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 2018.[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 2018.

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.

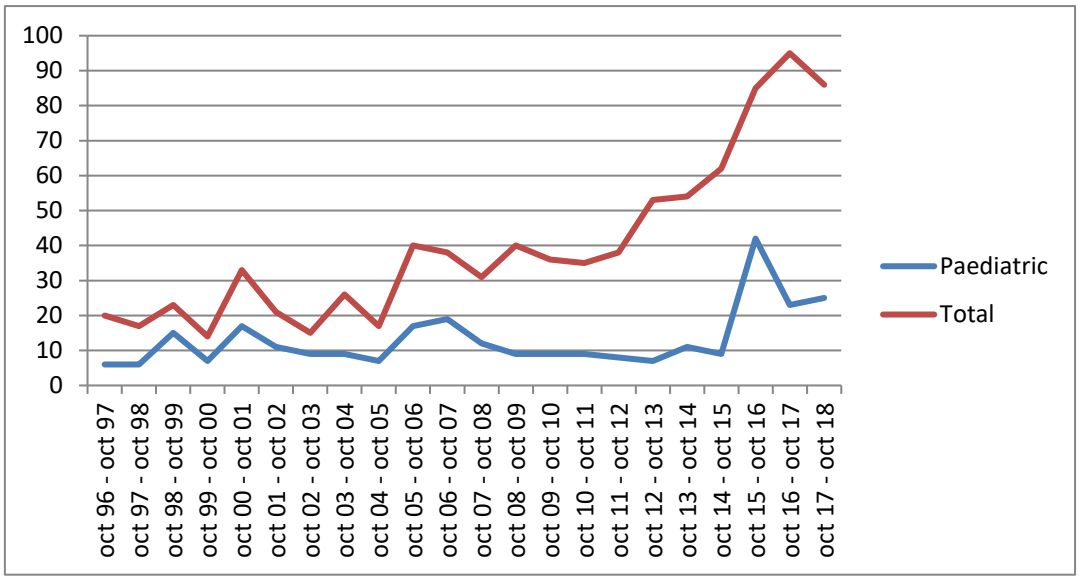
4. Results

4.1. Number and percentage of paediatric medicines

In the period October 1995 – October 2018, 783 active substances (ASs) have been approved by EMA under the Centralised Procedure: 253 of them were paediatric (32%).[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. 2018)

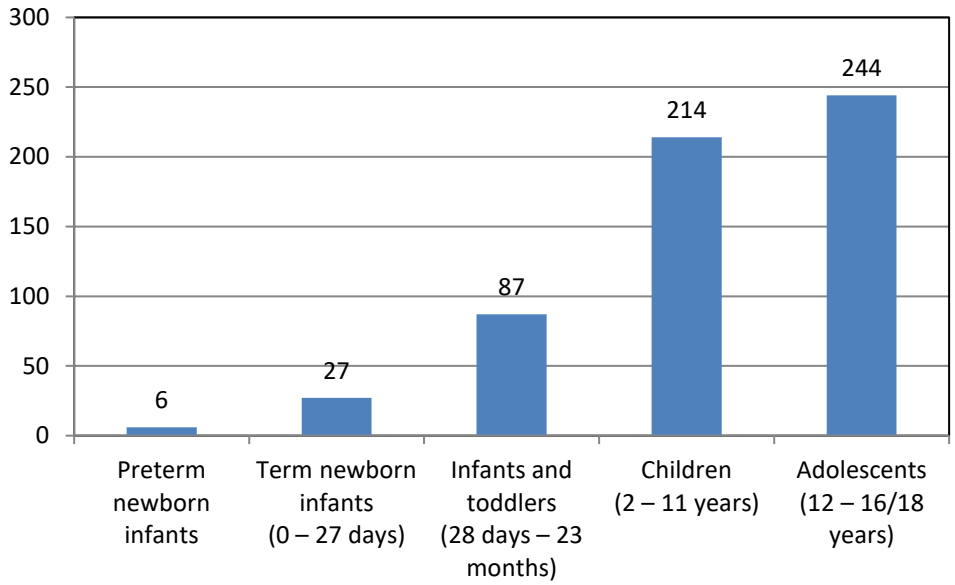


[1] In the first ten years period covered by this report (1995-2005), medicines that included in their documentation (Summary of Product Characteristics – SPC/PL) a paediatric dosages information, but not a paediatric indication, were also considered as paediatric.

