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

(period: January 2023 – December 2023)

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 October 1995 to December 2023.[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. The Regulation is currently under revision by European Commission.

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; three publications are available [2,3,4].

The aim of this report is to present the status of paediatric medicines licensed by EMA. An insight on authorisations/variations until 2023 is also reported (paragraph 5).

3. Methodology

3.1. Data collection and storing

The EMA public website (section "What's new") 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 on each medicinal product approved by EMA 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
- Orphan Drug status

3.3. Data Analysis

General descriptive statistics 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

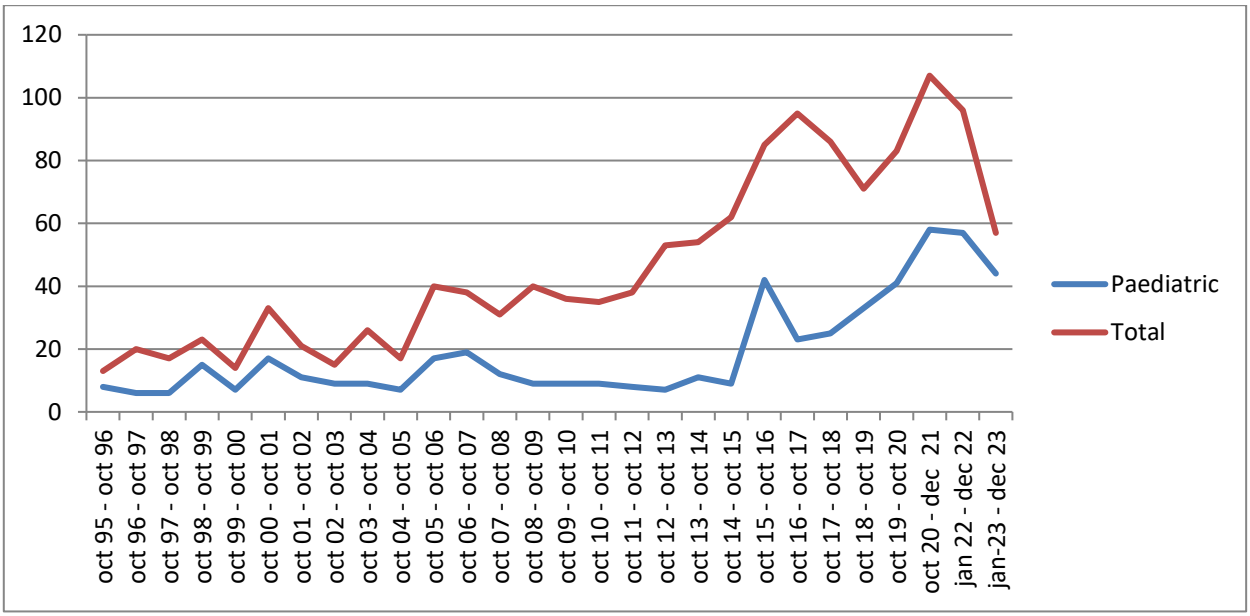
4.1. Number and percentage of paediatric medicines

From the EMA institution to December 2023, 1042 active substances (ASs) have been approved under the Centralised Procedure (corresponding to a total of 1703 Medicinal Products): 402 of them were paediatric (38%) on a total of 651 paediatric Medicinal Products.[1]

12 active substances are exclusively authorized for the pediatric population.

Figure 1 reports the number of paediatric medicines and the total of medicines approved by EMA under the centralised procedure over the years. New 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 and the gap between always for adults and paediatric population in 2022/2023 appears particularly reduced.

Figure 1 - Medicinal products authorised by EMA divided by year (Oct. 1995 – Dec. 2023)

