Periodic report on drugs approved for children under the EU Centralised Procedure

Index

1. Abstract

This is the periodic report prepared by the TEDDY Network on paediatric medicines registered in Europe under the EMA Centralised Procedure from the beginning to October 1995 to October 2020.[i]

2. Introduction

In the pharmaceutical field the main goal is to guarantee that efficacious, high quality and safe medicines are available to European citizens, regardless of income or social status. The proper use of medicines depends on a wide dissemination of relevant information to all the interested stakeholders (regulatory agencies, medical doctors, pharmacists, patient associations, industries, etc).

For many years, a lack of information on drugs continued to affect the paediatric population. It is well known that approved medicines are used in children without proper information on: dosage, potential toxicity, evidence of clinical safety and efficacy at the recommended dosages.

The specific issue of paediatric medicines has been considered by the European Institutions since 1997. For this purpose, a number of initiatives have been developed during the last years, culminating with the entering into force of the European Paediatric Regulation [1] in January 2007.

TEDDY collects and stores in its database EPMD (European Paediatric Medicines Database) data on paediatric medicines registered in Europe under the EMA Centralised Procedure from October 1995. Reports are released regularly; two publications are available [2,3].

The aim of this report is to present the status of paediatric medicines licensed by EMA. An insight on authorisations/variations until 2020.

3. Methodology

3.1. Data collection and storing

The EMA public website represents the source of information. For each new medicine approved, including new Marketing Authorisations (MAs) and variations listed on the EMA website, the European Public Assessment Reports (EPARs) of human medicines are analysed. Information derived by EPARs is collected in a standardised way and stored in TEDDY European Paediatric Medicines Database (EPMD). Data are collected and validated by two researchers. Discrepancies are solved with the support of a supervisor.

3.2. Collected data

EPMD includes a number of information including:

- Year of approval
- Active substance
- Tradename
- Anatomical Therapeutic Chemical (ATC) code - first-level

- Indication and Paediatric Indication
- Ages for which the drug is intended
- Dosages
- Orphan Drug status
- Paediatric trials and studies included in the EPAR at the time of approval.

3.3. Data Analysis

General descriptive statistics analyses are performed on annual basis providing details on: a) year of MA, b) age of population for which the drug is approved, c) ATC code, and d) orphan status. In addition, the database allows to perform other analyses according to specific request.

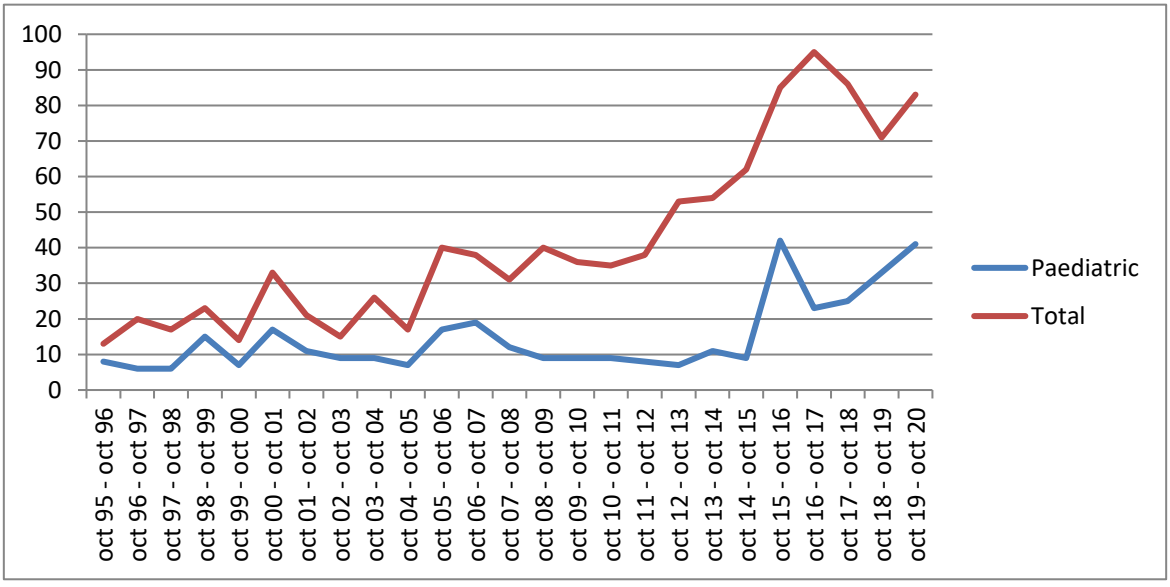
4. Results

4.1. Number and percentage of paediatric medicines

In the period October 1995 – October 2020, 877 active substances (ASs) have been approved by EMA under the Centralised Procedure: 300 of them were paediatric (34%).[1]

