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 2017.[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 2017.

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.

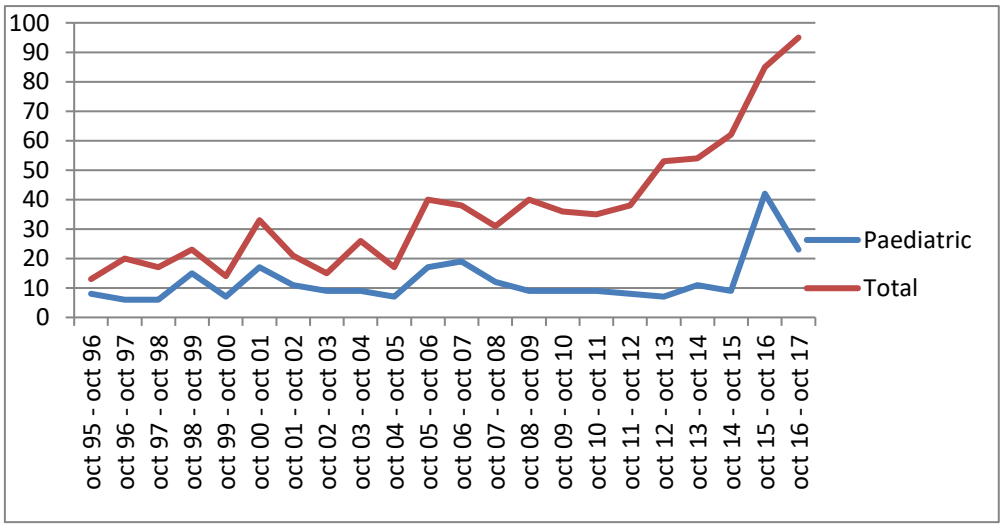
4. Results

4.1. Number and percentage of paediatric medicines

In the period October 1995 – October 2017, 733 active substances (ASs) have been approved by EMA under the Centralised Procedure: 228 of them were paediatric (31%).[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. 2017)

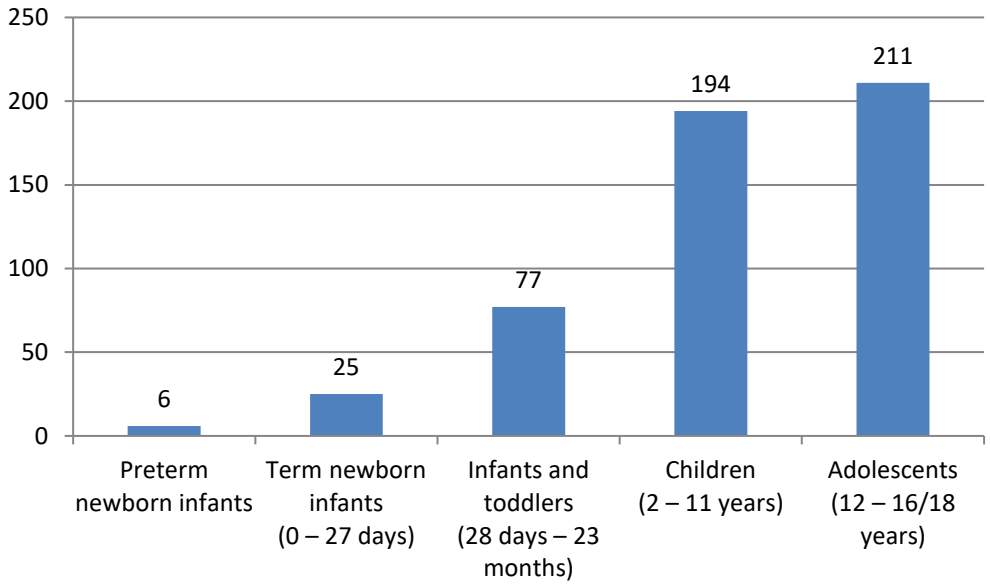


[1] In the first ten years period covered by this report (1995-2005), medicines that included in their documentation (Summary of Product Characteristics – SPC/PL) a paediatric dosages information, but not a paediatric indication, were also considered as paediatric.

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, while D-ATC (D – Dermatologicals), G-ATC (Genito-urinary system and sex hormones), M-ATC (Musculo-skeletal system) and P-ATC (Antiparasitic) the lowest ones. Table 1 provides additional details.

