



AVAILABILITY OF SOME CARDIOVASCULAR MEDICINES AUTHORIZED IN ALBANIA FOR PEDIATRIC POPULATION

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Article Received on
08 Feb 2016,

Revised on 28 Feb 2016,
Accepted on 19 Mar 2016

DOI: 10.20959/wjpps20164-6500

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ABSTRACT

Objectives: The aim of this study was to evaluate the number of medicines and active ingredients for pediatric population that are authorized and marketed in Albania, for nine active ingredients which belong to medicinal products used for treatment of cardiovascular diseases. **Methods:** The availability of pediatric medicines and active ingredients was studied with the help of the database of the Albanian National Agency for Medicine and Medical Devices and SmPC. Selected active ingredients were categorized based on their route of administration, type of pharmaceutical form, dosage, therapeutic indication, dose capability and suitability of the pharmaceutical form for use in children. **Results:** Evaluation of the SmPCs of the products suggested that only two active substances are authorized for use in

children; all were for solid oral forms. Approved pharmaceutical forms are as follows: 78.5% tablets, 7.4% coated tablets, 12.4% modified-release film-coated tablets and 1.7% film coated tablets. For any active ingredient wasn't found authorized liquid formulations, which are more appropriate for use in children. **Conclusion:** This study shows lack of availability of pediatric medicines for selected products and shows that pediatric medicines may not be age-appropriate; even they are authorized for such use. It was shown that few medicinal products are specifically studied in children. Therefore, are needed more efforts to increase the number of drugs authorized for the pediatric groups. Even more, it is required by pharmaceutical companies to supply data on the effects of new drugs in children.

KEYWORDS: pediatric, medicines, forms, authorized, cardiovascular.

INTRODUCTION

Due to limited studies designed to evaluate pharmacological and toxicological aspects in pediatric populations, many approved drugs have been used in children without appropriate dosage form or proper information on dosage and potential toxicity.^[1,2,3]

In order to provide medical assistance to children, physicians often have prescribed unauthorized medicinal products due to lack of suitable and authorized medicine for children.^[4-8] This attitude seems to lead to an increased rate of adverse drug reactions and medical errors.^[9,10] With coming into force of Pediatric Regulation in the European Union, on January 2007, based on multiple strategies, development and accessibility of authorized pediatric medicine were more facilitated. One of these strategies obliges pharmaceutical industry to plan clinical trials in children at an early stage of the development of medicines containing a new active substance. The same requirement applies to the development of a new indication for existing medicinal drug products. As clinical trials and marketing authorizations take quite an amount of time, the real effect of this Regulation on the availability of authorized medicines for children in Europe is still to be shown.^[10-13]

The design of currently authorized pediatric medicines is not always optimal.^[9,14,15] This is understandable as scientific evidence on the impact of pharmaceutical technology aspects of pediatric products of child patient outcomes is scarce.^[16] Moreover, tablets have been authorized for children below the age of 6 years, even though they may be not able to swallow tablets.^[14,15] Therefore, it is very important to study at what rate authorized medicines are really adequate for use in children.

Therefore, the first objective of this study was to evaluate the number of medicines and active ingredients for pediatric population that are authorized and marketed in Albania, for five selected groups. The second objective was to evaluate the age-appropriateness of the selected medicines evaluated in two aspects: dose capability and suitability of the pharmaceutical form for use in children.

METHODS

With the help of database of medicines of the Albanian National Agency for Medicine and Medical Devices, till 10 April 2015, was identifies authorized medicines for selected active ingredients.^[17]

For this study was selected and evaluated below mentions products:

- Medicinal products for the treatment of cardiovascular diseases:
 - ACE Inhibitors: Captopril, Ramipril, Enalapril;
 - Calcium antagonists: Nifedipine, Verapamil, Amlodipine;
 - β – Blockers: Propranolol, Carvedilol, Atenolol.

In total was studies 118 medicinal products from selected active ingredients for treatment of cardiovascular diseases.

This database doesn't allow extraction of marketed products and active ingredients classified based on age-appropriateness. For this reason were evaluated Patients Information Leaflet and/or Summary of Product Characteristics. From these two available sources information documents were analyzed sections: pharmaceutical form, therapeutic indications, posology and route of administration.^[18-20]

A special focus was dedicated to age-appropriateness of selected products. First investigated aspect was if recommended dose is prescribed to children based on classification of pediatric age: preterm newborn infants, term newborn infants, infants and toddlers, children and adolescents.^[21] Second investigated aspect was if approved pharmaceutical form, for selected products in this study, were suitable for use in children. For solid forms (such as tablets and capsules) were evaluated presence of the score line and the possibility of opening or not contains of capsules.

Based on all prescribed methodology use for this study were collected these data: authorized indications; authorized age-group; pharmaceutical form; authorized dosage; presence of score line; information on possibility for opening capsules contains.

RESULTS AND DISCUSSION

The availability of medicines and active ingredients selected for treatment of cardiovascular diseases are described in Table 1.

