenario 1b – Paediatric +	0,5-18	NA		NA

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
			Adult indication				
Eurartesim	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-0,5	NA		NA
Eurartesim	NA	4.2 Posology and method of administration	Scenario 1b – Paediatric + Adult indication	0,5-18	NA		NA
Eurartesim	NA	4.4 Special warnings and precautions for use	Scenario 1b – Paediatric + Adult indication	0,5-18	NA		NA
Eurartesim	NA	4.5 Interaction with other medicinal products and other forms of interaction	Scenario 1b – Paediatric + Adult indication	0,5-18	NA		NA
Eurartesim	NA	4.8 Undesirable effects	Scenario 1b – Paediatric + Adult indication	0,5-18	NA		NA
Eurartesim	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1b – Paediatric + Adult indication	0,5-18	NA		NA
Eurartesim	NA	5.2 Pharmacokinetic properties	Scenario 1b – Paediatric + Adult indication	0,5-18	NA		NA
Fluenz Tetra	NA	4.1 Therapeutic indications	Scenario 1d - Paediatric only indication	2-18	NA		NA
Fluenz Tetra	NA	4.2 Posology and method of administration	Scenario 3a – Should not be used	0-2	NA		NA
Fycompa	NA	4.1 Therapeutic indications	Scenario 1a - Adult focussed indication	12-18	NA		Indication 1
Fycompa	NA	4.1 Therapeutic indications	Scenario 1a - Adult focussed indication	12-18	NA		Indication 2
Fycompa	NA	4.2 Posology and method of administration	Scenario 1a - Adult focussed indication	12-18	NA		Indication 2
Fycompa	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-12	NA		Indication 1
Fycompa	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-12	NA		Indication 2
Fycompa	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-12	NA		Indication 3
Fycompa	NA	4.2 Posology and method of administration	Scenario 1a - Adult focussed indication	12-18	NA		Indication 1
Fycompa	NA	4.8 Undesirable effects	Scenario 1a - Adult focussed indication	12-18	NA		Indication 1
Fycompa	NA	4.8 Undesirable effects	Scenario 1a - Adult focussed indication	12-18	NA		Indication 2
Fycompa	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1a - Adult focussed indication	12-18	NA		Indication 1
Fycompa	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1a - Adult focussed indication	12-18	NA		Indication 2
Fycompa	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Deferral	one or more subsets	Indication 3
Fycompa	NA	5.2 Pharmacokinetic properties	Scenario 1a - Adult focussed indication	12-18	NA		Indication 1

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
Fycompa	NA	5.2 Pharmacokinetic properties	Scenario 1a - Adult focussed indication	12-18	NA		Indication 2
Gardasil 9	NA	4.1 Therapeutic indications	Scenario 1b – Paediatric + Adult indication	9-18	NA		NA
Gardasil 9	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-9	NA		NA
Granupas	NA	4.1 Therapeutic indications	Scenario 1a or 1b	0,083-18	NA		NA
Granupas	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-0,083	NA		NA
Granupas	NA	4.2 Posology and method of administration	Scenario 1a or 1b	0,083-18	NA		NA
Granupas	NA	4.8 Undesirable effects	Scenario 1a or 1b	0,083-18	NA		NA
Hemangiol	NA	4.1 Therapeutic indications	Scenario 1d - Paediatric only indication	0,104-0,417	NA		NA
Hexacima	NA	4.1 Therapeutic indications	Scenario 1d - Paediatric only indication	0,125-2	NA		NA
Hizentra	NA	4.1 Therapeutic indications	Scenario 1a or 1b	0-18	NA		NA
Hizentra	NA	4.2 Posology and method of administration	Scenario 1a or 1b	0-18	NA		NA
Hizentra	NA	4.4 Special warnings and precautions for use	Scenario 1a or 1b	0-18	NA		NA
Hizentra	NA	4.5 Interaction with other medicinal products and other forms of interaction	Scenario 1a or 1b	0-18	NA		NA
Hizentra	NA	4.8 Undesirable effects	Scenario 1a or 1b	0-18	NA		NA
Hizentra	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1a or 1b	0-18	NA		NA
Hizentra	NA	5.2 Pharmacokinetic properties	Scenario 1a or 1b	0-18	NA		NA
Ilaris	NA	4.1 Therapeutic indications	Scenario 1a or 1b	2-18	Deferral	one or more subsets	Indication 1
Ilaris	NA	4.1 Therapeutic indications	Scenario 1c - Paediatric fo-cussed indication	2-18	Deferral	one or more subsets	Indication 2
Ilaris	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-18	Waiver	0-18	Indication 3
Ilaris	NA	4.2 Posology and method of administration	Scenario 1a or 1b	2-18	Deferral	one or more subsets	Indication 1
Ilaris	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-2	Deferral	one or more subsets	Indication 2
Ilaris	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-2	Deferral	one or more subsets	Indication 1
Ilaris	NA	4.8 Undesirable effects	Scenario 1a or 1b	2-18	Deferral	one or more subsets	Indication 1
Ilaris	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1a or 1b	2-18	Deferral	one or more subsets	Indication 1
Ilaris	NA	5.2 Pharmacokinetic properties	Scenario 1a or 1b	2-18	Deferral	one or more subsets	Indication 1
Kalydeco	Kalydeco 150 mg film-coated tablets	4.1 Therapeutic indications	Scenario 1a - Adult focussed indication	6-18	Deferral	one or more subsets	Indication 1
Kalydeco	Kalydeco 50 mg granules in sachet Kalydeco 75 mg	4.1 Therapeutic indications	Scenario 1a - Adult focussed indication	2-18	Deferral	one or more subsets	Indication 1