Figure 1 reports the number of paediatric medicines and the total of medicines approved by EMA under the centralised procedure. MAs and variations are included. Notwithstanding the increase observed in 2007, the number of paediatric medicines remains low till 2015. A new increase is observed from 2015.

Figure 1 - Medicinal products authorised by EMA divided by year (Oct. 1995 – Oct. 2020)

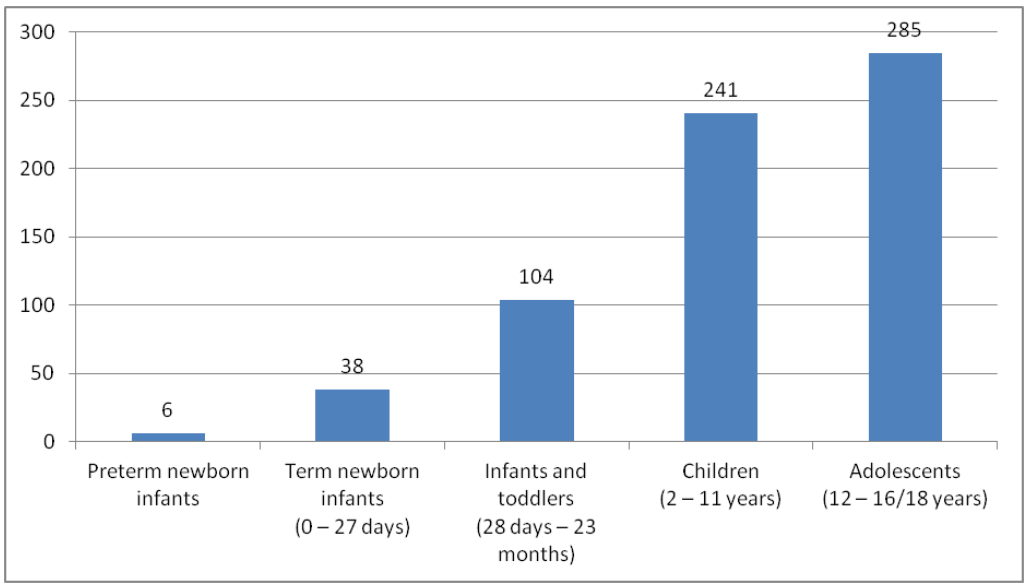


[1] In the first ten years period covered by this report (1995-2005), medicines that included in their documentation (Summary of Product Characteristics – SPC/PL) a paediatric dosages information, but not a paediatric indication, were also considered as paediatric.

4.2. Distribution of paediatric medicines by age

Figure 2 reports the distribution of the paediatric medicines by age for which the drug is approved. It is evident that the lower number of medicines refers to neonates and younger children, while this number increases for older children and is the highest for adolescents.

Figure 2 – Paediatric Medicines: age distribution



4.3. Distribution of paediatric medicines by ATC

Authorised paediatric medicines belong to 14 ATC first-level categories. The percentage of paediatric medicines for each therapeutic area significantly varies among ATC codes: J-ATC (anti-infectives for systemic use) represents the group with the highest ratio on the total of authorised medicines, G-ATC (Genito-urinary system and sex hormones), and C-ATC (Cardiovascular system) the lowest ones. Table 1 provides additional details.

Table 1: EMA Paediatric Medicines by ATC code

	Paediatric/Total	
	N	**%**
A -Alimentary tract and metabolism	49/103	47
B - Blood and blood forming organs	34/72	47
C - Cardiovascular system	5/42	12
D - Dermatologicals	4/11	36
G- Genito-urinary system and sex hormones	2/32	6
H - Systemic hormonal preparations, excluding sex hormones and insulins	5/16	31
J - Anti-infectives for systemic use	85/163	52

