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

(period: October 2020 – October 2021)

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 October 2021.[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].

The aim of this report is to present the status of paediatric medicines licensed by EMA. An insight on authorisations/variations until 2021.

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

- Dosages
- Orphan Drug status
- Paediatric trials and studies included in the EPAR at the time of approval of the paediatric indication or variation.

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.

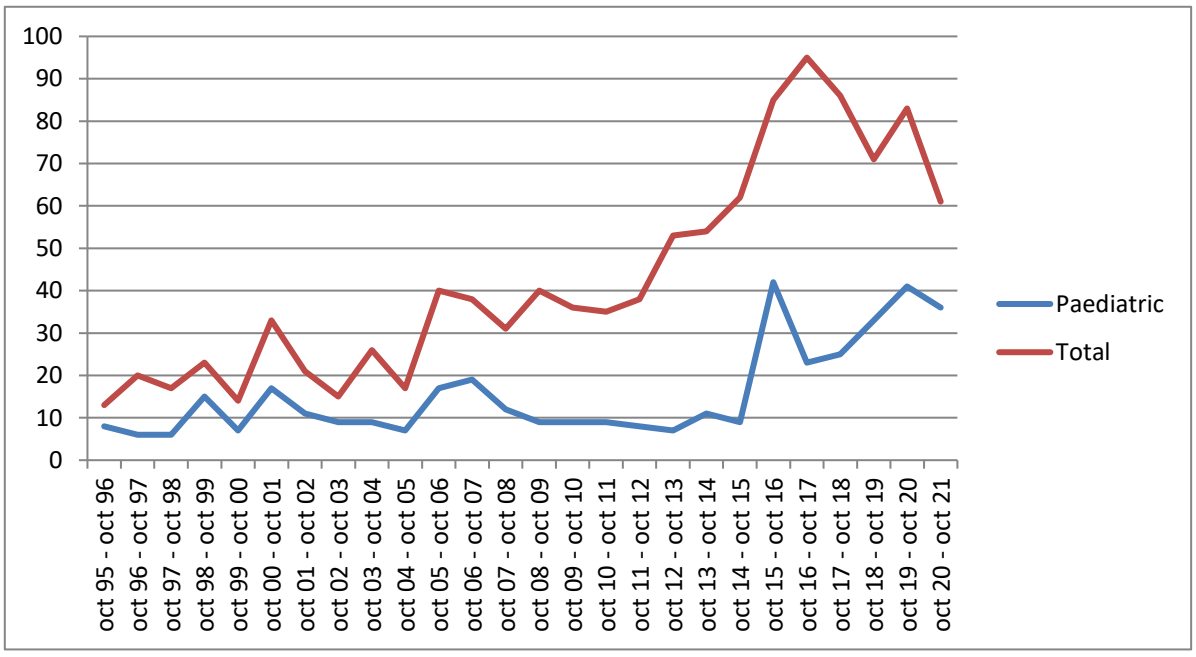
4. Results

4.1. Number and percentage of paediatric medicines

In the period October 1995 – October 2021, 927 active substances (ASs) have been approved by EMA under the Centralised Procedure: 333 of them were paediatric (36%).[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. 2021)