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
	granules in sachet						
Kalydeco	Kalydeco 150 mg film-coated tablets	4.2 Posology and method of administration	Scenario 2a – No data	0-6	Deferral	one or more subsets	Indication 1
Kalydeco	Kalydeco 50 mg granules in sachet Kalydeco 75 mg granules in sachet	4.2 Posology and method of administration	Scenario 1a - Adult focussed indication	2-18	Deferral	one or more subsets	Indication 1
Kalydeco	Kalydeco 50 mg granules in sachet Kalydeco 75 mg granules in sachet	4.2 Posology and method of administration	Scenario 2a – No data	0-2	Deferral	one or more subsets	Indication 1
Kalydeco	Kalydeco all dosage forms	4.2 Posology and method of administration	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	Indication 2
Kalydeco	Kalydeco 150 mg film-coated tablets	4.2 Posology and method of administration	Scenario 1a - Adult focussed indication	6-18	Deferral	one or more subsets	Indication 1
Kalydeco	Kalydeco 50 mg granules in sachet Kalydeco 75 mg granules in sachet	4.4 Special warnings and precautions for use	Scenario 1a - Adult focussed indication	2-18	Deferral	one or more subsets	Indication 1
Kalydeco	Kalydeco 150 mg film-coated tablets	4.4 Special warnings and precautions for use	Scenario 1a - Adult focussed indication	6-18	Deferral	one or more subsets	Indication 1
Kalydeco	Kalydeco all dosage forms	4.4 Special warnings and precautions for use	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	Indication 2
Kalydeco	Kalydeco all dosage forms	4.8 Undesirable effects	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	Indication 2
Kalydeco	Kalydeco 50 mg granules in sachet Kalydeco 75 mg granules in sachet	4.8 Undesirable effects	Scenario 1a - Adult focussed indication	2-18	Deferral	one or more subsets	Indication 1
Kalydeco	Kalydeco 150	4.8 Undesirable effects	Scenario 1a - Adult focussed	6-18	Deferral	one or more subsets	Indication 1