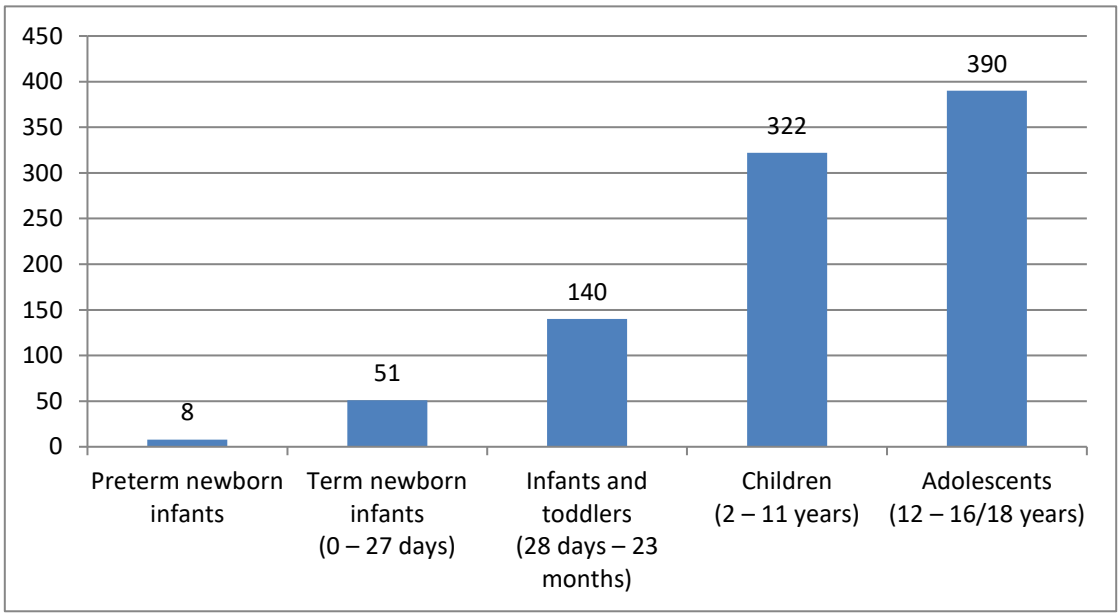


[1] In the first ten years period covered by this report (1995-2005), medicines that included in their documentation (Summary of Product Characteristics – SPC/PL) a paediatric dosages information, but not a paediatric indication, were also considered as paediatric.

4.2. Distribution of paediatric medicines by age

Figure 2 shows the distribution of paediatric medicines approved for different age groups. It is clear that the number of available medicines is lower for neonates and younger children, while it gradually increases for older children and reaches its peak in 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" (55%) represents the group with the highest ratio on the total of authorised medicines, followed by B-ATC "Blood and blood forming organs" (54%) and A-ATC "Alimentary tract and metabolism" (52%); C-ATC "Cardiovascular system" (24%) and G-ATC "Genito-urinary system and sex hormones" (18%) the lowest ones. Table 1 provides additional details.

Table 1: EMA Paediatric Medicines by ATC code	**Paediatric/Total**	
	N	**%**
A -Alimentary tract and metabolism	61/118	52
B - Blood and blood forming organs	40/74	54
C - Cardiovascular system	12/50	24
D - Dermatologicals	7/17	41
G - Genito-urinary system and sex hormones	6/34	18
H - Systemic hormonal preparations, excluding sex hormones and insulins	8/21	38
J - Anti-infectives for systemic use	105/192	55

Table 1: EMA Paediatric Medicines by ATC code	Paediatric/Total	
	N	%
L - Antineoplastic and immunomodulating agents	75/279	27
M - Musculo-skeletal system	7/28	25
N - Nervous system	28/86	32
P - Antiparasitic products, insecticides and repellents	2/2	100
R - Respiratory system	16/39	41
S - Sensory organs	7/28	25
V - Various	17/57	30
Not assigned yet	11/17	65
TOTAL	***402/1042***	***38%***

4.4. Distribution of paediatric medicines by orphan status

With reference to orphan drugs, it should be noted that out of the 139 orphan drugs authorised from the EMA institution to December 2023 under the OD Regulation rules, 65 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 (47% and 38%, respectively).

Table 2 – Paediatric orphan drugs and ATC distribution

ATC	Orphan medicinal products authorised	Paediatric orphan drugs authorised	Percentage
A -Alimentary tract and metabolism	23	18	78
B - Blood and blood forming organs	10	6	60
C - Cardiovascular system	3	0	-
D - Dermatologicals	2	1	50
G- Genito-urinary system and sex hormones	0	0	-
H - Systemic hormonal preparations, excluding sex hormones and insulins	6	3	50
J - Anti-infectives for systemic use	11	5	45
L - Antineoplastic and immunomodulating agents	49	8	16
M - Musculo-skeletal system	5	4	80
N - Nervous system	12	8	67
P -Antiparasitic products, insecticides and repellents	1	1	100
R - Respiratory system	2	2	100
S - Sensory organs	4	2	50
V -Various	3	1	33
Not assigned yet	8	6	75
TOTAL	**139**	**65**	***47%***