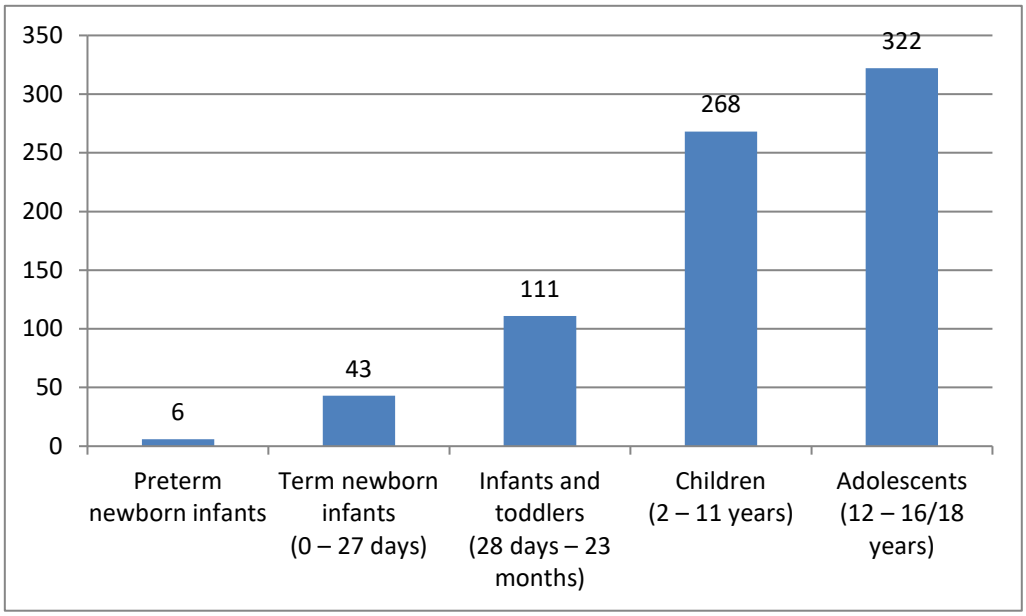


[1] In the first ten years period covered by this report (1995-2005), medicines that included in their documentation (Summary of Product Characteristics – SPC/PL) a paediatric dosages information, but not a paediatric indication, were also considered as paediatric.

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" (51%) and B-ATC "Blood and blood forming organs" (51%) represents the group with the highest ratio on the total of authorised medicines, followed by A-ATC "Alimentary tract and metabolism" (49%) ; C-ATC "Cardiovascular system" (17%) and G-ATC "Genito-urinary system and sex hormones" (12%) the lowest ones. Table 1 provides additional details.

Table 1: EMA Paediatric Medicines by ATC code

	Paediatric/Total	
	N	**%**
A -Alimentary tract and metabolism	52/107	49
B - Blood and blood forming organs	36/70	51
C - Cardiovascular system	8/45	17
D - Dermatologicals	4/13	31
G - Genito-urinary system and sex hormones	4/34	12
H - Systemic hormonal preparations, excluding sex hormones and insulins	5/17	29
J - Anti-infectives for systemic use	87/172	51

Table 1: EMA Paediatric Medicines by ATC code	Paediatric/Total	
	N	%
L - Antineoplastic and immunomodulating agents	64/230	28
M - Musculo-skeletal system	7/27	26
N - Nervous system	24/77	31
P - Antiparasitic products, insecticides and repellents	1/1	100
R - Respiratory system	15/36	42
S - Sensory organs	6/27	22
V - Various	15/52	29
Not assigned yet	5/19	26
TOTAL	***333/927***	***36%***

4.4. Distribution of paediatric medicines by orphan status

With reference to orphan drugs, it should be noted that out of the 125 orphan drugs authorised by the EMA in the period October 1995 – October 2021 under the OD Regulation rules, 63 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 (50% and 36%, respectively).

Table 2 – Paediatric orphan drugs and ATC distribution

ATC	Orphan medicinal products authorised	Paediatric orphan drugs authorised	Percentage
A -Alimentary tract and metabolism	21	18	86
B - Blood and blood forming organs	10	8	80
C - Cardiovascular system	4	1	25
D - Dermatologicals	2	0	0
G- Genito-urinary system and sex hormones	0	0	-
H - Systemic hormonal preparations, excluding sex hormones and insulins	4	0	-
J - Anti-infectives for systemic use	11	6	54
L - Antineoplastic and immunomodulating agents	41	11	27
M - Musculo-skeletal system	5	5	100
N - Nervous system	10	6	60
P -Antiparasitic products, insecticides and repellents	0	0	-
R - Respiratory system	4	3	75
S - Sensory organs	4	2	50
V -Various	2	0	-
Not assigned yet	7	3	43
TOTAL	**125**	**63**	***50%***