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
	mg film-coated tablets		indication				
Kalydeco	Kalydeco 50 mg granules in sachet Kalydeco 75 mg granules in sachet	5.1 Pharmacodynamic properties - Studies	Scenario 1a - Adult focussed indication	2-18	Deferral	one or more subsets	Indication 1
Kalydeco	Kalydeco 150 mg film-coated tablets	5.1 Pharmacodynamic properties - Studies	Scenario 1a - Adult focussed indication	6-18	Deferral	one or more subsets	Indication 1
Kalydeco	Kalydeco all dosage forms	5.1 Pharmacodynamic properties - Studies	Scenario 2b – Limited data	0-18	Deferral	one or more subsets	Indication 2
Kalydeco	Kalydeco 150 mg film-coated tablets	5.2 Pharmacokinetic properties	Scenario 1a - Adult focussed indication	6-18	Deferral	one or more subsets	Indication 1
Kalydeco	Kalydeco 50 mg granules in sachet Kalydeco 75 mg granules in sachet	5.2 Pharmacokinetic properties	Scenario 1a - Adult focussed indication	2-18	Deferral	one or more subsets	Indication 1
Ketoconazole HRA	NA	4.1 Therapeutic indications	Scenario 1a - Adult focussed indication	12-18	NA		NA
Ketoconazole HRA	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-12	NA		NA
Ketoconazole HRA	NA	4.2 Posology and method of administration	Scenario 1a - Adult focussed indication	12-18	NA		NA
Ketoconazole HRA	NA	4.8 Undesirable effects	Scenario 1a - Adult focussed indication	12-18	NA		NA
Ketoconazole HRA	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1a - Adult focussed indication	12-18	NA		NA
Ketoconazole HRA	NA	5.2 Pharmacokinetic properties	Scenario 1a - Adult focussed indication	12-18	NA		NA
Menveo	NA	4.1 Therapeutic indications	Scenario 1c - Paediatric focussed indication	2-18	NA		NA
Menveo	NA	4.2 Posology and method of administration	Scenario 2b – Limited data	0-2	NA		NA
Menveo	NA	5.1 Pharmacodynamic properties - Studies	Scenario 2b – Limited data	0,125-2	NA		NA
Nimenrix	NA	4.1 Therapeutic indications	Scenario 1c - Paediatric focussed indication	1-18	Deferral	one or more subsets	NA
Nimenrix	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-1	Deferral	one or more subsets	NA
NovoEight	NA	4.1 Therapeutic indications	Scenario 1b – Paediatric + Adult indication	0-18	NA		NA

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
NovoEight	NA	4.2 Posology and method of administration	Scenario 1b – Paediatric + Adult indication	0-18	NA		NA
NovoEight	NA	4.4 Special warnings and precautions for use	Scenario 1b – Paediatric + Adult indication	0-18	NA		NA
NovoEight	NA	4.8 Undesirable effects	Scenario 1b – Paediatric + Adult indication	0-18	NA		NA
NovoEight	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1b – Paediatric + Adult indication	0-18	NA		NA
NovoEight	NA	5.2 Pharmacokinetic properties	Scenario 1b – Paediatric + Adult indication	0-18	NA		NA
NovoThirteen	NA	4.1 Therapeutic indications	Scenario 1b – Paediatric + Adult indication	0-18	NA		NA
NovoThirteen	NA	4.2 Posology and method of administration	Scenario 1b – Paediatric + Adult indication	0-18	NA		NA
NovoThirteen	NA	4.8 Undesirable effects	Scenario 1b – Paediatric + Adult indication	0-18	NA		NA
NovoThirteen	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1b – Paediatric + Adult indication	0-18	NA		NA
NovoThirteen	NA	5.2 Pharmacokinetic properties	Scenario 1b – Paediatric + Adult indication	0-18	NA		NA
Nuwiq	NA	4.1 Therapeutic indications	Scenario 1b – Paediatric + Adult indication	0-18	Deferral	one or more subsets	NA
Nuwiq	NA	4.2 Posology and method of administration	Scenario 1b – Paediatric + Adult indication	0-18	Deferral	one or more subsets	NA
Nuwiq	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-2	Deferral	one or more subsets	NA
Nuwiq	NA	4.4 Special warnings and precautions for use	Scenario 1b – Paediatric + Adult indication	0-18	Deferral	one or more subsets	NA
Nuwiq	NA	4.8 Undesirable effects	Scenario 1b – Paediatric + Adult indication	0-18	Deferral	one or more subsets	NA
Nuwiq	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1b – Paediatric + Adult indication	0-18	Deferral	one or more subsets	NA
Nuwiq	NA	5.2 Pharmacokinetic properties	Scenario 1b – Paediatric + Adult indication	0-18	Deferral	one or more subsets	NA
Orphacol	NA	4.1 Therapeutic indications	Scenario 1c - Paediatric focussed indication	0,083-18	NA		NA
Pandemic Influenza Vaccine H5N1 Baxter AG	NA	4.1 Therapeutic indications	Scenario 1a - Adult focussed indication	0,5-18	NA		NA
Pandemic Influenza Vaccine H5N1 Baxter AG	NA	4.2 Posology and method of administration	Scenario 1a - Adult focussed indication	0,5-18	NA		NA
Pandemic Influen-	NA	4.8 Undesirable effects	Scenario 1a - Adult focussed	0,5-18	NA		NA

