Periodic report on paediatric drugs available for children

Index

1. Abstract

This is the periodic report prepared by the TEDDY Network on paediatric medicines registered in Europe under the EMEA Centralised Procedure (EMEA-CP) from October 1995. The report is updated with data on medicines registered in 2014.[i]

2. Introduction

The main goal in the pharmaceutical field 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 is dependent upon a wide dissemination of relevant information to all 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 within 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 EMEA Centralised Procedure (EMEA-CP) from October 1995. Regularly reports are released. 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 in 2014 is provided.

3. Methodology

3.1. Definitions

To the aim of EPMD the following definitions apply

- Paediatric medicines: medicines with registered labels including information to allow paediatric use. The inclusion of information about both label and Package Leaflet (PL) were related to paediatric indication and dosage (by age(s) and/or by weight).
- Paediatrics age groups: the groups of ages defined according to the ICH Topic E11 'Clinical Investigation of Medicinal Products in the Paediatric Population' Guideline (2000) [4].
- 'Orphan Drugs' and 'Orphan-like drugs': as defined in the Regulation n. 141/2000/EC [5] and in the "Status Report on the implementation of the European Parliament Legislation on Orphan Medicinal Products" [6], respectively.

3.2. Data collection and storing

The EMA public website represent the source of information. For each new medicines approved, including new MA and variations listed on the EMA website homepage (http://www.ema.europa.eu/ema/index.jsp?curl=pages/home/Home_Page.jsp&mid=), the European public assessment reports (EPAR) for human medicines are analysed. Information derived by EPARs are collected in a standardised way and stored in TEDDY European Paediatric Medicines Database (EPMD). Data are collected and validated by two researchers. Doubts and discrepancies are solved with the support of a supervisor.

3.3. Data collected

EPMD includes the following information:

- Year of approval
- Active substance
- Trade Name
- Anatomical Therapeutic Chemical – ATC code (first-level)
- Indication and Paediatric Indication
- Ages for which the drug is intended
- Dosages
- Orphan drug status
- Orphan condition
- Paediatric trials and studies included in the EPAR at the time of approval

3.4. Data Analysis

General descriptive statistics analyses are performed on annual basis providing details on: a) year of Marketing Authorisation (MA), b) age of population for which the drug is approved, c) ATC code, and d) orphan status.Other analyses can be done according to specific request.

4. Results

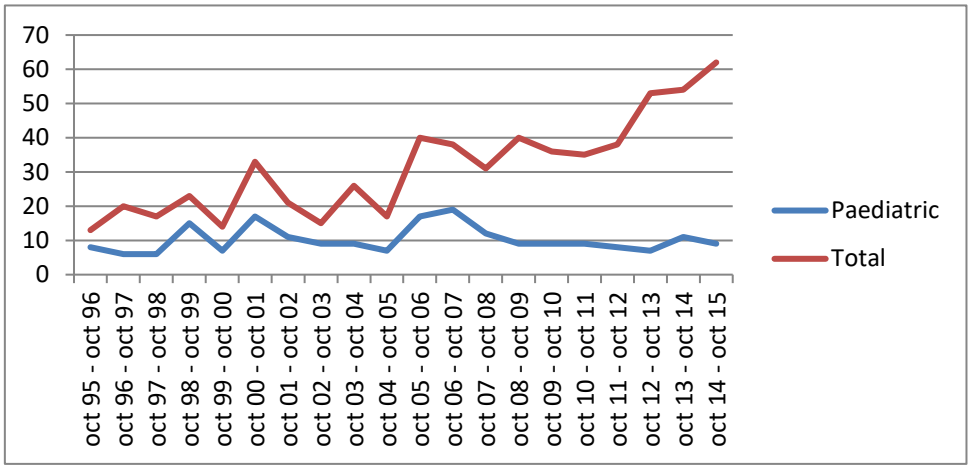
4.1. Paediatric medicines number and percentage

In the period October 1995 – October 2015, 626 active substances (AS) have been approved by EMA under the Centralised Procedure, of which 206 are paediatric.[1]

Figure 1 reports a comparison of the percentage of paediatric medicines on the total of medicines approved by EMA under the centralised procedure. Marketing Authorisations and Variations are included. Notwithstanding the increase observed in 2007, the percentage remains very low.

[1] In the first period covered by this report (from 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.