	Paediatric/Total	
	N	**%**
L - Antineoplastic and immunomodulating agents	57/213	27
M - Musculo-skeletal system	5/27	18
N - Nervous system	19/72	26
P -Antiparasitic products, insecticides and repellents	1/1	100
R - Respiratory system	12/33	36
S - Sensory organs	6/26	23
V -Various	13/51	25
Not assigned yet	3/15	20
TOTAL	***300/877***	***34%***

4.4. Distribution of paediatric medicines by orphan status

With reference to orphan drugs, it should be noted that out of the 127 orphan drugs authorised by the EMA in the period October 1995 – October 2020 under the OD Regulation rules, 57 were paediatric. Thus, comparing the rate of paediatric medicines between orphan and non-orphan drug groups, a significant difference in favour of paediatric medicines in the orphan drug group is evident (46% and 34%, respectively).

Table 2 – Paediatric orphan drugs and ATC distribution

ATC	Orphan drugs authorised	Paediatric orphan drugs authorised	Percentage
A -Alimentary tract and metabolism	24	19	88
B - Blood and blood forming organs	11	9	91
C - Cardiovascular system	6	1	-
D - Dermatologicals	2	0	-
G- Genito-urinary system and sex hormones	0	0	-
H - Systemic hormonal preparations, excluding sex hormones and insulins	5	0	-
J - Anti-infectives for systemic use	10	5	54
L - Antineoplastic and immunomodulating agents	42	10	26
M - Musculo-skeletal system	3	4	100
N - Nervous system	9	2	45
P -Antiparasitic products, insecticides and repellents	0	0	-
R - Respiratory system	4	3	75
S - Sensory organs	4	2	50
V -Various	2	0	25
Not assigned yet	5	2	50
TOTAL	**127**	**57**	***46%***

5. New paediatric drug from October 2019 to October 2020

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
Clofarabine	L01BB06	Treatment of acute lymphoblastic leukaemia (ALL) in paediatric patients who have relapsed or are refractory after receiving at least two prior regimens and where there is no other treatment option anticipated to result in a durable response. Safety and efficacy have been assessed in studies of patients ≤ 21 years old at initial diagnosis	NO	> 1 year		NO
Miglustat	A16AX06	Miglustat Dipharma is indicated for the treatment of progressive neurological manifestations in adult patients and paediatric patients with Niemann-Pick type C disease	NO	> 4 years		NO
Glucagon	H04AA01	Baqsimi is indicated for the treatment of severe hypoglycaemia in adults, adolescents, and children aged 4 years and over with diabetes mellitus.	NO	> 4 years		YES
Bedaquiline fumarate	J04AK05	SIRTURO is indicated for use as part of an appropriate combination regimen for pulmonary multidrug-resistant tuberculosis (MDR-TB) in adults and adolescent patients (12 years to less than 18 years of age and weighing at least 30 kg) when an effective treatment regimen cannot otherwise be composed for reasons of resistance or tolerability	YES	> 12 years weighing at least 30 kg	12/12/19 (23/01/20): The extension of indication is supported by the Week 24 analysis of Cohort 1 (adolescent subjects aged ≥12 to <18 years) of Study TMC207-C211.	YES
Adalimumab	L04AB04	**Juvenile idiopathic arthritis:** Polyarticular juvenile idiopathic arthritis: Amsparity in combination with methotrexate is indicated for the treatment of active polyarticular juvenile idiopathic arthritis, in patients from the age of 2 years who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs). Amsparity can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate. Adalimumab has not been studied in patients aged less than 2 years. Enthesitis-related arthritis: Amsparity is indicated for the treatment of active enthesitis-related arthritis in patients, 6 years of age and older, who have had an inadequate response to, or who are intolerant of, conventional therapy. **Paediatric plaque psoriasis:** Amsparity is indicated for the treatment of severe chronic plaque psoriasis in children and adolescents from 4 years of age who have had an inadequate response to or are inappropriate candidates for topical therapy and phototherapies. **Paediatric Crohn's disease:** Amsparity is indicated for the treatment of moderately to severely active Crohn's disease in paediatric patients (from 6 years of age) who have had an inadequate response to conventional therapy including primary nutrition therapy and a corticosteroid and/or an immunomodulator, or who are intolerant to or have contraindications for such therapies. **Adolescent hidradenitis suppurativa:** Amsparity is indicated for the treatment of active moderate to severe hidradenitis suppurativa (HS) (acne inversa) in adolescents from 12 years of age with an inadequate response to conventional systemic HS therapy . **Paediatric uveitis:** Amsparity is indicated for the treatment of paediatric chronic non-infectious	NO	> 2 years > 4 years > 6 years > 12 years		NO