5. New paediatric drug from October 2020 to October 2021

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
defatted powder of Arachis hypogaea L., semen (peanuts)	V01	**PALFORZIA** is indicated for the treatment of patients aged 4 to 17 years with a confirmed diagnosis of peanut allergy. PALFORZIA may be continued in patients 18 years of age and older. PALFORZIA should be used in conjunction with a peanut-avoidant diet.	NO	> 4 years		YES
Autologous CD34+ cells encoding ARSA gene	N07	**Libmeldy** is indicated for the treatment of metachromatic leukodystrophy (MLD) characterized by biallelic mutations in the arylsulfatase A (ARSA) gene leading to a reduction of the ARSA enzymatic activity: - in children with late infantile or early juvenile forms, without clinical manifestations of the disease, - in children with the early juvenile form, with early clinical manifestations of the disease, who still have the ability to walk independently and before the onset of cognitive decline	YES	children		YES
COVID-19 mRNA vaccine (nucleoside-modified)	J07BX	Comirnaty is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus, in individuals 12 years of age and older.	NO	> 12 years	28/05/2021 (31/05/21): Extension of the existing indication from "individuals 16 years of age and older" to "individuals 12 years of age and older" for Comirnaty	YES
Rituximab (Biosimilar)	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
sodium oxybate	N07XX04	**Xyrem**: Treatment of narcolepsy with cataplexy in adult patients, adolescents and children from the age of 7 years	NO	> 7 years	12/11/20 (17/12/20): extension to the existing indication as follows: Treatment of narcolepsy with cataplexy in adult patients, adolescents and children from the age of 7 years.	NO
fenfluramine	N03	**Fintepla** is indicated for the treatment of seizures associated with Dravet syndrome as an add-on therapy to other anti-epileptic medicines for patients 2 years of age and older	YES	> 2 years		YES
dabigatran etexilate	B01AE07	**Pradaxa** Treatment of VTE and prevention of recurrent VTE in paediatric patients from birth to less than 18 years of age.	NO	all ages	12/11/20 (11/01/21): Extension application to add two new pharmaceutical forms for PRADAXA (coated granules (20 mg, 30 mg, 40 mg, 50 mg, 110 mg, 150 mg) and powder and solvent for oral solution (6.25 mg/mL)) and five new strengths (related to the coated granules), grouped with: -A type II variation (C.I.6.a) - Extension of Indication to	YES

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
					include new indication for Pradaxa 75 mg, 110 mg, 150 mg capsules based on the paediatric trials 1160.106 and 1160.108.	
Baloxavir marboxil	Not yet assigned	Treatment of influenza: **Xofluza** is indicated for the treatment of uncomplicated influenza in patients aged 12 years and above. Post-exposure prophylaxis of influenza: Xofluza is indicated for post-exposure prophylaxis of influenza in individuals aged 12 years and above.	NO	> 12 years		NO
rivaroxaban	B01AF01	**Xarelto** - Paediatric population: Treatment of venous thromboembolism (VTE) and prevention of VTE recurrence in children and adolescents aged less than 18 years and weighing from 30 kg to 50 kg after at least 5 days of initial parenteral anticoagulation treatment. Treatment of venous thromboembolism (VTE) and prevention of VTE recurrence in term neonates, infants and toddlers, children, and adolescents aged less than 18 years after at least 5 days of initial parenteral anticoagulation treatment	NO	all ages	12/11/2020 (21/01/2021): Extension of indication to include treatment of venous thromboembolism (VTE) and prevention of VTE recurrence in term neonates, infants and toddlers, children, and adolescents aged less than 18 years following initiation of standard anticoagulation treatment for Xarelto 15 and 20 mg tablets.	YES
Rituximab (biosimilar)	L01XC02	Non-Hodgkin's lymphoma (NHL): **Ritemvia** 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: Ritemvia, 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
Adalimumab (biosimilar)	L04AB04	Juvenile idiopathic arthritis Polyarticular juvenile idiopathic arthritis: **Yuflyma** 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). Yuflyma 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: Yuflyma is indicated for the treatment of active enthesitis-related arthritis in patients, 6 years of age and older. Paediatric plaque psoriasis: Yuflyma 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. Hidradenitis suppurativa (HS): Yuflyma is indicated for the treatment of active moderate to severe hidradenitis suppurativa (acne inversa) in adults and adolescents from 12 years of age with an inadequate response to conventional systemic HS therapy. Paediatric Crohn's disease: Yuflyma is indicated for the treatment of moderately to severely active	NO	> 2 years > 4 years > 6 years > 12 years		NO