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
za Vaccine H5N1 Baxter AG			indication				
Pandemic Influenza Vaccine H5N1 Baxter AG	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1a - Adult focussed indication	0,5-18	NA		NA
Pheburane	NA	4.1 Therapeutic indications	Scenario 1a or 1b	0-18	NA		NA
Pheburane	NA	4.2 Posology and method of administration	Scenario 1a or 1b	0-18	NA		NA
Pheburane	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1a or 1b	0-18	NA		NA
Prevenar 13	NA	4.1 Therapeutic indications	Scenario 1b – Paediatric + Adult indication	0,125-18	NA		NA
Prevenar 13	NA	4.2 Posology and method of administration	Scenario 1b – Paediatric + Adult indication	0,125-18	NA		NA
Prevenar 13	NA	4.4 Special warnings and precautions for use	Scenario 1b – Paediatric + Adult indication	0,125-18	NA		NA
Prevenar 13	NA	4.5 Interaction with other medicinal products and other forms of interaction	Scenario 1b – Paediatric + Adult indication	0,125-18	NA		NA
Prevenar 13	NA	4.8 Undesirable effects	Scenario 1b – Paediatric + Adult indication	0,125-18	NA		NA
Prevenar 13	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1b – Paediatric + Adult indication	0,125-18	NA		NA
Procysbi	NA	4.1 Therapeutic indications	Scenario 1c - Paediatric focussed indication	0-18	NA		NA
Relvar Ellipta	NA	4.1 Therapeutic indications	Scenario 1a or 1b	12-18	Deferral	one or more subsets	Indication 1
Relvar Ellipta	NA	4.2 Posology and method of administration	Scenario 1a or 1b	12-18	Deferral	one or more subsets	Indication 1
Relvar Ellipta	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-12	Waiver	0-18	Indication 2
Relvar Ellipta	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-12	Deferral	one or more subsets	Indication 1
Relvar Ellipta	NA	5.2 Pharmacokinetic properties	Scenario 1a or 1b	12-18	Deferral	one or more subsets	Indication 1
Repatha	NA	4.1 Therapeutic indications	Scenario 1a - Adult focussed indication	12-18	NA		Indication 2
Repatha	NA	4.2 Posology and method of administration	Scenario 1a - Adult focussed indication	12-18	NA		Indication 2
Repatha	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver+Deferral	see 5.1	Indication 1
Repatha	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-12	NA		Indication 2
Repatha	NA	4.8 Undesirable effects	Scenario 1a - Adult focussed indication	12-18	NA		Indication 2
Repatha	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1a - Adult focussed indication	12-18	NA		Indication 2
Repatha	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Waiver	0-18	Indication 1
Repatha	NA	5.1 Pharmacodynamic properties - Waiv-	Scenario 2a – No data	0-18	Deferral	one or more subsets	Indication 1