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
		anterior uveitis in patients from 2 years of age who have had an inadequate response to or are intolerant to conventional therapy, or in whom conventional therapy is inappropriate.				
Deferasirox	V03AC03	Deferasirox Accord is indicated for the treatment of chronic iron overload due to frequent blood transfusions (≥7 ml/kg/month of packed red blood cells) in patients with beta thalassaemia major aged 6 years and older. Deferasirox Accord is also indicated for the treatment of chronic iron overload due to blood transfusions when deferoxamine therapy is contraindicated or inadequate in the following patient groups: - in paediatric patients with beta thalassaemia major with iron overload due to frequent blood transfusions (≥7 ml/kg/month of packed red blood cells) aged 2 to 5 years, - in adult and paediatric patients with beta thalassaemia major with iron overload due to infrequent blood transfusions (<7 ml/kg/month of packed red blood cells) aged 2 years and older, - in adult and paediatric patients with other anaemias aged 2 years and older. Deferasirox Accord is also indicated for the treatment of chronic iron overload requiring chelation therapy when deferoxamine therapy is contraindicated or inadequate in patients with non-transfusiondependent thalassaemia syndromes aged 10 years and older.	NO	> 2 years		NO
Givosiran	-	Givlaari is indicated for the treatment of acute hepatic porphyria (AHP) in adults and adolescents aged 12 years and older.	YES	> 12 years		YES
Fidaxomicin	A07AA12	DIFICLIR film-coated tablets is indicated for the treatment of Clostridioides difficile infections (CDI) also known as C. difficile-associated diarrhoea (CDAD) in adult and paediatric patients with a body weight of at least 12.5 kg DIFICLIR granules for oral suspension is indicated for the treatment of Clostridioides difficile infections (CDI) also known as C. difficile-associated diarrhoea (CDAD) in adults and paediatric patients from birth to < 18 years of age	NO	all ages	12/12/19 (13/02/20): Extension application to introduce a new pharmaceutical form associated with new strength (40 mg/ml granules for oral suspension) for paediatric use of Dificlir in children from birth to less than 18 years of age. This is grouped with a type II variation (C.I.6.a) for the film-coated tablet formulation, to include paediatric use of Dificlir in children with body weight of at least 12.5 kg.	YES
Rituximab	L01XC02	Non-Hodgkin's lymphoma (NHL): MabThera in combination with chemotherapy is indicated for the treatment of paediatric patients (aged ≥ 6 months to < 18 years old) with previously untreated advanced stage CD20 positive diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma (BL)/Burkitt leukaemia (mature B-cell acute leukaemia) (BAL) or Burkitt-like lymphoma (BLL). Granulomatosis with polyangiitis and microscopic polyangiitis: MabThera, in combination with glucocorticoids, is indicated for the induction of remission in paediatric patients (aged ≥ 2 to < 18 years old) with severe, active GPA (Wegener's) and MPA.	NO	> 6 months	30/01/20 (03/03/20): Extension of indication to include treatment of paediatric patients (aged ≥6 months to <18 years old) with previously untreated advanced stage diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma (BL)/Burkitt leukaemia (mature B-cell acute leukaemia) (BAL) or Burkitt-like lymphoma (BLL) in combination with chemotherapy for MabThera. Extension of indication to	YES