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
		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 cortico Paediatric uveitis: Yuflyma is indicated for the treatment of paediatric chronic non-infectious 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.				
Glucagon	H04AA01	**Ogluo** is indicated for the treatment of severe hypoglycaemia in adults, adolescents, and children aged 2 years and over with diabetes mellitus.	NO	> 2 years		NO
insulin aspart (Biosimilar)	A10AB05	**Kirsty** is indicated for treatment of diabetes mellitus in adults, adolescents and children aged 1 year and above.	NO	> 1 year		NO
fluticasone propionate salmeterol xinafoate	R03AK06	**Seffalair Spiromax** is indicated in the regular treatment of asthma in adults and adolescents aged 12 years and older not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short-acting β2 agonists.	NO	> 12 years		YES
salmeterol xinafoate fluticasone propionate	R03AK06	**BroPair Spiromax** is indicated in the regular treatment of asthma in adults and adolescents aged 12 years and older not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short-acting β2 agonists.	NO	> 12 years		YES
selpercatinib	L01EX22	**Retsevmo** as monotherapy is indicated for the treatment of adults and adolescents 12 years and older with advanced RET-mutant medullary thyroid cancer (MTC) who require systemic therapy following prior treatment with cabozantinib and/or vandetanib.	NO	> 12 years		YES
Thiotepa (Generic)	L01AC01	**Thiotepa Riemser** is indicated, in combination with other chemotherapy medicinal products: • with or without total body irradiation (TBI), as conditioning treatment prior to allogeneic or autologous haematopoietic progenitor cell transplantation (HPCT) in haematological diseases in adult and paediatric patients; • when high dose chemotherapy with HPCT support is appropriate for the treatment of solid tumours in adult and paediatric patients.	NO	children		NO
Potassium citrate monohydrated Potassium hydrogen carbonate	A12BA30	**Sibnayal** is indicated for the treatment of distal renal tubular acidosis (dRTA) in adults, adolescents and children aged one year and older.	NO	> 1 year		YES
Risdiplam	M09AX10	**Evrysdi** is indicated for the treatment of 5q spinal muscular atrophy (SMA) in patients 2 months of age and older, with a clinical diagnosis of SMA Type 1, Type 2 or Type 3 or with one to four SMN2 copies.	YES	2 months		YES
berotralstat	B06AC	**Orladeyo** is indicated for routine prevention of recurrent attacks of hereditary angioedema (HAE) in adult and adolescent patients aged 12 years and older.	NO	> 12 years		YES
estetrol monohydrate drospirenone	G03	Oral contraception. The decision to prescribe **Lydisilka** should take into consideration the individual woman's current risk factor	NO	> 16 years		YES
drospirenone estetrol monohydrate	G03	Oral contraception. The decision to prescribe **Drovelis** should take into consideration the individual woman's current risk facto	NO	> 16 years		YES
liraglutide	A10BJ02	Adolescents (≥12 years): **Saxenda** can be used as an adjunct to a healthy nutrition and increased physical activity for weight management in adolescent patients from the age of 12 years and above with:	NO	> 12 years	25/03/21 (26/04/21): Extension of Indication to include treatment as an adjunct to a healthy nutrition and increased physical	YES