5. New paediatric drug from January 2023 to December 2023

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
dengue tetravalent vaccine (live, attenuated)	J07BX04	**Qdenga** is indicated for the prevention of dengue disease in individuals from 4 years of age.	NO	> 4 years		YES
dimethyl fumarate (generic)	L04AX07	**Dimethyl fumarate Neuraxpharm** is indicated for the treatment of adult and paediatric patients aged 13 years and older with relapsing remitting multiple sclerosis (RRMS).	NO	> 13 years		NO
Tabelecleucel	Not yet assigned	**Ebvallo** is indicated as monotherapy for treatment of adult and paediatric patients 2 years of age and older with relapsed or refractory Epstein-Barr virus positive post-transplant lymphoproliferative disease (EBV+ PTLD) who have received at least one prior therapy. For solid organ transplant patients, prior therapy includes chemotherapy unless chemotherapy is inappropriate.	YES	> 2 years		YES
Plerixafor (generic)	L03AX16	Paediatric patients (1 to less than 18 years) **Plerixafor Accord** is indicated in combination with G-CSF to enhance mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in children with lymphoma or solid malignant tumours, either: - pre-emptively, when circulating stem cell count on the predicted day of collection after adequate mobilization with G-CSF (with or without chemotherapy) is expected to be insufficient with regards to desired hematopoietic stem cells yield, or - who previously failed to collect sufficient haematopoietic stem cells	NO	> 1 year		NO
aflibercept	S01LA05	**EYLEA** is indicated in preterm infants for the treatment of • retinopathy of prematurity (ROP) with zone I (stage 1+, 2+, 3 or 3+), zone II (stage 2+ or 3+) or AP-ROP (aggressive posterior ROP) disease.	NO	Preterm infants		YES
dimethyl fumarate (generic)	L04AX07	**Dimethyl fumarate Accord** is indicated for the treatment of adult and paediatric patients aged 13 years and older with relapsing remitting multiple sclerosis (RRMS).	NO	> 13 years		NO
Sugammadex (generic)	V03AB35	For the paediatric population: sugammadex is only recommended for routine reversal of rocuronium induced blockade in children and adolescents aged 2 to 17 years.	NO	> 2 years		NO
dulaglutide	A10BJ05	**Trulicity** is indicated for the treatment of patients 10 years and above with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise • as monotherapy when metformin is considered inappropriate due to intolerance or contraindications • in addition to other medicinal products for the treatment of diabetes	NO	> 10 years	26/01/23 (06/03/23): Extension of indication to include treatment of type 2 diabetes mellitus (T2DM) in children and adolescents aged 10 to less than 18 years based on final results from study H9X-MC-GBGC; this is a phase 3, double-blind, randomised, multi-centre, placebo-controlled superiority trial to evaluate PK, PD, safety and efficacy of dulaglutide in children from 10 to less than 18 years of age, with an open label extension to evaluate safety	YES