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
		er/Deferral					
Repatha	NA	5.2 Pharmacokinetic properties	Scenario 1a - Adult focussed indication	12-18	NA		Indication 2
Rixubis	NA	4.1 Therapeutic indications	Scenario 1a or 1b	0-18	NA		Indication 1
Rixubis	NA	4.2 Posology and method of administration	Scenario 1a or 1b	0-18	NA		Indication 1
Rixubis	NA	4.4 Special warnings and precautions for use	Scenario 1a or 1b	0-18	NA		Indication 1
Rixubis	NA	4.8 Undesirable effects	Scenario 1a or 1b	0-18	NA		Indication 1
Rixubis	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1a or 1b	0-18	NA		Indication 1
Rixubis	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Waiver	0-18	Indication 2
Rixubis	NA	5.2 Pharmacokinetic properties	Scenario 1a or 1b	0-18	NA		Indication 1
Somatropin Biopartners	10, 20 mg powder and solvent for prolonged-release suspension for injection	4.1 Therapeutic indications	Scenario 1d - Paediatric only indication	2-18	NA		NA
Somatropin Biopartners	10, 20 mg powder and solvent for prolonged-release suspension for injection	4.2 Posology and method of administration	Scenario 3a – Should not be used	0-2	NA		NA
Tivicay	NA	4.1 Therapeutic indications	Scenario 1a - Adult focussed indication	12-18	Deferral	0,083-12	NA
Tivicay	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-12	Deferral	0,083-12	NA
Tivicay	NA	4.2 Posology and method of administration	Scenario 1a - Adult focussed indication	12-18	NA		NA
Tivicay	NA	4.8 Undesirable effects	Scenario 1a - Adult focussed indication	12-18	NA		NA
Tivicay	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1a - Adult focussed indication	12-18	NA		NA
Tivicay	NA	5.2 Pharmacokinetic properties	Scenario 1a - Adult focussed indication	12-18	NA		NA
Tobi Podhaler	NA	4.1 Therapeutic indications	Scenario 1b – Paediatric + Adult indication	6-18	NA		NA
Tobi Podhaler	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-6	NA		NA
Tobi Podhaler	NA	4.2 Posology and method of administration	Scenario 1b – Paediatric + Adult indication	6-18	NA		NA
Tobi Podhaler	NA	4.4 Special warnings and precautions for use	Scenario 1b – Paediatric + Adult indication	6-18	NA		NA
Tobi Podhaler	NA	4.8 Undesirable effects	Scenario 1b – Paediatric +	6-18	NA		NA

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
			Adult indication				
Tobi Podhaler	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1b – Paediatric + Adult indication	6-18	NA		NA
Tobi Podhaler	NA	5.2 Pharmacokinetic properties	Scenario 1b – Paediatric + Adult indication	6-18	NA		NA
Translarna	NA	4.1 Therapeutic indications	Scenario 1c - Paediatric focussed indication	5-18	Waiver+Deferral	see 5.1	NA
Translarna	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0,5-5	Deferral	0,5-5	NA
Translarna	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-0,5	Waiver	0-0,5	NA
Tresiba	NA	4.1 Therapeutic indications	Scenario 1a - Adult focussed indication	1-18	Waiver	see 5.1	Indication 2
Tresiba	NA	4.1 Therapeutic indications	Scenario 1a - Adult focussed indication	1-18	Waiver	see 5.1	Indication 1
Tresiba	NA	4.2 Posology and method of administration	Scenario 1a - Adult focussed indication	1-18	Waiver	see 5.1	Indication 1
Tresiba	NA	4.2 Posology and method of administration	Scenario 1a - Adult focussed indication	1-18	Waiver	see 5.1	Indication 2
Tresiba	NA	4.8 Undesirable effects	Scenario 1a - Adult focussed indication	1-18	Waiver	see 5.1	Indication 2
Tresiba	NA	4.8 Undesirable effects	Scenario 1a - Adult focussed indication	1-18	Waiver	see 5.1	Indication 1
Tresiba	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1a - Adult focussed indication	1-18	NA		Indication 2
Tresiba	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1a - Adult focussed indication	1-18	NA		Indication 1
Tresiba	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-10	Waiver	0-10	Indication 2
Tresiba	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-1	Waiver	0-1	Indication 1
Tresiba	NA	5.2 Pharmacokinetic properties	Scenario 1a - Adult focussed indication	1-18	Waiver	see 5.1	Indication 1
Tresiba	NA	5.2 Pharmacokinetic properties	Scenario 1a - Adult focussed indication	1-18	Waiver	see 5.1	Indication 2
Triumeq	NA	4.1 Therapeutic indications	Scenario 1a - Adult focussed indication	12-18	NA		NA
Triumeq	NA	4.2 Posology and method of administration	Scenario 1a - Adult focussed indication	12-18	NA		NA
Triumeq	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-12	NA		NA
Triumeq	NA	4.8 Undesirable effects	Scenario 1a - Adult focussed indication	12-18	NA		NA