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
		• obesity (BMI corresponding to ≥30 kg/m2 for adults by international cut-off points) and • body weight above 60 kg. Treatment with Saxenda should be discontinued and re-evaluated if patients have not lost at least 4% of their BMI or BMI z score after 12 weeks on the 3.0 mg/day or maximum tolerated dose.			activity for weight management in adolescent patients from the age of 12 years and above with obesity (BMI corresponding to ≥30 kg/m2 for adults) and body weight above 60 kg, based on Study NN8022-4180 that evaluated the efficacy of liraglutide 3.0 mg in adolescents aged 12 to less than 18 years with obesity	
budesonide formoterol fumarate dihydrate	R03AK07	Asthma **BiResp Spiromax** is indicated in adults and adolescents (12 years and older) for the regular treatment of asthma, where use of a combination (inhaled corticosteroid and long-acting β2 adrenoceptor agonist) is appropriate: -in patients not adequately controlled with inhaled corticosteroids and "as needed" inhaled short-acting β2 adrenoceptor agonists. or -in patients already adequately controlled on both inhaled corticosteroids and long-acting β2 adrenoceptor agonists.	NO	> 12 years	22/04/21 (21/05/21): Extension of Indication to include adolescents (12 years and older) for the regular treatment of asthma, where use of a combination (inhaled corticosteroid and long-acting β2 adrenoceptor agonist) is appropriate: in patients not adequately controlled with inhaled corticosteroids and "as needed" inhaled short-acting β2 adrenoceptor agonists; or in patients already adequately controlled on both inhaled corticosteroids and long-acting β2 adrenoceptor agonists	NO
budesonide formoterol fumarate dihydrate	R03AK07	Asthma **DuoResp Spiromax** is indicated in adults and adolescents (12 years and older) for the regular treatment of asthma, where use of a combination (inhaled corticosteroid and long-acting β2 adrenoceptor agonist) is appropriate: -in patients not adequately controlled with inhaled corticosteroids and "as needed" inhaled short-acting β2 adrenoceptor agonists. or -in patients already adequately controlled on both inhaled corticosteroids and long-acting β2 adrenoceptor agonists.	NO	> 12 years	22/04/21 (21/05/21): Extension of Indication to include adolescents (12 years and older) for the regular treatment of asthma, where use of a combination (inhaled corticosteroid and long-acting β2 adrenoceptor agonist) is appropriate: in patients not adequately controlled with inhaled corticosteroids and "as needed" inhaled short-acting β2 adrenoceptor agonists; or in patients already adequately controlled on both inhaled corticosteroids and long-acting β2 adrenoceptor agonists.	NO
hydrocortisone	H02AB09	**Efmody** Treatment of congenital adrenal hyperplasia (CAH) in adolescents aged 12 years and over and adults.	NO	> 12 years		NO
Rituximab (biosimilar)	L01XC02	Non-Hodgkin's lymphoma (NHL): **Rixathon** 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 Bcell lymphoma (DLBCL), Burkitt lymphoma (BL)/Burkitt leukaemia (mature B-cell acute leukaemia) (BAL) or Burkitt-like lymphoma (BLL). Granulomatosis with polyangiitis and microscopic polyangiitis: Rixathon, in combination with glucocorticoids, is indicated for the treatment of adult patients with severe, active granulomatosis	NO	>6 months (NHL) > 2 years Granulomatosis		NO

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
		with polyangiitis (Wegener's) (GPA) and microscopic polyangiitis (MPA). Rixathon, 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.				
Evinacumab	C10AX	**Evkeeza** is indicated as an adjunct to diet and other low-density lipoprotein-cholesterol (LDL-C) lowering therapies for the treatment of adult and adolescent patients aged 12 years and older with homozygous familial hypercholesterolaemia (HoFH).	NO	> 12 years		YES
teriflunomide	L04AA31	**AUBAGIO** is indicated for the treatment of adult patients and paediatric patients aged 10 years and older with relapsing remitting multiple sclerosis (MS) (please refer to section 5.1 for important information on the population for which efficacy has been established)	NO	> 10 years	22/04/21 (17/06/21): Extension of a marketing authorisation for Aubagio to add a new strength, 7 mg film-coated tablet, for use in paediatric patients from 10 years of age and older with relapsing remitting multiple sclerosis (MS). Extension of indication to include treatment of paediatric patients aged 10 years and older with relapsing remitting multiple sclerosis (MS) for Aubagio.	YES
azathioprine	L04AX01	Jayempi is indicated in combination with other immunosuppressive agents for the prophylaxis of transplant rejection in patients receiving allogenic kidney, liver, heart, lung or pancreas transplants. Azathioprine is indicated in immunosuppressive regimens as an adjunct to immunosuppressive agents that form the mainstay of treatment (basis immunosuppression). Jayempi is used as an immunosuppressant antimetabolite either alone or, more commonly, in combination with other agents (usually corticosteroids) and/ or procedures which influence the immune response. Jayempi is indicated in patients who are intolerant to glucocorticosteroids or if the therapeutic response is inadequate despite treatment with high doses of glucocorticosteroids, in the following diseases: - severe active rheumatoid arthritis (chronic polyarthritis) that cannot be kept under control by less toxic agents (disease-modifying anti-rheumatic -medicinal products – DMARDs) - auto-immune hepatitis - systemic lupus erythematosus - dermatomyositis - polyarteritis nodosa - pemphigus vulgaris and bullous pemphigoid - Behçet's disease - refractory auto-immune haemolytic anaemia, caused by warm IgG antibodies - chronic refractory idiopathic thrombocytopenic purpura Jayempi is used for the treatment of moderately severe to severe forms of chronic inflammatory bowel disease (IBD) (Crohn's disease or ulcerative colitis) in patients in whom glucocorticosteroid therapy is necessary, but where glucocorticosteroids are not tolerated, or in whom the disease is untreatable with other common means of first choice.	NO	all ages		NO