Table 1: EMA Paediatric Medicines by ATC code

	Paediatric/Total	
	N	**%**
A -Alimentary tract and metabolism	41/91	45
B - Blood and blood forming organs	25/58	43
C - Cardiovascular system	5/38	13
D - Dermatologicals	2/10	10
G- Genito-urinary system and sex hormones	2/31	6
H - Systemic hormonal preparations, excluding sex hormones and insulins	3/14	21

	Paediatric/Total	
	N	**%**
J - Anti-infectives for systemic use	70/139	50
L - Antineoplastic and immunomodulating agents	39/173	22
M - Musculo-skeletal system	2/21	9
N - Nervous system	15/58	26
P -Antiparasitic products, insecticides and repellents	1/1	100
R - Respiratory system	8/25	32
S - Sensory organs	4/23	17
V -Various	11/45	24
Not assigned yet	0/6	-
TOTAL	***228/733***	***31%***

4.4. Distribution of paediatric medicines by orphan status

With reference to orphan drugs, it should be noted that out of the 112 orphan drugs authorised by the EMA in the period October 1995 – October 2017 under the OD Regulation rules, 44 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 (39% and 31%, respectively).

Table 2 – Paediatric orphan drugs and ATC distribution

ATC	Orphan drugs authorised	Paediatric orphan drugs authorised	Percentage
A -Alimentary tract and metabolism	19	17	89
B - Blood and blood forming organs	5	4	80
C - Cardiovascular system	5	0	-
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	7	4	57
L - Antineoplastic and immunomodulating agents	49	10	20
M - Musculo-skeletal system	1	1	100
N - Nervous system	8	5	62
P -Antiparasitic products, insecticides and repellents	0	0	-
R - Respiratory system	2	1	50
S - Sensory organs	3	1	33
V -Various	4	1	25
Not assigned yet	2	0	-
TOTAL	**112**	**44**	***39%***

5. New paediatric drug from October 2016 to October 2017

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations
Darunavir (generic)	J05AE10	Darunavir Mylan tablets may be used to provide suitable dose regimens: For the treatment of HIV-1 infection in paediatric patients from the age of 3 years and at least 15 kg body weight. Darunavir Mylan tablets may be used to provide suitable dose regimens for the treatment of HIV-1 infection in adult and paediatric patients from the age of 3 years and at least 40 kg body weight who are: antiretroviral therapy (ART)-naïve. ART-experienced with no darunavir resistance associated mutations (DRV-RAMs) and who have plasma HIV-1 RNA < 100,000 copies/ml and CD4+ cell count ≥ 100 cells x 106/l. In deciding to initiate treatment with darunavir in such ART-experienced patients, genotypic testing should guide the use of darunavir.	NO	> 3 years	
tenofovir disoproxil (generic)	J05AF07	**HIV-1 infection:** Tenofovir disoproxil 245 mg film-coated tablets are also indicated for the treatment of HIV-1 infected adolescents, with NRTI resistance or toxicities precluding the use of first line agents, aged 12 to < 18 years. **Hepatitis B infection**: Tenofovir disoproxil 245 mg film-coated tablets are indicated for the treatment of chronic hepatitis B in adolescents 12 to < 18 years of age with compensated liver disease and evidence of immune active disease, i.e. active viral replication, persistently elevated serum ALT levels and histological evidence of active inflammation and/or fibrosis.	NO	>12 years	
tenofovir alafenamide	J05AF13	Vemlidy is indicated for the treatment of chronic hepatitis B in adults and adolescents (aged 12 years and older with body weight at least 35 kg)	NO	>12 years with body weight at least 35 kg	
Sildenafil (generic)	G04BE03	Treatment of paediatric patients aged 1 year to 17 years old with pulmonary arterial hypertension. Efficacy in terms of improvement of exercise capacity or pulmonary haemodynamics has been shown in primary pulmonary hypertension and pulmonary hypertension associated with congenital heart disease	NO	> 1 year	
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 **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 > 6 years > 12 years	
insulin glargine	A10AE04	Treatment of diabetes mellitus in adults, adolescents and children aged 2 years and above.	NO	> 2 years	
lonoctocog alfa	B02BD02	Treatment and prophylaxis of bleeding in patients with	NO	All ages	