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), 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	46/100	46
B - Blood and blood forming organs	28/62	45
C - Cardiovascular system	6/38	16
D - Dermatologicals	2/10	20
G- Genito-urinary system and sex hormones	2/32	6
H - Systemic hormonal preparations, excluding sex hormones and insulins	4/14	28

	Paediatric/Total	
	N	**%**
J - Anti-infectives for systemic use	71/145	49
L - Antineoplastic and immunomodulating agents	46/190	24
M - Musculo-skeletal system	3/23	13
N - Nervous system	17/64	26
P -Antiparasitic products, insecticides and repellents	1/1	100
R - Respiratory system	10/27	37
S - Sensory organs	5/24	20
V -Various	12/47	25
Not assigned yet	0/6	-
TOTAL	***253/783***	***32%***

4.4. Distribution of paediatric medicines by orphan status

With reference to orphan drugs, it should be noted that out of the 129 orphan drugs authorised by the EMA in the period October 1995 – October 2018 under the OD Regulation rules, 57 were paediatric. Thus, comparing the rate of paediatric medicines between orphan and non-orphan drug groups, a significant difference in favour of paediatric medicines in the orphan drug group is evident (42% and 32%, respectively).

Table 2 – Paediatric orphan drugs and ATC distribution

ATC	Orphan drugs authorised	Paediatric orphan drugs authorised	Percentage
A -Alimentary tract and metabolism	24	21	87
B - Blood and blood forming organs	6	5	83
C - Cardiovascular system	5	1	20
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	8	4	50
L - Antineoplastic and immunomodulating agents	55	14	25
M - Musculo-skeletal system	2	2	100
N - Nervous system	10	5	50
P -Antiparasitic products, insecticides and repellents	0	0	-
R - Respiratory system	2	2	100
S - Sensory organs	4	2	50
V -Various	4	1	25
Not assigned yet	2	0	-
TOTAL	**129**	**57**	***42%***

5. New paediatric drug from October 2017 to October 2018

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations
Buprenorphine / naloxone	N07BC51	Substitution treatment for opioid drug dependence, within a framework of medical, social and psychological treatment. The intention of the naloxone component is to deter intravenous misuse. Treatment is intended for use in adults and adolescents over 15 years of age who have agreed to be treated for addiction.	NO	> 15 years	
Anakinra	L04AC03	*Cryopyrin-Associated Periodic Syndromes (CAPS)*: Kineret is indicated in adults, adolescents, children and infants aged 8 months and older with a body weight of 10 kg or above for the treatment of CAPS, including: - Neonatal-Onset Multisystem Inflammatory Disease (NOMID) / Chronic Infantile Neurological, Cutaneous, Articular Syndrome (CINCA) - Muckle-Wells Syndrome (MWS) - Familial Cold Autoinflammatory Syndrome (FCAS) *Still's Disease*: Kineret is indicated in adults, adolescents, children and infants aged 8 months and older with a body weight of 10 kg or above for the treatment of Still's disease, including Systemic Juvenile Idiopathic Arthritis (SJIA) and Adult-Onset Still's Disease (AOSD), with active systemic features of moderate to high disease activity, or in patients with continued disease activity after treatment with non-steroidal anti-inflammatory drugs (NSAIDs) or glucocorticoids. Kineret can be given as monotherapy or in combination with other anti-inflammatory drugs and disease-modifying antirheumatic drugs (DMARDs).	NO	> 8 months body weight of 10 kg	22/02/18 (06/04/18): Extension of indication to include a new indication for Kineret 100 mg/0.67 ml solution for injection in prefilled syringe for the treatment of Still's disease, including Systemic Juvenile Idiopathic Arthritis and Adult-Onset Still's Disease.
Darunavir (generic)	J05AE10	400mg and 800 mg Film-coated Tablets Darunavir Krka d.d., co-administered with low dose ritonavir is indicated in combination with other antiretroviral medicinal products for the treatment of patients with human immunodeficiency virus (HIV-1) infection. Darunavir Krka d.d., co-administered with cobicistat is indicated in combination with other antiretroviral medicinal products for the treatment of patients with human immunodeficiency virus (HIV-1) infection in adult patients . Darunavir Krka d.d. 400 mg and 800 mg 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). 600mg Film-coated Tablets: Darunavir Krka d.d., co-administered with low dose ritonavir is indicated in combination with other antiretroviral medicinal products for the treatment of patients with human immunodeficiency virus (HIV-1) infection. Darunavir Krka d.d. 600 mg tablets may be used to provide suitable dose regimens: For the treatment of HIV-1 infection in antiretroviral treatment (ART)-experienced adult patients, including those that have been highly pre-treated.	NO	> 3 years	