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
		It is also indicated in adult patients in relapsing multiple sclerosis, if an immunomodulatory therapy is indicated but beta interferon therapy is not possible, or a stable course has been achieved with previous treatment with azathioprine. Jayempi is indicated for the treatment of generalised myasthenia gravis. Depending on the severity of the disease, Jayempi should be given in combination with glucocorticosteroids because of slow onset of action at the beginning of treatment and the glucocorticosteroid dose should be gradually reduced after several months of treatment.				
satralizumab	L04AC	**Enspryng** is indicated as a monotherapy or in combination with immunosuppressive therapy (IST) for the treatment of neuromyelitis optica spectrum disorders (NMOSD) in adult and adolescent patients from 12 years of age who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive	YES	> 12 years		YES
Cinacalcet (Generic)	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. **Cinacalcet Mylan** may be used as part of a therapeutic regimen including phosphate binders and/or vitamin D sterols, as appropriate.	NO	> 3 years		NO
spheroids of human autologous matrix-associated chondrocytes	M09AX02	**Spherox** Repair of symptomatic articular cartilage defects of the femoral condyle and the patella of the knee (International Cartilage Regeneration & Joint Preservation Society [ICRS] grade III or IV) with defect sizes up to 10 cm2 in adults and adolescents with closed epiphyseal growth plate in the affected joint.	NO	adolescent	20/05/21 (28/06/21): Extension of the indication to include treatment of adolescents with closed epiphyseal growth plate in the affected joint	YES
COVID-19 mRNA Vaccine (nucleoside modified)	J07BX03	**Spikevax** is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 12 years of age and older.	NO	> 12 years	23/07/21 (23/07/21): Extension of indication to include use in adolescents from 12 to 17 years of age for Spikevax;	YES
setmelanotide	A08AA	**IMCIVREE** is indicated for the treatment of obesity and the control of hunger associated with genetically confirmed loss-of-function biallelic pro-opiomelanocortin (POMC), including PCSK1, deficiency or biallelic leptin receptor (LEPR) deficiency in adults and children 6 years of age and above.	YES	> 6 years		YES
odevixibat	A05AX	**Bylvay** is indicated for the treatment of progressive familial intrahepatic cholestasis (PFIC) in patients aged 6 months or older	YES	> 6 months		YES
Rituximab (biosimilar)	L01XC02	Non-Hodgkin's lymphoma (NHL): **Truxima** 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: Truxima, 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

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
Fingolimod (Generic)	L04AA27	**Fingolimod Mylan** 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: · Patients with highly active disease despite a full and adequate course of treatment with at least one disease modifying therapy. 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 magnetic resonance imaging (MRI) or a significant increase in T2 lesion load as compared to a previous recent MRI.	NO	> 10 years		NO
elivaldogene autotemcel	N07	**Skysona** is indicated for the treatment of early cerebral adrenoleukodystrophy in patients less than 18 years of age, with an ABCD1 genetic mutation, and for whom a human leukocyte antigen (HLA)-matched sibling haematopoietic stem cell (HSC) donor is not available	YES	3 to 18 years		YES
Icatibant (Generic)	B06AC02	**Icatibant Accord** is indicated for symptomatic treatment of acute attacks of hereditary angioedema (HAE) in adults, adolescents and children aged 2 years and older, with C1-esterase-inhibitor deficiency.	NO	> 2 years		NO
upadacitinib	L04AA	Atopic dermatitis: **RINVOQ** is indicated for the treatment of moderate to severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy.	NO	> 12 years	24/06/21 (20/08/21): Extension application to introduce a new strength (30 mg prolonged-release tablet), grouped with a type II variation (C.I.6.a) to add a new indication (treatment of moderate to severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy for Rinvoq).	YES
vosoritide	M05BX	**Voxzogo** is indicated for the treatment of achondroplasia in patients 2 years of age and older whose epiphyses are not closed. The diagnosis of achondroplasia should be confirmed by appropriate genetic testing.	YES	> 2 years		YES
tofacitinib	L04AA29	**Xeljanz** Juvenile idiopathic arthritis (JIA): Tofacitinib is indicated for the treatment of active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+]or negative [RF-] polyarthritis and extended oligoarthritis), and juvenile psoriatic arthritis (PsA) in patients 2 years of age and older, who have responded inadequately to previous therapy with DMARDs. Tofacitinib can be given in combination with methotrexate (MTX) or as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.	NO	> 2 years	24/06/21 (18/08/21): Extension application to introduce a new pharmaceutical form (oral solution, 1mg/ml) grouped with a type II variation (C.I.6.a) to add a new indication (treatment of active polyarticular course juvenile idiopathic arthritis (pJIA) in patients 2 years of age and older)	YES
Rituximab (biosimilar)	L01XC02	Non-Hodgkin's lymphoma (NHL): **Riximyo** 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 Bcell lymphoma (DLBCL), Burkitt lymphoma (BL)/Burkitt leukaemia (mature B-cell acute leukaemia) (BAL) or Burkitt-like lymphoma (BLL).	NO	> 6 months		NO