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
Triumeq	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1a - Adult focussed indication	12-18	NA		NA
Triumeq	NA	5.2 Pharmacokinetic properties	Scenario 1a - Adult focussed indication	12-18	NA		NA
Vantobra	NA	4.1 Therapeutic indications	Scenario 1a or 1b	6-18	NA		NA
Vantobra	NA	4.2 Posology and method of administration	Scenario 1a or 1b	6-18	NA		NA
Vantobra	NA	4.2 Posology and method of administration	Scenario 4 – Not relevant	0-6	NA		NA
Vantobra	NA	4.8 Undesirable effects	Scenario 1a or 1b	6-18	NA		NA
Vepacel	NA	4.1 Therapeutic indications	Scenario 1a - Adult focussed indication	0,5-18	NA		NA
Vepacel	NA	4.2 Posology and method of administration	Scenario 1a - Adult focussed indication	0,5-18	NA		NA
Vepacel	NA	4.8 Undesirable effects	Scenario 1a - Adult focussed indication	0,5-18	NA		NA
Vepacel	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1a - Adult focussed indication	0,5-18	NA		NA
Vimizim	NA	4.1 Therapeutic indications	Scenario 1c - Paediatric focussed indication	0-18	Deferral	one or more subsets	NA
Voncento	NA	4.1 Therapeutic indications	Scenario 1a or 1b	0-18	NA		Indication 1
Voncento	NA	4.1 Therapeutic indications	Scenario 1a or 1b	12-18	Deferral	0-12	Indication 2
Voncento	NA	4.2 Posology and method of administration	Scenario 1a or 1b	12-18	NA		Indication 2
Voncento	NA	4.2 Posology and method of administration	Scenario 1a or 1b	0-18	NA		Indication 1
Voncento	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-12	Deferral	0-12	Indication 2
Voncento	NA	4.4 Special warnings and precautions for use	Scenario 1a or 1b	0-18	NA		Indication 1
Voncento	NA	4.4 Special warnings and precautions for use	Scenario 1a or 1b	12-18	NA		Indication 2
Voncento	NA	4.8 Undesirable effects	Scenario 1a or 1b	12-18	NA		Indication 2
Voncento	NA	4.8 Undesirable effects	Scenario 1a or 1b	0-18	NA		Indication 1
Voncento	NA	5.2 Pharmacokinetic properties	Scenario 1a or 1b	0-18	NA		Indication 1
Voncento	NA	5.2 Pharmacokinetic properties	Scenario 1a or 1b	12-18	NA		Indication 2
Votubia	Votubia 2/3/5 mg dispersible tablets	4.1 Therapeutic indications	Scenario 1c - Paediatric focussed indication	1-18	NA		NA
Votubia	Votubia 2/3/5 mg dispersible tablets	4.2 Posology and method of administration	Scenario 2a – No data	0-1	NA		NA
Vpriv	NA	4.1 Therapeutic indications	Scenario 1a - Adult focussed indication	0-18	Waiver+Deferral	see 5.1	Indication 1
Vpriv	NA	4.2 Posology and method of administration	Scenario 1a - Adult focussed indication	0-18	Waiver+Deferral	see 5.1	Indication 1