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
					include the induction of remission in paediatric patients (aged ≥ 2 to <18 years old) with severe, active granulomatosis with polyangiitis (GPA) (Wegener's) and microscopic polyangiitis (MPA)	
Darunavir / cobicistat	J05	REZOLSTA is indicated, in combination with other antiretroviral medicinal products, for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults and adolescents (aged 12 years and older, weighing at least 40 kg).	NO	> 12 years	30/01/20 (09/03/20): To extend the approved therapeutic indication of Rezolsta to include the adolescent population (aged 12 years old and older with body weight at least 40 kg).	YES
Cholera vaccine (recombinant, live, oral)	J07AE02	Vaxchora is indicated for active immunisation against disease caused by Vibrio cholerae serogroup O1 in adults and children aged 6 years and older.	NO	> 6 years		YES
Cinacalcet	H05BX01	Secondary hyperparathyroidism: Paediatric population: Treatment of secondary hyperparathyroidism (HPT) in children aged 3 years and older with end-stage renal disease (ESRD) on maintenance dialysis therapy in whom secondary HPT is not adequately controlled with standard of care therapy.	NO	> 3 years		NO
Crisaborole	D11AH06	Staquis is indicated for treatment of mild to moderate atopic dermatitis in adults and paediatric patients from 2 years of age with ≤ 40% body surface area (BSA) affected.	NO	> 2 years		YES
Tigecycline	J01AA12	Tigecycline Accord is indicated in adults and in children from the age of eight years for the treatment of the following infections: • Complicated skin and soft tissue infections (cSSTI), excluding diabetic foot infections; • Complicated intra-abdominal infections (cIAI). Tigecycline Accord should be used only in situations where other alternative antibiotics are not suitable	NO	> 8 years		NO
Onasemnogene abeparvovec	M09AX09		YES	all ages		YES
Etanercept	L04AB01	Juvenile idiopathic arthritis: Treatment of polyarthritis (rheumatoid factor positive or negative) and extended oligoarthritis in children and adolescents from the age of 2 years who have had an inadequate response to, or who have proved intolerant of, methotrexate. Treatment of psoriatic arthritis in adolescents from the age of 12 years who have had an inadequate response to, or who have proved intolerant of, methotrexate. Treatment of enthesitis-related arthritis in adolescents from the age of 12 years who have had an inadequate response to, or who have proved intolerant of, conventional therapy. Etanercept has not been studied in children aged less than 2 years. Paediatric plaque psoriasis: Treatment of chronic severe plaque psoriasis in children and adolescents from the age of 6 years who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies.	NO	> 2 years		NO

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
Ixekizumab	L04AC	Paediatric plaque psoriasis: Taltz is indicated for the treatment of moderate to severe plaque psoriasis in children from the age of 6 years and with a body weight of at least 25 kg and adolescents who are candidates for systemic therapy.	NO	> 6 years	28/05/20 (26/06/20): Extension of Indication to include the treatment of moderate to severe plaque psoriasis in children from the age of 6 years and with a body weight of at least 25 kg and adolescents who are candidates for systemic therapy	YES
Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence	L03		YES	all ages		YES
Cobicistat on silicon dioxide	V03AX03	Tybost is indicated as a pharmacokinetic enhancer of atazanavir 300 mg once daily or darunavir 800 mg once daily as part of antiretroviral combination therapy in human immunodeficiency virus-1 (HIV-1) infected adults and adolescents aged 12 years and older: • weighing at least 35 kg co-administered with atazanavir or • weighing at least 40 kg co-administered with darunavir.	NO	> 12 years	30/01/20 (09/03/20): Extension of Indication to modify the approved therapeutic indication for Tybost to include the adolescent population aged 12 years old and older weighing at least 35kg when Tybost is used in combination with ATV and at least 40 kg when it is used in combination with Darunavir.	YES
Secukinumab	L04AC10	Paediatric plaque psoriasis: Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in children and adolescents from the age of 6 years who are candidates for systemic therapy.	NO	> 6 years	25/06/20(31/07/20): Extension of Indication to include the treatment of moderate to severe plaque psoriasis in children and adolescents from the age of 6 years who are candidates for systemic therapy;	YES
Indacaterol/Mometasone	R03AK	Atectura Breezhaler is indicated as a maintenance treatment of asthma in adults and adolescents 12 years of age and older not adequately controlled with inhaled corticosteroids and inhaled short-acting beta2-agonists.	NO	> 12 years		YES
Indacaterol/Mometasone	R03AK	Bemrist Breezhaler is indicated as a maintenance treatment of asthma in adults and adolescents 12 years of age and older not adequately controlled with inhaled corticosteroids and inhaled short-acting beta2-agonists.	NO	> 12 years		YES
Anidulafungin	J02AX06	Treatment of invasive candidiasis in adults and paediatric patients aged 1 month to < 18 years	NO	> 1 month	30/04/20 (03/06/20): Extension of the approved indication "treatment of invasive candidiasis (ICC)" to include paediatric patients aged from 1 month to less than 18 years of age;	YES
Caplacizumab	B01A	Cablivi is indicated for the treatment of adults and adolescents of 12 years of age and older weighing at least 40 kg experiencing an episode of acquired thrombotic thrombocytopenic purpura (aTTP), in conjunction with plasma exchange and immunosuppression.	YES	> 12 years	30/04/20 (09/06/20): Extension of indication to include adolescents weighing over 40 kg in the authorised indication for Cablivi	YES
Fingolimod	L04AA27	Fingolimod Accord is indicated as single disease modifying therapy in highly active relapsing remitting multiple sclerosis for the following groups of adult patients and paediatric patients aged 10 years and older:	NO	> 10 years		NO