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
		Granulomatosis with polyangiitis and microscopic polyangiitis: Riximyo, 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.				
ambrisentan	C02KX02	**Volibris** is indicated for treatment of PAH in adolescents and children (aged 8 to less than 18 years) of WHO Functional Class (FC) II to III including use in combination treatment. Efficacy has been shown in IPAH, familial, corrected congenital and in PAH associated with connective tissue disease.	NO	> 8 years	**22/7/21 (22/9/21):** Extension application to introduce a new strength (2.5 mg film-coated tablet), grouped with an extension of indication to include treatment of PAH in adolescents and children (8 to less than 18 years).	YES
Imatinib (generic)	L01EA01	**Imatinib Koanaa** is indicated for the treatment of • adult and paediatric patients with newly diagnosed Philadelphia chromosome (bcr-abl) positive (Ph+) chronic myeloid leukaemia (CML) for whom bone marrow transplantation is not considered as the first line of treatment. • adult and paediatric patients with Ph+ CML in chronic phase after failure of interferon-alpha therapy, or in accelerated phase or blast crisis. • adult and paediatric patients with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) integrated with chemotherapy. In adult and paediatric patients, the effectiveness of imatinib is based on overall haematological and cytogenetic response rates and progression-free survival in CML, on haematological and cytogenetic response rates in Ph+ ALL, MDS/MPD, on haematological response rates in HES/CEL and on objective response rates in adult patients with unresectable and/or metastatic GIST and DFSP and on recurrence-free survival in adjuvant GIST. The experience with imatinib in patients with MDS/MPD associated with PDGFR gene re-arrangements is very limited (see section 5.1). Except in newly diagnosed chronic phase CML, there are no controlled trials demonstrating a clinical benefit or increased survival for these diseases.	NO	> 2 years		NO
selumetinib	Not yet assigned	**Koselugo** as monotherapy is indicated for the treatment of symptomatic, inoperable plexiform neurofibromas (PN) in paediatric patients with neurofibromatosis type 1 (NF1) aged 3 years and above.	YES	> 3 years		YES
sofosbuvir velpatasvir voxilaprevi	J05A	**Vosevi** is indicated for the treatment of chronic hepatitis C virus (HCV) infection in patients aged 12 years and older and weighing at least 30 kg	NO	> 12 years	**22/07/21 (16/09/21):** Extension application to introduce a new strength (200 mg /50 mg /50 mg film-coated tablets). The new presentation is indicated for the treatment of chronic hepatitis C virus (HCV) infection in patients aged 12 years and older or weighing at least 30 kg,	YES
Pembrolizumab	L01XC18	Classical Hodgkin lymphoma (cHL) **KEYTRUDA** as monotherapy is indicated for the treatment of adult and paediatric patients aged 3 years and older with relapsed or refractory classical Hodgkin lymphoma who have failed autologous stem cell transplant (ASCT) or following at least two prior therapies when ASCT is not a treatment option.	NO	> 3 years	28/01/21 (09/03/21): Extension of the currently approved therapeutic indication for the treatment of relapsed or refractory classical Hodgkin lymphoma (rrcHL) in adults to an earlier line of therapy and to	YES