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations
		For the treatment of HIV-1 infection in paediatric patients from the age of 3 years and at least 15 kg body weight. In deciding to initiate treatment with darunavir co-administered with low dose ritonavir, careful consideration should be given to the treatment history of the individual patient and the patterns of mutations associated with different agents. Genotypic or phenotypic testing (when available) and treatment history should guide the use of darunavir.			
Ipilimumab	L01XC11	Yervoy is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults, and adolescents 12 years of age and older.	NO	> 12 years	26/04/18 (31/05/18): Extension of indication to include the treatment of advanced (unresectable or metastatic) melanoma in adults in combination with nivolumab for Yervoy. 14/12/17 (18/1/18): Extension of indication to include the treatment of advanced (unresectable or metastatic) melanoma in adults and adolescents 12 years of age and older for Yervoy
Icatibant	B06AC02	Firazyr 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	YES	> 2 years	14/09/17 (19/10/17): Extension of Indication to include adolescents and children aged 2 years and older, with C1-esteraseinhibitor deficiency, for the use of Firazyr for symptomatic treatment of acute attacks of hereditary angioedema
Naloxone	V03AB15	Nyxoid is intended for immediate administration as emergency therapy for known or suspected opioid overdose as manifested by respiratory and/or central nervous system depression in both non-medical and healthcare settings. Nyxoid is indicated in adults and adolescents aged 14 years and over. Nyxoid is not a substitute for emergency medical care.	NO	> 14 years	
Darunavir (generic)	J05AE10	Darunavir Krka 400 mg and 800 mg 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 Darunavir Krka 600 mg tablets may be used to provide suitable dose regimens: For the treatment of HIV-1 infection in antiretroviral treatment (ART)-experienced adult patients, including those that have been highly pre-treated. For the treatment of HIV-1 infection in paediatric patients from the age of 3 years and at least 15 kg body weight.	NO	> 3 years	
Rurioctocog alfa pegol	B02BD02	Treatment and prophylaxis of bleeding in patients 12 years and above with haemophilia A (congenital factor VIII deficiency).	NO	> 12 years	

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations
Travoprost	S01EE04	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.
Hydrocortisone	H02AB09	Replacement therapy of adrenal insufficiency in infants, children and adolescents (from birth to < 18 years old).	NO	all ages	
Emicizumab	B02BX	Hemlibra is indicated for routine prophylaxis of bleeding episodes in patients with haemophilia A with factor VIII inhibitors. Hemlibra can be used in all age groups.	NO	> 1 year	
Romiplostim	B02BX04	Nplate is indicated for chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients one year of age and older who are refractory to other treatments (e.g. corticosteroids, immunoglobulins)	YES	> 1 year	09/11/17 (30/01/18): Extension of Indication to include paediatric population for Nplate: to register Nplate for the use in the paediatric chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients: 1 year of age and older.
Burosumab	M05BX05	CRYSVITA is indicated for the treatment of X-linked hypophosphataemia with radiographic evidence of bone disease in children 1 year of age and older and adolescents with growing skeletons.	YES	> 1 year	
Imatinib (generic)	L01XE01	Imatinib Teva B.V. is indicated for the treatment of •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. •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. There are no controlled trials demonstrating a clinical benefit or increased survival for these diseases.	NO	> 2 years	09/10/18: withdrawal - commercial reasons
Nilotinib	L01XE08	Tasigna is indicated for the treatment of: - adult and paediatric patients with newly diagnosed Philadelphia chromosome positive chronic myelogenous leukaemia (CML) in the chronic phase, - paediatric patients with chronic phase Philadelphia chromosome positive CML with resistance or intolerance to prior therapy including imatinib.	YES	Paediatric patients	14/09/17 (15/11/17): Extension of Indication to include treatment of paediatric patients with newly diagnosed Philadelphia chromosome-positive chronic myelogenous leukaemia in chronic phase (Ph+ CML-CP), or with Ph+CML-CP resistant or intolerant to prior