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
		- Patients with highly active disease despite a full and adequate course of treatment with at least one disease modifying therapy (for exceptions and information about washout periods see sections 4.4 and 5.1). or - Patients with rapidly evolving severe relapsing remitting multiple sclerosis defined by 2 or more disabling relapses in one year, and with 1 or more Gadolinium enhancing lesions on brain MRI or a significant increase in T2 lesion load as compared to a previous recent MRI.				
Insulin aspart	A10AB05	Insulin aspart Sanofi is indicated for the treatment of diabetes mellitus in adults, adolescents and children aged 1 year and above.	NO	> 1 year		NO
Ravulizumab	L04AA	Ultomiris is indicated in the treatment of patients with a body weight of 10 kg or above with atypical haemolytic uremic syndrome (aHUS) who are complement inhibitor treatment-naïve or have received eculizumab for at least 3 months and have evidence of response to eculizumab	NO	children with a body weight of 10 kg	30/04/20 (25/06/20): Extension of Indication to include the treatment of patients with atypical hemolytic uremic syndrome (aHUS) for Ultomiris	YES
Remdesivir		Veklury is indicated for the treatment of coronavirus disease 2019 (COVID-19) in adults and adolescents (aged 12 years and older with body weight at least 40 kg) with pneumonia requiring supplemental oxygen	NO	> 12 years with body weight at least 40 kg		YES
Ebola vaccine (rDNA, replication-incompetent)	J07BX	Mvabea, as part of the Zabdeno, Mvabea vaccine regimen, is indicated for active immunisation for prevention of disease caused by Ebola virus (Zaire ebolavirus species) in individuals ≥1 year of age	NO	> 1 year		YES
Ebola vaccine (rDNA, replication-incompetent)	J07	Zabdeno, as part of the Zabdeno, Mvabea vaccine regimen, is indicated for active immunisation for prevention of disease caused by Ebola virus (Zaire ebolavirus species) in individuals ≥1 year of age	NO	> 1 year		YES
Tedizolid phosphate	J01	Sivextro is indicated for the treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults and adolescents 12 years of age and older.	NO	> 12 years	28/05/20 (26/06/20): Extension of Indication (treatment of ABSSSI in adults) to include adolescent population from 12 years old and older for Sivextro	YES
Ivacaftor / tezacaftor / elexacaftor	R07AX	Kaftrio is indicated in a combination regimen with ivacaftor 150 mg tablets for the treatment of cystic fibrosis (CF) in patients aged 12 years and older who are homozygous for the F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene or heterozygous for F508del in the CFTR gene with a minimal function (MF) mutation	YES	> 12 years		YES
Caffeine citrate	N06BC01	Treatment of primary apnoea of premature newborns	NO	premature newborns		NO
Entrectinib	L01XE56	Rozlytrek as monotherapy is indicated for the treatment of adult and paediatric patients 12 years of age and older with solid tumours expressing a neurotrophic tyrosine receptor kinase (NTRK) gene fusion, • who have a disease that is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity, and • who have not received a prior NTRK inhibitor • who have no satisfactory treatment options. Rozlytrek as monotherapy is indicated for the treatment of adult patients with ROS1-positive, advanced non-small cell lung cancer (NSCLC) not previously treated with ROS1 inhibitors.	NO	> 12 years		YES