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
					include paediatric patients - as follows: KEYTRUDA as monotherapy is indicated for the treatment of adult and paediatric patients aged 3 years and older with relapsed or refractory classical Hodgkin lymphoma (cHL) who have failed autologous stem cell transplant (ASCT) following at least one prior therapy when ASCT is not a treatment option.	
melphalan	L01AA03	High-dose of **PHELINUN** used alone or in combination with other cytotoxic medicinal products and/or total body irradiation is indicated in the treatment of: - multiple myeloma, - acute lymphoblastic and myeloblastic leukemia, - childhood neuroblastoma, PHELINUN in combination with other cytotoxic medicinal products is indicated as conditioning regimen prior to allogeneic haematopoietic stem cell transplantation in haematological diseases in the paediatric population as: - Myeloablative conditioning (MAC) treatment in case of malignant haematological diseases - RIC treatment in case of non-malignant haematological diseases.	NO	> 2 years		NO
Sucroferric oxyhydroxide	V03AE05	**Velphoro** is indicated for the control of serum phosphorus levels in paediatric patients 2 years of age and older with CKD stages 4-5 (defined by a glomerular filtration rate <30 mL/min/1.73 m²) or with CKD on dialysis.	NO	> 2 years	17/09/20 (16/11/20): extension of indication to add an indication to use Velphoro for the control of serum phosphorus levels in paediatric patients 2 years of age and older with CKD stages 4-5 (defined by a glomerular filtration rate <30 mL/min/1.73 m2) or with CKD on dialysis, based on the results from an open-label, randomised, active-controlled, parallel group, multicentre, phase 3 study investigating the safety and efficacy of Velphoro and calcium acetate in paediatric and adolescent CKD patients with hyperphosphataemia (Study PA-CL-PED-01).	YES
meningococcal group A, C, W-135 and Y conjugate vaccine	J07AH08	**MenQuadfi** is indicated for active immunisation of individuals from the age of 12 months and older against invasive meningococcal disease caused by Neisseria meningitidis serogroups A, C, W, and Y. The use of this vaccine should be in accordance with available official recommendations.	NO	> 12 months		YES
Obiltoxaximab	J06BB22	**Obiltoxaximab SFL** is indicated in combination with appropriate antibacterial drugs in all age groups for treatment of inhalational anthrax due to Bacillus anthracis. Obiltoxaximab SFL is indicated in all age groups for post-exposure prophylaxis of inhalational anthrax when alternative therapies are not appropriate or are not available	YES	all ages		YES

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

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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.

7. ANNEX 1 - Drug approved in the period November-December 2021

[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.*

ANNEX 1

In the period November – December 2021, 14 active substances (ASs) have been approved by EMA under the Centralised Procedure: 3 of them were paediatric (21%)

1. Drug approved in the period November-December 2021

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations	PIP
casirivimab/imdevimab	J06BD	**Ronapreve** is indicated for:Treatment of COVID-19 in adults and adolescents aged 12 years and older weighing at least 40 kg who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19. Prevention of COVID-19 in adults and adolescents aged 12 years and older weighing at least 40 kg. The use of Ronapreve should take into account information on the activity of Ronapreve against viral variants of concern	NO	> 12 years		YES
atazanavir/cobicistat	J05AR15	**EVOTAZ** is indicated in combination with other antiretroviral medicinal products for the treatment of HIV-1 infected adults and adolescents (aged 12 years and older weighing at least 35 kg) without known mutations associated with resistance to atazanavir	NO	> 12 years	20/05/21 (21/06/21): Extension of indication to include the use of EVOTAZ in combination with other antiretroviral agents in the treatment of HIV-1 infection in adolescent patients aged ≥ 12 to < 18 years, weighing ≥ 35 kg without known mutations associated with resistance to atazanavir	YES
Sugammadex (generic)	V03AB35	**Sugammadex Mylan** 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
Rivaroxaban (generic)	B01AF01	**Rivaroxaban Mylan** **Paediatric population** Treatment of venous thromboembolism (VTE) and prevention of VTE recurrence in children and adolescents aged less than 18 years and weighing from 30 kg to 50 kg after at least 5 days of initial parenteral anticoagulation treatment.	NO	children from 30 kg		NO
casirivimab/imdevimab	J06BD05	**Xevudy** is indicated for the treatment of adults and adolescents (aged 12 years and over and weighing at least 40 kg) with coronavirus disease 2019 (COVID-19) who do not require oxygen supplementation and who are at increased risk of progressing to severe COVID-19	NO	> 12 years weighing 40 kg		YES