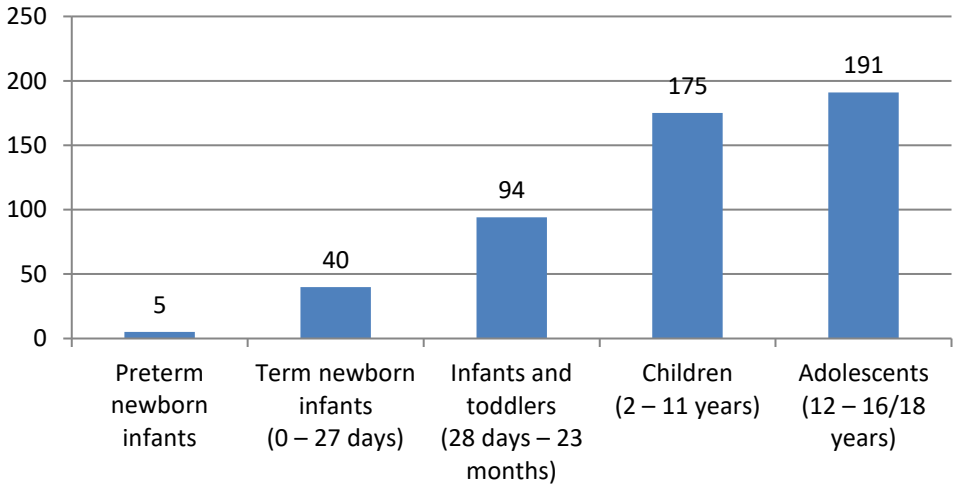
Figure 1 - Medicinal products authorised by EMA divided by year (Oct. 1995 – Oct. 2015)



4.2. Paediatric medicines age distribution

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

Figure 2 – Paediatric Medicines: age distribution



4.3. ATC and orphan status

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 while G-ATC (Genito-urinary system and sex hormones), M-ATC (Musculo-skeletal system) and P-ATC (Antiparasitic) the lowest ones.

Of a total of 206 paediatric medicines, 41 are Orphan MP, eleven in the Alimentary-metabolism (A) ATC and ten in the oncology ATC (L). Table 1 provides additional details.

Table 1: EMA Paediatric and Orphan Medicines by ATC code

	Paediatric/Total		**Orphan/Paediatric**	
	N	**%**	**N**	**%**
A -Alimentary tract and metabolism	29/76	38	11/29	39
B - Blood and blood forming organs	15/48	31	1/15	7
C - Cardiovascular system	5/37	13	0/5	-
D - Dermatologicals	3/7	43	0/3	-
G- Genito-urinary system and sex hormones	1/27	4	1/1	100
H - Systemic hormonal preparations, excluding sex hormones and insulins	3/12	2	1/3	33
J - Anti-infectives for systemic use	83/125	66	4/83	5
L - Antineoplastic and immunomodulating agents	31/137	23	10/31	32
M - Musculo-skeletal system	1/18	5	0/1	-
N - Nervous system	12/53	23	4/12	33
P -Antiparasitic products, insecticides and repellents	1/1	100	0/1	-
R - Respiratory system	8/20	40	1/8	12
S - Sensory organs	3/21	14	0/3	-
V -Various	9/39	23	1/9	11
Not assigned yet	2/5	40	2/2	100
TOTAL	***206/626***	***33%***	***41/206***	***20%***

It should be noted that, referring to orphan drugs, out of the 83 orphan drugs authorised by the EMA in the period October 1995 – October 2015, 36 were paediatric. Thus, comparing the rate of paediatric medicines in orphan and non orphan drug groups, a significant difference in favour of paediatric medicines in the orphan drug group is evident (43% and 33%, respectively). In particular in some diseases categories such as A, J, N, the majority of the approved OMP are licensed for children (Table 2).

Table 2 – Paediatric orphan drugs and ATC distribution

ATC	Orphan drugs authorised	Paediatric orphan drugs authorised	Percentage
A -Alimentary tract and metabolism	13	11	85
B - Blood and blood forming organs	2	1	50
C - Cardiovascular system	5	0	-
D - Dermatologicals	2	0	-
G- Genito-urinary system and sex hormones	0	1	-
H - Systemic hormonal preparations, excluding sex hormones and insulins	4	1	25
J - Anti-infectives for systemic use	6	4	67
L - Antineoplastic and immunomodulating agents	37	10	26
M - Musculo-skeletal system	0	0	-
N - Nervous system	7	4	57
P -Antiparasitic products, insecticides and repellents	0	0	-
R - Respiratory system	2	1	50
S - Sensory organs	1	0	-
V -Various	2	1	50
Not assigned yet	2	2	
TOTAL	**83**	**36**	***43%***

5. 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.

4. ICH. Clinical Investigation of Medicinal Products in the Paediatric Population. ICH/Topic E11 (2000)

5. European Parliament and Council Regulation 141/2000/EC, 16 December 1999 on Orphan Medicinal Products

6. EMEA. Status Report on the implementation of the European Parliament Legislation on Orphan Medicinal Products. EMEA/7381/01 (March 30th 2001)

[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.