Medicine Name	Dosage forms / strengths	Section EU	Scenario	Age range use	Waiver / Deferral	Age range waiver / deferral	Multiple indication
Vpriv	NA	4.8 Undesirable effects	Scenario 1a - Adult focussed indication	0-18	Waiver+Deferral	see 5.1	Indication 1
Vpriv	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1a - Adult focussed indication	0-18	Waiver+Deferral	see 5.1	Indication 1
Vpriv	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 1a - Adult focussed indication	0-18	Deferral	one or more subsets	Indication 1
Vpriv	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Deferral	one or more subsets	Indication 3
Vpriv	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Waiver	0-18	Indication 2
Xaluprine	NA	4.1 Therapeutic indications	Scenario 1a or 1b	2-18	NA		NA
Xaluprine	NA	4.2 Posology and method of administration	Scenario 1a or 1b	2-18	NA		NA
Xaluprine	NA	4.4 Special warnings and precautions for use	Scenario 1a or 1b	2-18	NA		NA
Xgeva	NA	4.1 Therapeutic indications	Scenario 1a - Adult focussed indication	12-18	Waiver	0-12	Indication 2
Xgeva	NA	4.2 Posology and method of administration	Scenario 1a - Adult focussed indication	12-18	Waiver	0-12	Indication 2
Xgeva	NA	4.2 Posology and method of administration	Scenario 2a – No data	0-18	Waiver	0-18	Indication 1
Xgeva	NA	4.8 Undesirable effects	Scenario 1a - Adult focussed indication	12-18	Waiver	0-12	Indication 2
Xgeva	NA	5.1 Pharmacodynamic properties - Studies	Scenario 1a - Adult focussed indication	12-18	Waiver	0-12	Indication 2
Xgeva	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-18	Waiver	0-18	Indication 1
Xgeva	NA	5.1 Pharmacodynamic properties - Waiver/Deferral	Scenario 2a – No data	0-12	Waiver	0-12	Indication 2
Xgeva	NA	5.3 Preclinical safety data	Scenario 1a - Adult focussed indication	12-18	Waiver	0-12	Indication 2

Annex III: Results from the comparison of EU SmPCs and US PIs

Table 15: Results from the comparison of EU SmPCs and US PIs for the individual medicinal products

Medicine Name EU	Active Substance	Paediatric indication	Scenario EU	Age range use EU	Medicine Name US	Scenario US	Age range use US
Defitelio	defibrotide	Yes	Scenario 1b – Paediatric + Adult indication	0,083-18	NA	not registered	NA
Granupas	para-aminosalicylic acid	Yes	Scenario 1a or 1b	0,083-18	PASER	Scenario 1a or 1b	0-18
Kalydeco	ivacaftor	Yes	Scenario 1a - Adult focussed indication	6-18	KALYDECO	Scenario 1a - Adult focussed indication	6-18
Kalydeco	ivacaftor	Yes	Scenario 1a - Adult focussed indication	2-18	KALYDECO	Scenario 1a - Adult focussed indication	2-18
Ketoconazole HRA	ketoconazole	Yes	Scenario 1a - Adult focussed indication	12-18	NA	not registered	NA
Orphacol	cholic acid	Yes	Scenario 1c - Paediatric focussed indication	0,083-18	CHOLBAM	Scenario 1c - Paediatric focussed indication	0,058-18
Procysbi	mercaptamine bitartrate	Yes	Scenario 1c - Paediatric focussed indication	0-18	PROCYSBI	Scenario 1c - Paediatric focussed indication	2-18
Tobi Podhaler	tobramycin	Yes	Scenario 1b – Paediatric + Adult indication	6-18	TOBI Podhaler	Scenario 1a - Adult focussed indication	6-18
Translarna	ataluren	Yes	Scenario 1c - Paediatric focussed indication	5-18	NA	not registered	NA
Vimizim	recombinant human n-acetylgalactosamine-6-sulfatase (rhgalns)	Yes	Scenario 1c - Paediatric focussed indication	0-18	Vimizim	Scenario 1c - Paediatric focussed indication	5-18
Votubia	everolimus	Yes	Scenario 1c - Paediatric focussed indication	1-18	AFINITOR Tablets and AFINITOR®	Scenario 1a - Adult focussed indication	1-18