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
Lurasidone	N05AE05	Latuda is indicated for the treatment of schizophrenia in adults and adolescent aged 13 years and over.	NO	> 13 years	23/07/20 (25/08/20): Extension of Indication for the treatment of schizophrenia in adolescent from 13 years and over;	YES
Rituximab	L01XC02	Non-Hodgkin's lymphoma (NHL): Ruxience in combination with chemotherapy is indicated for the treatment of paediatric patients (aged ≥ 6 months to < 18 years old) with previously untreated advanced stage CD20 positive diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma (BL)/Burkitt leukaemia (mature B-cell acute leukaemia) (BAL) or Burkitt-like lymphoma (BLL). Granulomatosis with polyangiitis and microscopic polyangiitis Ruxience, in combination with glucocorticoids, is indicated for the treatment of adult patients with severe, active granulomatosis with polyangiitis (Wegener's) (GPA) and microscopic polyangiitis (MPA). Ruxience, in combination with glucocorticoids, is indicated for the induction of remission in paediatric patients (aged ≥ 2 to < 18 years old) with severe, active GPA (Wegener's) and MPA.	NO	> 6 months		NO
Ceftazidime Avibactam	J01	Zavicefta is indicated in adults and paediatric patients aged 3 months and older for the treatment of the following infections: · Complicated intra-abdominal infection (cIAI) · Complicated urinary tract infection (cUTI), including pyelonephritis · Hospital-acquired pneumonia (HAP), including ventilator associated pneumonia (VAP) Zavicefta is also indicated for the treatment of infections due to aerobic Gram-negative organisms in adults and paediatric patients aged 3 months and older with limited treatment options. Consideration should be given to official guidance on the appropriate use of antibacterial agents.	NO	> 3 months	17/09/20 (22/10/20): Extension of indication to include paediatric patients aged 3 months to less than 18 years for Zavicefta (for the treatment of cIAI and cUTI), based on data from paediatric studies D4280C00014, C3591004 and C3591005 and the population PK modelling/simulation analyses (CAZ-MS-PED-01 and CAZ-MS-PED-02).	YES
Crizanlizumab	B06AX01	Adakveo is indicated for the prevention of recurrent vaso-occlusive crises (VOCs) in sickle cell disease patients aged 16 years and older. It can be given as an add-on therapy to hydroxyurea/hydroxycarbamide (HU/HC) or as monotherapy in patients for whom HU/HC is inappropriate or inadequate.	YES	> 16 years		YES
Sofosbuvir velpatasvir	J05A	Epclusa is indicated for the treatment of chronic hepatitis C virus (HCV) infection in patients aged 6 years and older and weighing at least 17 kg	NO	> 6 years	25/06/20 (25/08/20): Extension application to introduce a new strength (200/50 mg film-coated tablets). The new presentation is indicated for the treatment of chronic hepatitis C virus (HCV) infection in patients 6 years and older. The extension application is grouped with a type II variation (C.I.6.a) to include paediatric use in patients aged 6 to < 18 years to the existing strength of 400/100 mg film-coated tablets	YES
Delamanid	J04AK06	Deltyba is indicated for use as part of an appropriate combination regimen for pulmonary multi-drug resistant tuberculosis (MDR-TB) in adults, adolescents and c hildren with a body weight of at least 30 kg when an effective	YES	children with a body weight of at least 30 kg	17/09/20 (27/10/20): Extension of indication to include adolescents and children with a body weight of at least 30 kg	YES

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
		treatment regimen cannot otherwise be composed for reasons of resistance or tolerability				
Rituximab	L01XC02	Non-Hodgkin's lymphoma (NHL): Blitzima in combination with chemotherapy is indicated for the treatment of paediatric patients (aged ≥ 6 months to < 18 years old) with previously untreated advanced stage CD20 positive diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma (BL)/Burkitt leukaemia (mature B-cell acute leukaemia) (BAL) or Burkitt-like lymphoma (BLL). Granulomatosis with polyangiitis and microscopic polyangiitis: Blitzima, in combination with glucocorticoids, is indicated for the induction of remission in paediatric patients (aged ≥ 2 to < 18 years old) with severe, active GPA (Wegener's) and MPA.	NO	> 6 months (NHL) > 2 years GPA and MPA		NO

6. References

1. European Parliament and Council Regulation (EC) No 1901/2006, 12 December 2006, on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004

2. Ceci A, Felisi M, Baiardi P, Bonifazi F, Catapano M, Giaquinto C, Nicolosi A, Sturkenboom M, Neubert A, Wong I. Medicines for children licensed by the European Medicines Agency (EMEA): the balance after 10 years Eur J Clin Pharmacol 2006. Nov;62(11):947-52.

3. Ceci A, Felisi M, Catapano M, Baiardi P, Cipollina L, Ravera S, Bagnulo S, Reggio S, Rondini G. Medicines for children licensed by the European Agency for the Evaluation of Medicinal Products. Eur J Clin Pharmacol. 2002 Nov;58(8):495-500.

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