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
selvacovatein	J07BN	**BIMERVAX** is indicated as a booster for active immunisation to prevent COVID-19 in individuals 16 years of age and older who have previously received a mRNA COVID-19 vaccine. The use of this vaccine should be in accordance with official recommendations	NO	> 16 years		YES
dapagliflozin	A10BK01	Type 2 diabetes mellitus **Dapagliflozin Viatris** is indicated in adults and children aged 10 years and above for the treatment of insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise - as monotherapy when metformin is considered inappropriate due to intolerance. - in addition to other medicinal products for the treatment of type 2 diabetes. For study results with respect to combination of therapies, effects on glycaemic control, cardiovascular and renal events, and the populations studied	NO	> 10 years	26/01/23 (06/03/23): Extension of indication to include treatment of type 2 diabetes mellitus (T2DM) in children and adolescents aged 10 to less than 18 years based on final results from study H9X-MC-GBGC; this is a phase 3, double-blind, randomised, multi-centre, placebo-controlled superiority trial to evaluate PK, PD, safety and efficacy of dulaglutide in children from 10 to less than 18 years of age, with an open label extension to evaluate safety	NO
insulin lispro	A10AB04	Treatment of diabetes mellitus in adults, adolescents and children aged 1 year and above	NO	> 1 year		NO
pitolisant	N07XX11	**Wakix** is indicated in adults, adolescents and children from the age of 6 years for the treatment of narcolepsy with or without cataplexy	YES	> 6 years	26/01/23 (24/02/23): Extension of indication to include treatment of narcolepsy with or without cataplexy in adolescents and children from the age of 6 years, based on results from Study P11-06; an ongoing phase III, double-blind, multicentre, randomized, placebo-controlled trial undertaken to evaluate safety and efficacy of pitolisant in children from 6 to less than 18 years with narcolepsy with/without cataplexy.	YES
ruxolitinib	D11AH	**Opzelura** is indicated for the treatment of non-segmental vitiligo with facial involvement in adults and adolescents from 12 years of age	NO	> 12 years		YES
human fibrinogen human thrombin	B02BC30	**TachoSil** is indicated in adults and children from 1 month of age for supportive treatment in surgery for improvement of haemostasis, to promote tissue sealing and for suture support in vascular surgery where standard techniques are insufficient.	NO	> 1 month	23/02/23 (24/03/23): Extension of indication to include treatment of children aged 1 month to 18 years, based on available bibliographical data, results from study TC-2402-040-SP which compared TachoSil with Surgicel Original as adjunct to primary surgical treatment in both adult and paediatric subjects, and results from Study TC019-IN; a prospective, uncontrolled study in paediatric subjects	NO
tadalafil	G04BE08	Paediatric population: Treatment of paediatric patients aged 2 years and above with pulmonary arterial hypertension (PAH) classified as WHO functional class II and III.	NO	> 2 years	15/12/22 (24/02/23): Extension application to introduce a new pharmaceutical form	YES

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
					associated with a new strength (2 mg/ml oral suspension) grouped with a type II variation (C.I.6.a) to include paediatric use (from 6 months to 17 years) based on study 4 (H6D-MC-LVHV [LVHV]) - A 24-week placebo-controlled efficacy and safety study with an open-label long-term extension phase	
Eculizumab (biosimilar)	L04AA25	**BEKEMV** is indicated in adults and children for the treatment of paroxysmal nocturnal haemoglobinuria (PNH). Evidence of clinical benefit is demonstrated in patients with haemolysis with clinical symptom(s) indicative of high disease activity, regardless of transfusion history	NO	> 2 years		NO
oritavancin	J01XA05	**Tenkasi** is indicated for the treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults and paediatric patients aged 3 months and older	NO	> 3 months	30/03/23 (15/05/23): Extension of indication to include treatment of paediatric population, aged between 3 months and less than 18 years for Tenkasi (oritavancin) 400 mg based on interim results from study TMC-ORI-11-01	YES
Lacosamide (generic)	N03AX18	**Lacosamide Adroiq** is indicated as monotherapy in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 2 years of age with epilepsy. Lacosamide Adroiq is indicated as adjunctive therapy • in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 2 years of age with epilepsy. • in the treatment of primary generalised tonic-clonic seizures in adults, adolescents and children from 4 years of age with idiopathic generalised epilepsy	NO	> 2 years		NO
sodium thiosulfate	Not yet assigned	**Pedmarqsi** is indicated for the prevention of ototoxicity induced by cisplatin chemotherapy in patients 1 month to < 18 years of age with localised, non-metastatic, solid tumours.	NO	> 1 month		YES
dabigatran etexilate (generic)	B01AE07	Treatment of VTE and prevention of recurrent VTE in paediatric patients from birth to less than 18 years of age.	NO	all ages		NO
Eculizumab	L04AA25	**Epysqli** is indicated in adults and children for the treatment of Paroxysmal nocturnal haemoglobinuria (PNH). Evidence of clinical benefit is demonstrated in patients with haemolysis with clinical symptom(s) indicative of high disease activity, regardless of transfusion history	NO	all ages > 5kg		NO
semaglutide	A10BJ06	Adolescents (≥12 years) **Wegovy** is indicated as an adjunct to a reduced-calorie diet and increased physical activity for weight management in adolescents ages 12 years and above with • obesity* and • body weight above 60 kg. Treatment with Wegovy should be discontinued and re-evaluated if adolescent patients have not	NO	> 12 years	30/03/23 (28/04/23): Extension of indication to include treatment of adolescents for weight management based on the final results from study NN9536-4451; this trial was conducted to assess the efficacy and safety of semaglutide in paediatric	YES