Medicine Name EU	Active Substance	Paediatric indication	Scenario EU	Age range use EU	Medicine Name US	Scenario US	Age range use US
					DISPERZ		
Vpriv	velaglucerase alfa	Yes	Scenario 1a - Adult focussed indication	0-18	VPRIV	Scenario 1a - Adult focussed indication	4-18
Xaluprine	6-mercaptopurine monohydrate	Yes	Scenario 1a or 1b	2-18	PURIXAN	Scenario 2b – Limited data	0-18
Adcetris	brentuximab vedotin	No	Scenario 2b – Limited data	0-18	ADCETRIS	Scenario 2b – Limited data	0-18
Adempas	riociguat	No	Scenario 3a – Should not be used	0-18	ADEMPAS	Scenario 2a – No data	0-18
Arzerra	ofatumumab	No	Scenario 2a – No data	0-18	ARZERRA	Scenario 2a – No data	0-18
Bosulif	bosutinib (as monohydrate)	No	Scenario 2a – No data	0-18	BOSULIF	Scenario 2a – No data	0-18
Bronchitol	mannitol	No	Scenario 2b – Limited data	6-18	NA	not registered	NA
Bronchitol	mannitol	No	Scenario 2a – No data	0-6	NA	not registered	NA
Cerdelga	eliglustat	No	Scenario 2a – No data	0-18	CERDELGA	Scenario 2a – No data	0-18
Cometriq	cabozantinib	No	Scenario 2a – No data	0-18	COMETRIQ	Scenario 2a – No data	0-18
Cyramza	ramucirumab	No	Scenario 4 – Not relevant	0-18	CYRAMZA	Scenario 2b – Limited data	0-18
Dacogen	decitabine	No	Scenario 2a – No data	0-18	DACOGEN	Scenario 2a – No data	0-18
Deltyba	delamanid	No	Scenario 2a – No data	0-18	NA	not registered	NA
Esbriet	pirfenidone	No	Scenario 4 – Not relevant	0-18	ESBRIET	Scenario 2a – No data	0-18
Gazyvaro	obinutuzumab	No	Scenario 2a – No data	0-18	GAZYVA	Scenario 2a – No data	0-18
Glybera	alipogene tiparvovec	No	Scenario 2a – No data	0-18	NA	not registered	NA
Hetlioz	tasimelteon	No	Scenario 2a – No data	0-18	HETLIOZ	Scenario 2a – No data	0-18
Holoclar	ex vivo expanded autologous human corneal epithelial cells containing stem cells	No	Scenario 2b – Limited data	0-18	NA	not registered	NA
Iclusig	ponatinib	No	Scenario 2a – No data	0-18	ICLUSIG	Scenario 2a – No data	0-18

Medicine Name EU	Active Substance	Paediatric indication	Scenario EU	Age range use EU	Medicine Name US	Scenario US	Age range use US
Imbruvica	ibrutinib	No	Scenario 2a – No data	0-18	IMBRUVICA	Scenario 2a – No data	0-18
Imnovid	pomalidomide	No	Scenario 4 – Not relevant	0-18	POMALYST	Scenario 2a – No data	0-18
Lenvima	lenvatinib mesylate	No	Scenario 2a – No data	2-18	LENVIMA	Scenario 2b – Limited data	0-18
Lenvima	lenvatinib mesylate	No	Scenario 3a – Should not be used	0-2	LENVIMA	Scenario 2b – Limited data	0-18
Lynparza	olaparib	No	Scenario 2a – No data	0-18	LYNPARZA	Scenario 2a – No data	0-18
NexoBrid	concentrate of proteolytic enzymes enriched in bromelain	No	Scenario 3a – Should not be used	0-18	NA	not registered	NA
Ofev	nintedanib	No	Scenario 2a – No data	0-18	OFEV	Scenario 2a – No data	0-18
Opsumit	macitentan	No	Scenario 2a – No data	0-18	OPSUMIT	Scenario 2a – No data	0-18
Plenadren	hydrocortisone	No	Scenario 2a – No data	0-18	NA	not registered	NA
Revestive	teduglutide	No	Scenario 2a – No data	0-18	GATTEX	Scenario 2a – No data	0-18
Scenesse	afamelanotide	No	Scenario 2a – No data	0-18	NA	not registered	NA
Signifor	pasireotide	No	Scenario 2a – No data	0-18	SIGNIFOR	Scenario 2a – No data	0-18
Sirturo	bedaquiline fumarate	No	Scenario 2a – No data	0-18	SIRTURO	Scenario 2a – No data	0-18
Sylvant	siltuximab	No	Scenario 2a – No data	0-18	SYLVANT	Scenario 2a – No data	0-18
Vyndaqel	tafamidis	No	Scenario 4 – Not relevant	0-18	NA	not registered	NA

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Eidesstattliche Versicherung

Hiermit erkläre ich an Eides statt, die Arbeit selbständig verfasst und keine anderen als die angegebenen Hilfsmittel verwendet zu haben.

Ort, Datum	Unterschrift