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations
		haemophilia A (congenital factor VIII deficiency). Afstyla can be used for all age groups.			
Adalimumab	L04AB04	**Enthesitis-related arthritis:** SOLYMBIC 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:** SOLYMBIC 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:** SOLYMBIC 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, a corticosteroid, and an immunomodulator, or who are intolerant to or have contraindications for such therapies.	YES	> 4 years > 6 years	
adalimumab	L04AB04	***Juvenile Idiopathic Arthritis*** -Polyarticular juvenile idiopathic arthritis: AMGEVITA 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). AMGEVITA 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: AMGEVITA 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***: AMGEVITA 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***: AMGEVITA 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, a corticosteroid, and an immunomodulator, or who are intolerant to or have contraindications for such therapies.	NO	> 2 years > 4 years > 6 years	
simoctocog alfa	B02BD02	Treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency). Vihuma can be used for all age groups.	NO	all ages	
methotrexate	L01BA01	**In rheumatological and dermatological diseases** -Polyarthritic forms of active, severe juvenile idiopathic arthritis (JIA) in adolescents and children aged 3 years and over when the response to non-steroidal anti-inflammatory drugs (NSAIDs) has been inadequate. **In oncology** Maintenance treatment of acute lymphoblastic leukaemia (ALL) in adults, adolescents and children aged 3 years and over.	NO	> 3 years	
meningococcal group b vaccine (recombinant,	J07AH09	Trumenba is indicated for active immunisation of individuals 10 years and older to prevent invasive meningococcal disease caused by Neisseria	NO	> 10 years	

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations
adsorbed)		meningitidis serogroup B. The use of this vaccine should be in accordance with official recommendations.			
dinutuximab beta	L01XC	Qarziba is indicated for the treatment of high-risk neuroblastoma in patients aged 12 months and above, who have previously received induction chemotherapy and achieved at least a partial response, followed by myeloablative therapy and stem cell transplantation, as well as patients with history of relapsed or refractory neuroblastoma, with or without residual disease. Prior to the treatment of relapsed neuroblastoma, any actively progressing disease should be stabilised by other suitable measures. In patients with a history of relapsed/refractory disease and in patients who have not achieved a complete response after first line therapy, Qarziba should be combined with interleukin-2 (IL-2).	YES	> 1 year	
nusinersen	M09AX07	Treatment and prophylaxis of bleeding in patients 12 years and above with haemophilia B (congenital factor IX deficiency).	YES	all ages	
cerliponase alfa	A16AB	**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.	YES	all ages	
nonacog beta pegol	B02BD04		NO	> 12 years	
etanercept	L04AB01	For the treatment of adults and children with diabetes mellitus who require insulin for the maintenance of normal glucose homeostasis. Insulin lispro Sanofi is also indicated for the initial stabilisation of diabetes mellitus.	NO	> 2 years > 6 years > 12 years	
carglumic acid (generic)	A16AA05	**Juvenile idiopathic arthritis** -Polyarticular juvenile idiopathic arthritis: Imraldi 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). Imraldi 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: Imraldi 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:** Imraldi 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	NO	all ages	

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations
		phototherapies. **Hidradenitis suppurativa (HS):** Imraldi 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:** Imraldi 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.			
insulin lispro	A10AB04	Treatment of adult and paediatric (in any age range) patients with confirmed diagnosis of hereditary tyrosinemia type 1 (HT 1) in combination with dietary restriction of tyrosine and phenylalanine.	NO	> 2 years	
adalimumab	L04AB04	Cuprior is indicated for the treatment of Wilson's disease in adults, adolescents and children ≥ 5 years intolerant to D-penicillamine therapy.	NO	> 2 years > 4 years > 6 years > 12 years	
Nitisinone (generic)	A16AX04	Treatment and prophylaxis of bleeding in patients 12 years and above with haemophilia B (congenital factor IX deficiency).	NO	all ages, dosage for weight	
trientine	A16AX	**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	> 5 years	
Entecavir (generic)	J05AF10	Entecavir Mylan is also indicated for the treatment of chronic HBV infection in nucleoside naive paediatric patients from 2 to <18 years of age with compensated liver disease who have evidence of active viral replication and persistently elevated serum ALT levels, or histological evidence of moderate to severe inflammation and/or fibrosis. With respect to the decision to initiate treatment in paediatric patients.	NO	> 2 years	
Lacosamide (generic)	N03AX18	Lacosamide Accord is indicated as monotherapy and adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 4 years of age with epilepsy.	NO	> 4 years	
darunavir/cobicistat /emtricitabine/tenofovir alafenamide	J05AR22	Symtuza is indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults and adolescents (aged 12 years and older with body weight at least 40 kg).	NO	> 12 years 40 kg	
Adalimumab	L04AB04	**Juvenile idiopathic arthritis** Polyarticular juvenile idiopathic arthritis: Adalimumab 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-	YES	> 2 years > 4 years > 6 years > 12 years	