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
		reduced their BMI by at least 5% after 12 weeks on the 2.4 mg or maximum tolerated dose.			patients of age 12 to <18 years with obesity.	
sirolimus	Not yet assigned	**Hyftor** is indicated for the treatment of facial angiofibroma associated with tuberous sclerosis complex in adults and paediatric patients aged 6 years and older.	YES	> 6 years		NO
Sugammadex (biosimilar)	V03AB	Reversal of neuromuscular blockade induced by rocuronium or vecuronium in adults. For the paediatric population: sugammadex is only recommended for routine reversal of rocuronium induced blockade in children and adolescents aged 2 to 17 years.	NO	> 2 years		NO
sacubitril valsartan	C09DX04	Paediatric heart failure: **Entresto** is indicated in children and adolescents aged one year or older for treatment of symptomatic chronic heart failure with left ventricular systolic dysfunction.	NO	> 1 year	30/03/23 (26/05/23): Extension application to introduce a new pharmaceutical form associated with two new strengths (6 mg/6 mg granules in capsule for opening and 15 mg/16 mg granules in capsule for opening), grouped with a type II variation (C.I.6.a) in order to extend the indication to include treatment of children and adolescents aged one year or older with chronic heart failure with left ventricular systolic dysfunction, based on the results of Study PANORAMA-HF (CLCZ696B2319)	YES
sacubitril valsartan	C09DX04	Paediatric heart failure: **Neparvis** is indicated in children and adolescents aged one year or older for treatment of symptomatic chronic heart failure with left ventricular systolic dysfunction	NO	> 1 year	30/03/23 (26/05/23): Extension application to introduce a new pharmaceutical form associated with two new strengths (6 mg/6 mg granules in capsule for opening and 15 mg/16 mg granules in capsule for opening), grouped with a type II variation (C.I.6.a) in order to extend the indication to include treatment of children and adolescents aged one year or older with chronic heart failure with left ventricular systolic dysfunction, based on the results of Study PANORAMA-HF (CLCZ696B2319)	YES
nivolumab	L01FF01	**Melanoma**: OPDIVO as monotherapy or in combination with ipilimumab is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults and adolescents 12 years of age and older. Relative to nivolumab monotherapy, an increase in progression-free survival (PFS) and overall survival (OS) for the combination of nivolumab with ipilimumab is established only in patients with low tumour PD-L1 expression **Adjuvant treatment of melanoma**: OPDIVO as monotherapy is indicated for the adjuvant treatment	NO	> 12 years	20/07/23 (21/08/23): Extension of indication to include OPDIVO for the adjuvant treatment of adults and adolescents 12 years of age and older with stage IIB or IIC melanoma who have undergone complete resection, based on results from study CA20976K. 26/04/23 (31/05/23): Extension of indication to	YES

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
		of adults and adolescents 12 years of age and older with Stage IIB or IIC melanoma, or melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection			include adolescent patients aged 12 years and older in treatment of advanced (unresectable or metastatic) melanoma (nivolumab monotherapy), treatment of advanced (unresectable or metastatic) melanoma (nivolumab in combination with ipilimumab) and adjuvant treatment of melanoma (nivolumab monotherapy) for Opdivo, based on results from a nonclinical biomarker study (Expression of PD-L1 (CD274), and characterization of tumor infiltrating immune cells in tumors of pediatric origin), also based on results from a Phase 1/2 clinical study (CA209070, A Phase 1/2 Study of Nivolumab (Ind# 124729) In Children, Adolescents, And Young Adults With Recurrent Or Refractory Solid Tumors As A Single Agent And In Combination With Ipilimumab) and a modelling and simulation study.	
sugammadex	V03AB35	Reversal of neuromuscular blockade induced by rocuronium or vecuronium in adults. For the paediatric population: sugammadex is only recommended for routine reversal of rocuronium induced blockade in children and adolescents aged 2 to 17 years.	NO	> 2 years		NO
spironolactone	C03DA01	In the management of refractory oedema associated with congestive cardiac failure; hepatic cirrhosis with ascites and oedema, malignant ascites, nephrotic syndrome, diagnosis and treatment of primary aldosteronism, essential hypertension. Neonates, children and adolescents should only be treated under guidance of a paediatric specialist. There is limited paediatric data available	NO	all ages		NO
somapacitan	H01AC07	**Sogroya** is indicated for the replacement of endogenous growth hormone (GH) in children aged 3 years and above, and adolescents with growth failure due to growth hormone deficiency (paediatric GHD), and in adults with growth hormone deficiency (adult GHD)	YES	> 3 years	25/05/23 (24/07/23): extension application to add a new strength of 15 mg/1.5 mL solution for injection in pre-filled pen grouped with a type II variation C.I.6 to add a new indication 'Replacement of endogenous growth hormone (GH) in children and adolescents with growth failure due to growth hormone deficiency (GHD)', based on results from the completed main 52-week period of the confirmatory phase 3 trial (4263), supported with long-term data from the phase 2 trial	YES