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations
					therapy including imatinib
Velmanase alfa	A16AB15		YES	> 6 years	
Peramivir	J05AH03	Alpivab is indicated for the treatment of uncomplicated influenza in adults and children from the age of 2 years	NO	> 2 years	
Fosaprepitant	A04AD12	Prevention of nausea and vomiting associated with highly and moderately emetogenic cancer chemotherapy in adults and paediatric patients aged 6 months and older	NO	> 6 months	22/03/18 (30/04/18): Extension of Indication to include adolescents, infants, toddlers and children aged 6 months and older for prevention of nausea and vomiting associated with highly and moderately emetogenic cancer chemotherapy
Insulin glargine	A10AE04	Treatment of diabetes mellitus in adults, adolescents and children aged 2 years and above.	NO	> 2 years	
Infliximab	L04AB02	Paediatric Crohn's disease: Zessly is indicated for treatment of severe, active Crohn's disease, in children and adolescents aged 6 to 17 years, who have not responded to conventional therapy including a corticosteroid, an immunomodulator and primary nutrition therapy; or who are intolerant to or have contraindications for such therapies. Infliximab has been studied only in combination with conventional immunosuppressive therapy. Paediatric ulcerative colitis Zessly is indicated for treatment of severely active ulcerative colitis, in children and adolescents aged 6 to 17 years, who have had an inadequate response to conventional therapy including corticosteroids and 6-MP or AZA, or who are intolerant to or have medical contraindications for such therapies.	NO	> 6 years	
Glibenclamide	A10BB01	Amglidia is indicated for the treatment of neonatal diabetes mellitus, for use in newborns, infants and children. Sulphonylureas like Amglidia have been shown to be effective in patients with mutations in the genes coding for the β-cell ATP-sensitive potassium channel and chromosome 6q24-related transient neonatal diabetes mellitus.	YES	newborns, infants, children	
Dasatinib	L01XE06	SPRYCEL is indicated for the treatment of paediatric patients with: - newly diagnosed Ph+ CML in chronic phase (Ph+ CML-CP) or Ph+ CML-CP resistant or intolerant to prior therapy including imatinib.	NO	> 1 year	26/04/18 (02/07/18): To include the treatment of paediatric patients with newly diagnosed Ph+ CML in chronic phase (Ph+ CML-CP) or Ph+ CML-CP resistant or intolerant to prior therapy including imatinib for Sprycel film-coated tablets.
Ciclosporin	S01XA18	Treatment of severe vernal keratoconjunctivitis (VKC) in children from 4 years of age and adolescents.	YES	> 4 to 18 years	
Adalimumab	L04AB04	Juvenile idiopathic arthritis Polyarticular juvenile idiopathic arthritis: Hyrimoz 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). Hyrimoz can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate. Adalimumab has not	NO	> 2 years > 4 years > 6 years > 12 years	

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations
		been studied in patients aged less than 2 years. Enthesitis-related arthritis: Hyrimoz 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: Hyrimoz 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): Hyrimoz 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: Hyrimoz 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: Hyrimoz 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.			
Adalimumab	L04AB04	Juvenile idiopathic arthritis: Polyarticular juvenile idiopathic arthritis Halimatoz 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). Halimatoz 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: Halimatoz 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: Halimatoz 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): Halimatoz 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 uveitis: Halimatoz 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.	NO	> 2 years > 4 years > 6 years > 12 years	