Evaluation of SmPCs, of the products suggested that only two active substances are also authorized for use in children; enalapril and amlodipine. All the other products are authorized for use only in adults. Furthermore, all these products were for solid oral intake forms and all were tablets (n = 118, 100%).

Table 1: Availability of selected medicines for treatment of cardiovascular diseases.

Active ingredient	Therapeutic class	Authorized indication	Authorized age-group	Authorized form and strength	Number of authorized products
Captopril	ACE Inhibitor	Hypertension, heart failure	Adults	Tablets; 25 mg and 50 mg	5
Ramipril	ACE Inhibitors	Hypertension, heart failure	Adults	Tablets; 2,5 mg, 5 mg and 10 mg	18
Enalapril	ACE Inhibitors	Hypertension, heart failure	Pediatric patients bodyweight 20 up to < 50 kg and patients with a bodyweight \geq 50 kg; Adults	Tablets; 5 mg, 10 mg and 20 mg	17
Nifedipine	Calcium antagonists	Hypertension	Adults	Modified-release film-coated tablets and film coated tablets; 10 mg, 20 mg, 30 mg and 60 mg	17
Verapamil	Calcium antagonists	Arrhythmias	Adults	Coated tablets; 40 mg and 80 mg	9
Amlodipine	Calcium antagonists	Hypertension	6-17 years; Adults	Tablets; 5 mg and 10 mg	19
Propranolol	β – Blockers	Hypertension, Arrhythmias	Adults	Tablets; 40 mg	1
Carvedilol	β – Blockers	Hypertension, heart failure, angina	Adults	Tablets; 3.125 mg, 6.25 mg, 12.5 mg and 25 mg	24
Atenolol	β – Blockers	Hypertension, Arrhythmias	Adults	Tablets; 100 mg	8

Evaluation of SmPCs for age-appropriateness of these products based on recommended dose and suitability of forms for use in children showed that all products are authorized only for use in adults and approved pharmaceutical form are as following: 78.5% tablets, 7.4% coated tablets, 12.4% modified-release film-coated tablets and 1.7% film coated tablets. For any active ingredient wasn't found authorized liquid formulations, which are more appropriate for use in children.

Evaluation of authorized pharmaceutical forms (tablets, coated tablets, modified-release film-coated tablets and film coated tablets) for the presence score line, in order to archives smaller dosages shows these results: 40.7% (n = 48) of medicinal products were without score line, 53.4% (n = 63) have a score line on one side of the tablet, 3.4% (n = 4) have a score line on both sides and for 2.5% (n = 3) information wasn't available in check SmPCs (Figure 1).

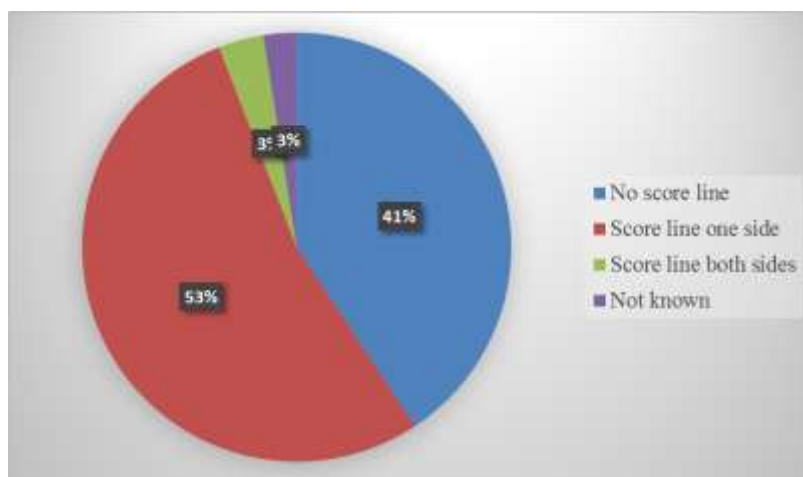


Fig 1: Presence of score line in studied products.

CONCLUSIONS

This study shows lack of availability of pediatric medicines for selected products and shows that pediatric medicines may not be age-appropriate; even they are authorized for such use. It was shown that few medicinal products are specifically studied in children. Therefore, are needed more efforts to increase the number of drugs authorized for the pediatric groups. Even more, it is required by pharmaceutical companies to supply data on the effects of new drugs in children.

The development of medicines for use in children requires that a specific active ingredient need to be available in different dosage forms and strengths. The dose capability was considered important criteria. A medicine is either dose capable or it is not. However, the suitability of pharmaceutical forms is not as absolute. According to EU reflection paper tablets and capsules are only suitable from the age of 6 years. However, recent studies have shown that small tablets can be swallowed by young children.^[22,23] Also, some capsules can be opened and can be ready for use.

Physicians and pharmacists should consider that by using formulation not appropriate for children may cause administration errors, lack of therapeutic compliance and unexpected side effects. In order to reduce the risk of any of below problems, they are encouraged to search between marketed products the most appropriate medicine for treating groups of pediatric population.

ACKNOWLEDGEMENT

A special thank you to the Department of Pharmaceutical Technology, Faculty of Pharmacy, and to my co-authors of this article for continued motivation and support.

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