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
					(4172), up to week 208 completed	
ganaxolone	N03AX	**ZTALMY** is indicated for the adjunctive treatment of epileptic seizures associated with cyclindependent kinase-like 5 (CDKL5) deficiency disorder (CDD) in patients 2 to 17 years of age. ZTALMY may be continued in patients 18 years of age and older.	YES	> 2 years		YES
riociguat	C02KX05	Pulmonary arterial hypertension (PAH) Paediatrics **Adempas** is indicated for the treatment of PAH in paediatric patients aged less than 18 years of age and body weight ≥ 50 kg with WHO Functional Class (FC) II to III in combination with endothelin receptor antagonists	NO	> 6 years	26/04/23 (31/05/23): Extension of indication to add the treatment of PAH in paediatric patients aged less than 18 years of age and body weight ≥ 50 kg with WHO Functional Class (FC) II to III in combination with endothelin receptor antagonists for ADEMPAS, based on results from pivotal study PATENT-CHILD (Study 15681); this is a Phase III, Open-label, individual dose titration study to evaluate safety, tolerability and pharmacokinetics of riociguat in children from 6 to less than 18 years of age with PAH	YES
Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live)	Not yet assigned	**Ervebo** is indicated for active immunisation of individuals 1 year of age or older to protect against Ebola Virus Disease (EVD) caused by Zaire Ebola virus	NO	> 1 year	20/07/23 (16/08/23): Extension of indication to include the paediatric population from 1 year to less than 18 years of age based on final results from study V920-016 (PREVAC)	YES
methoxy polyethylene glycol-epoetin beta	B03XA03	Treatment of symptomatic anaemia associated with chronic kidney disease (CKD) in paediatric patients from 3 months to less than 18 years of age who are converting from another erythropoiesis stimulating agent (ESA) after their haemoglobin level was stabilised with the previous ESA.	NO	> 3 months	22/06/23 (26/07/23): Extension of indication to include treatment of paediatric patients from 3 months to less than 18 years of age who are converting from another erythropoiesis stimulating agent (ESA) after their haemoglobin level was stabilised with the previous ESA	YES
ritlecitinib	L04AF08	**Litfulo** is indicated for the treatment of severe alopecia areata in adults and adolescents 12 years of age and older	NO	> 12 years		YES
cabotegravir	J05AJ04	**Apretude** is indicated in combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in high-risk adults and adolescents, weighing at least 35 kg. Apretude tablets may be used as: • oral lead-in to assess tolerability of Apretude prior to administration of long acting cabotegravir injection. • oral PrEP for individuals who will miss planned dosing with cabotegravir injection.	NO	adolescents weighing at least 35 kg		YES
baricitinib	L04AA37	Juvenile idiopathic arthritis: Baricitinib is indicated for the treatment of active juvenile idiopathic arthritis in patients 2 years of age and older who have had an inadequate response or intolerance to	NO	> 2 years	14/09/23 (18/10/23): Extension of indication to include the treatment of paediatric patients (from 2	YES