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations
Metreleptin	A16AA	Myalepta is indicated as an adjunct to diet as a replacement therapy to treat the complications of leptin deficiency in lipodystrophy (LD) patients: • with confirmed congenital generalised LD (Berardinelli-Seip syndrome) or acquired generalised LD (Lawrence syndrome) in adults and children 2 years of age and above • with confirmed familial partial LD or acquired partial LD (Barraquer-Simons syndrome), in adults and children 12 years of age and above for whom standard treatments have failed to achieve adequate metabolic control.	YES	> 2 years	
Adalimumab	L04AB04	Juvenile idiopathic arthritis Polyarticular juvenile idiopathic arthritis: Hefiya 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). Hefiya 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: Hefiya 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: Hefiya 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): Hefiya 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 uveitis: Hefiya 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.	NO	> 2 years > 4 years > 6 years > 12 years	
Gemtuzumab ozogamicin	L01XC05	MYLOTARG is indicated for combination therapy with daunorubicin (DNR) and cytarabine (AraC) for the treatment of patients age 15 years and above with previously untreated, de novo CD33-positive acute myeloid leukaemia (AML), except acute promyelocytic leukaemia (APL)	YES	> 15 years	
Nitisinone (generic)	A16AX04	Treatment of adult and paediatric patients with confirmed diagnosis of hereditary tyrosinemia type 1 (HT-1) in combination with dietary restriction of tyrosine and phenylalanine.	NO	all ages	
Vestronidase alfa	A16AB18		YES	all ages	
Adalimumab	L04AB04	Juvenile idiopathic arthritis Polyarticular juvenile idiopathic arthritis: Hulio 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). Hulio can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with	NO	> 2 years > 4 years > 6 years > 12 years	

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations
		methotrexate is inappropriate (for the efficacy in monotherapy see section 5.1). Adalimumab has not been studied in patients aged less than 2 years. Enthesitis-related arthritis: Hulio 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: Hulio 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: Hulio is indicated for the treatment of moderately to severely active Crohn's disease in paediatric patients (from 6 years of age) who have had an inadequate response to conventional therapy including primary nutrition therapy and a corticosteroid and/or an immunomodulator, or who are intolerant to or have contraindications for such therapies. Adolescent hidradenitis suppurativa: Hulio is indicated for the treatment of active moderate to severe hidradenitis suppurativa (acne inversa) in adolescents from 12 years of age with an inadequate response to conventional systemic HS therapy. Paediatric Uveitis: Hulio 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.			
Tisagenlecleucel	L01	Kymriah is indicated for the treatment of: - Paediatric and young adult patients up to 25 years of age with B-cell acute lymphoblastic leukaemia (ALL) that is refractory, in relapse post-transplant or in second or later relapse.	YES	> 3 years	
Mepolizumab	R03DX09	Nucala is indicated as an add-on treatment for severe refractory eosinophilic asthma in adults, adolescents and children aged 6 years and older.	NO	> 6 years	26/07/18 (27/08/18): Extension of Indication to include children and adolescents aged 6 to 17 years for Nucala
Melatonin	N05CH01	Slenyto is indicated for the treatment of insomnia in children and adolescents aged 2-18 with Autism Spectrum Disorder (ASD) and / or Smith-Magenis syndrome, where sleep hygiene measures have been insufficient.	NO	> 2 years	
Blinatumomab	L01XC	BLINCYTO is indicated as monotherapy for the treatment of paediatric patients aged 1 year or older with Philadelphia chromosome negative CD19 positive B-cell precursor ALL which is refractory or in relapse after receiving at least two prior therapies or in relapse after receiving prior allogeneic hematopoietic stem cell transplantation.	YES	> 1 year	15/11/18 (18/01/19): Extension of indication to include the treatment of adults with Philadelphia chromosome-negative CD19 positive B precursor ALL in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1% for BLINCYTO monotherapy. 26/07/18 (23/08/18): Extension of Indication to include the children 1 month and older to the authorised population for the treatment of adults with Philadelphia chromosome-negative

Active substance	ATC code	Paediatric indication	Orphan	Paediatric Age	Variations
					relapsed or refractory B-precursor acute lymphoblastic leukaemia (ALL) for BLINCYTO
Deferiprone (generic)	V03AC02		NO	> 6 years	
Vigabatrin	N03AG04	Kigabeq is indicated in infants and children from 1 month to less than 7 years of age for: - Treatment in monotherapy of infantile spasms (West's syndrome). - Treatment in combination with other antiepileptic medicinal products for patients with resistant partial epilepsy (focal onset seizures) with or without secondary generalisation, that is where all other appropriate medicinal product combinations have proved inadequate or have not been tolerated.	NO	1 month to 7 years	

6. References

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

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

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

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