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations
		modifying anti-rheumatic drugs (DMARDs). Adalimumab 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: Adalimumab 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:** Cyltezo 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):** Cyltezo is indicated for the treatment of active moderate to severe hidradenitis suppurativa (acne inversa) in adults and adolescents from 12 years of agewith an inadequate response to conventional systemic HS therapy. **Paediatric Crohn's disease:** Cyltezo 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. **Paediatric Uveitis:** Cyltezo 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.			
Ritonavir (generic)	J05AE03	Ritonavir is indicated in combination with other antiretroviral agents for the treatment of HIV 1 infected patients (adults and children of 2 years of age and older).	NO	> 2 years	
ledispavir 90 mg / sofosbuvir 400 mg	J05AX65	Harvoni is indicated for the treatment of chronic hepatitis C (CHC) in adults and in adolescents aged 12 to < 18 years	NO	> 12 years	11/11/16 (22/06/17): Extension of indication to add treatment of chronic hepatitis C in adolescents aged 12 to < 18 years.
vandetanib	L01XE	Caprelsa is indicated for the treatment of aggressive and symptomatic medullary thyroid cancer (MTC) in patients with unresectable locally advanced or metastatic disease. Caprelsa is indicated in adults, children and adolescents aged 5 years and older. For patients in whom re-arranged-during-transfection(RET) mutation is not known or is negative, a possible lower benefit should be taken into account before individual treatment decision.	NO	> 5 years	10/11/16 (16/12/16): Extension of Indication to include paediatric patients aged 5 to 18 with unresectable locally advanced or metastatic medullary thyroid carcinoma (MTC) for Caprelsa
eslicarbazepine acetate	N03AF04	Zebinix is indicated as: - adjunctive therapy in adults, adolescents and children aged above 6 years, with partial-onset seizures with or without secondary generalisation.	NO	> 6 years	23/03/17 (28/04/17): Extension of indication for the tablet formulation to include the use of Zebinix as monotherapy in the treatment of partial-onset seizures, with or without secondary generalisation, in adults with newly diagnosed epilepsy, in addition to the previously authorised indication as adjunctive therapy.

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations
					13/10/16 (08/12/16) Addition of a new therapeutic indication or modification of an approved one. In the opinion: "Zebinix is indicated as adjunctive therapy in adults, adolescents and children aged above 6 years, with partial-onset seizures with or without secondary generalisation". In addition, Zebinix will be available as an oral suspension (50 mg/ml)
mercaptamine hydrochloride	S01XA21	Cystadrops is indicated for the treatment of corneal cystine crystal deposits in adults and children from 2 years of age with cystinosis	YES	> 2 years	
elvitegravir / cobicistat / emtricitabine / tenofovir disoproxil fumarate	J05AR09	Stribild is also indicated for the treatment of HIV-1 infection in adolescents aged 12 to < 18 years weighing ≥ 35 kg who are infected with HIV-1 without known mutations associated with resistance to any of the three antiretroviral agents in Stribild and who have experienced toxicities which preclude the use of other regimens that do not contain tenofovir disoproxil fumarate (TDF)	NO	> 12 years	14/09/17 (19/10/17): Extension of Indication to include the treatment of HIV 1 infection in adolescents aged 12 to < 18 years weighing ≥ 35 kg without known mutations associated with resistance to any of the three antiretroviral agents in Stribild, and who have experienced toxicities which preclude the use of other regimens that do not contain tenofovir disoproxil fumarate (TDF);
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 > 6 years > 12 years	15/12/16 (27/01/17): Extension of indication to include two new indications for the treatment of juvenile idiopathic arthritis and paediatric plaque psoriasis already approved for the reference medicinal product (Enbrel) for Benepali.
emtricitabine / tenofovir disoproxil (generic)	J05AR03	Emtricitabine/Tenofovir disoproxil Zentiva is also indicated for the treatment of HIV-1 infected adolescents, with NRTI resistance or toxicities precluding the use of first line agents	NO	> 12 years weighing at least 35 kg	
emtricitabine / tenofovir disoproxil (generic)	J05AR03	Emtricitabine/Tenofovir disoproxil Krka d.d. is also indicated for the treatment of HIV-1 infected adolescents, with NRTI resistance or toxicities precluding the use of first line agents, aged 12 to < 18 years.	NO	> 12 years weighing at least 35 kg	
cinacalcet	H05BX01	Secondary hyperparathyroidism 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 Mimpara may be used as part of a therapeutic regimen including phosphate binders and/or Vitamin D sterols, as appropriate	NO	> 3 years	22/06/17 (28/08/17): Extension application to introduce a new pharmaceutical form associated with new strengths (1 mg, 2.5 mg and 5 mg hard capsules) grouped with a type II variation (C.1.6.a) to include paediatric use in the approved indication.