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
		one or more prior conventional synthetic or biologic DMARDs: - Polyarticular juvenile idiopathic arthritis (polyarticular rheumatoid factor positive [RF+] or negative [RF-], extended oligoarticular), - Enthesitis-related arthritis, and - Juvenile psoriatic arthritis. Atopic dermatitis: Baricitinib is indicated for the treatment of moderate to severe atopic dermatitis in adult and paediatric patients 2 years of age and older who are candidates for systemic therapy			years of age and older) with moderate to severe atopic dermatitis for OLUMIANT, based on the final results from study I4V-MC-JAIP	
Tocilizumab (biosimilar)	L04AC07	**Tyenne** is indicated for the treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 2 years of age and older, who have responded inadequately to previous therapy with NSAIDs and systemic corticosteroids. Tyenne can be given as monotherapy (in case of intolerance to MTX or where treatment with MTX is inappropriate) or in combination with MTX. Tyenne can be given as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.	NO	> 2 years		NO
pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted)	J07BB02	Prophylaxis of influenza in an officially declared pandemic situation.	NO	> 6 months	20/07/23 (16/08/23): Extension of indication to include children from 6 months to less than 18 years of age for Foclivia, based on final results from study V87_30; this is a phase 2, randomized, observer-blind, multicenter study to evaluate the immunogenicity and safety of several doses of antigen and MF59 adjuvant content in a monovalent H5N1 pandemic influenza vaccine in healthy pediatric subjects 6 months to less than 9 years of age	NO
crisantaspase	L01XX02	**Enrylaze** is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukaemia (ALL) and lymphoblastic lymphoma (LBL) in adult and paediatric patients (1 month and older) who developed hypersensitivity or silent inactivation to E. coli-derived asparaginase	NO	> 1 month		YES
Lebrikizumab	L04AC	**Ebglyss** is indicated for the treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years and older with a body weight of at least 40 kg who are candidates for systemic therapy.	NO	> 12 years		YES
Enalapril maleate	C09AA02	**AQUMELDI** is indicated for the treatment of heart failure in children from birth to less than 18 years.	NO	0-18 years		YES
dabrafenib	L01EC02	Low-grade glioma: **Finlee** in combination with trametinib is indicated for the treatment of paediatric patients aged 1 year and older with low-grade glioma (LGG) with a BRAF V600E mutation who require systemic therapy. High-grade glioma: Finlee in combination with trametinib is indicated for the treatment of paediatric patients aged 1 year and older with high-grade glioma (HGG) with a BRAF V600E mutation who have received at least one prior radiation and/or chemotherapy treatment.	YES	> 1 year		YES

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
Posaconazole (generic)	J02AC04	**Posaconazole Accord** gastro-resistant tablets are indicated for use in the treatment of the following fungal infections in paediatric patients from 2 years of age weighing more than 40 kg and adults: - Invasive aspergillosis in patients with disease that is refractory to amphotericin B or itraconazole or in patients who are intolerant of these medicinal products; - Fusariosis in patients with disease that is refractory to amphotericin B or in patients who are intolerant of amphotericin B; - Chromoblastomycosis and mycetoma in patients with disease that is refractory to itraconazole or in patients who are intolerant of itraconazole; - Coccidioidomycosis in patients with disease that is refractory to amphotericin B, itraconazole or fluconazole or in patients who are intolerant of these medicinal products. Refractoriness is defined as progression of infection or failure to improve after a minimum of 7 days of prior therapeutic doses of effective antifungal therapy. Posaconazole Accord is also indicated for prophylaxis of invasive fungal infections in the following paediatric patients from 2 years of age weighing more than 40 kg and adults: - Patients receiving remission-induction chemotherapy for acute myelogenous leukaemia (AML) or myelodysplastic syndromes (MDS) expected to result in prolonged neutropenia and who are at high -risk of developing invasive fungal infections; - Hematopoietic stem cell transplant (HSCT) recipients who are undergoing high-dose immunosuppressive therapy for graft versus host disease and who are at high-risk of developing invasive fungal infections.	NO	> 2 years		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. Toma M, Felisi M, Bonifazi D, Bonifazi F, Giannuzzi V, Reggiardo G, de Wildt S, Ceci A and al. Paediatric Medicines in Europe: The Paediatric Regulation – Is It Time for Reform? Front. Med., 02 February 2021 Vol.8 https://doi.org/10.3389/fmed.2021.593281

3. 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.

4. 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.

[i] *This document has been prepared by TEDDY Network as part of its research activity. It does not replace the official data that can be accessed directly from the EMA website. The material cannot be distributed nor re-utilised without acquiring a specific preliminary consent from TEDDY Network. Reference to this document and to TEDDY Network should be included when citing data deriving from it.*