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations
sofosbuvir	J05AX15	Sovaldi is indicated in combination with other medicinal products for the treatment of chronic hepatitis C (CHC) in adults and in adolescents aged 12 to <18 years	NO	> 12 years	20/07/17 (14/09/17): Extension of indication to add treatment of chronic hepatitis C in adolescents aged 12 to <18 years
emtricitabine / tenofovir disoproxil	J05AR03	Truvada is also indicated for the treatment of HIV-1 infected adolescents, with NRTI resistance or toxicities precluding the use of first line agents. Pre-exposure prophylaxis (PrEP): Truvada is indicated in combination with safer sex practices for pre-exposure prophylaxis to reduce the risk of sexually acquired HIV-1 infection in adults and adolescents at high risk	NO	> 12 years weighing at least 35 kg	23/02/17 (24/03/17): Extension of Indication for Truvada in the treatment of human immunodeficiency virus, type 1 (HIV-1) infected adolescents, with nucleoside reverse transcriptase inhibitor (NRTI) resistance or toxicities precluding the use of first line agents, aged 12 to <18 years.
emtricitabine / tenofovir disoproxil (generic)	J	Treatment of HIV-1 infection: Emtricitabine/Tenofovir disoproxil Krka is also indicated for the treatment of HIV-1 infected adolescents, with NRTI resistance or toxicities precluding the use of first line agents. Pre-exposure prophylaxis (PrEP): Emtricitabine/ Tenofovir disoproxil Krka is indicated in combination with safer sex practices for preexposure prophylaxis to reduce the risk of sexually acquired HIV-1 infection in adults and adolescents at high risk	NO	> 12 years weighing at least 35 kg	
Entecavir (generic)	J	Entecavir Accord is also indicated for the treatment of chronic HBV infection in nucleoside naive paediatric patients from 2 to < 18 years of age with compensated liver disease who have evidence of active viral replication and persistently elevated serum ALT levels, or histological evidence of moderate to severe inflammation and/or fibrosis. With respect to the decision to initiate treatment in paediatric patients	NO	> 2 years	
sevelamer carbonate	V	Renvela is indicated for the control of hyperphosphataemia in paediatric patients (>6 years of age and a Body Surface Area (BSA) of >0.75 m2) with chronic kidney disease.	NO	> 6 years	18/05/17 (26/06/17): Extension of indication for Renvela 1.6 g and 2.4 g powder for oral suspension and Sevelamer carbonate Zentiva 2.4 g powder for oral suspension to include the control of hyperphosphataemia in paediatric patients (>6 years of age and a Body Surface Area (BSA) of >0.75 m2) with chronic kidney disease
chenodeoxycholic acid	A	Chenodeoxycholic acid is indicated for the treatment of inborn errors of primary bile acid synthesis due to sterol 27 hydroxylase deficiency (presenting as cerebrotendinous xanthomatosis (CTX)) in infants, children and adolescents aged 1 month to 18 years and adults.	YES	> 1 month	
travoprost	S	Decrease of elevated intraocular pressure in adult patients with ocular hypertension or open-angle glaucoma. Decrease of elevated intraocular pressure in paediatric patients aged 3 years to < 18 years with ocular hypertension or paediatric glaucoma.	NO	> 3 years	18/05/17 (23/06/17): Extension of Indication to include treatment of paediatric patients aged 3 years to < 18 years with ocular hypertension or paediatric glaucoma in order to decrease of elevated intraocular pressure.
sevelamer carbonate	V	Sevelamer carbonate Zentiva is indicated for the control of hyperphosphataemia in paediatric patients (>6 years of age and a Body Surface Area (BSA) of >0.75 m2) with chronic kidney disease.	NO	> 6 years	18/05/17 (23/06/17): Extension of indication for Renvela 1.6 g and 2.4 g powder for oral suspension and Sevelamer carbonate Zentiva 2.4 g powder for oral suspension to include the control of hyperphosphataemia in

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations
					paediatric patients (>6 years of age and a Body Surface Area (BSA) of >0.75 m2) with chronic kidney disease
maraviroc	J	CELSENTRI, in combination with other antiretroviral medicinal products, is indicated for treatment-experienced adults, adolescents and children of 2 years of age and older and weighing at least 10 kg infected with only CCR5-tropic HIV-1 detectable	NO	> 2 years	21/04/17 (06/07/17): Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one - The MAH applied for the addition of a new pharmaceutical form (20mg/ml oral solution), and 2 new strengths for film coated tablets (25 mg, 75 mg). In addition, the MAH proposed to extend the indication for Celsentri, in combination with other antiretroviral medicinal products for treatment experienced adolescents and children of 2 years of age and older infected with only CCR5-tropic HIV-1 detectable

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.

[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.*