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Human Medicines Research and Development Support Division

Public summary of the evaluation of a proposed product-specific waiver

(R)-2-[3-({Benzoxazol-2-yl[3-(4-methoxyphenoxy)propyl]amino}methyl) phenoxy]butanoic acid for the reduction of residual cardiovascular events in patients with diabetes

On 18 July 2014, the Paediatric Committee of the European Medicines Agency refused a product-specific waiver* for (R)-2-[3-({Benzoxazol-2-yl[3-(4-methoxyphenoxy)propyl]amino}methyl)phenoxy] butanoic acid for the reduction of residual cardiovascular events in patients with diabetes (EMEA-001573-PIP01-13).

What is (R)-2-[3-({Benzoxazol-2-yl[3-(4-methoxyphenoxy)propyl]amino} methyl)phenoxy]butanoic acid, and how is it expected to work?

(R)-2-[3-({Benzoxazol-2-yl[3-(4-methoxyphenoxy)propyl]amino}methyl)phenoxy]butanoic acid is not authorised in the European Union. Studies in adults are currently on-going. This medicine is proposed in adults for the reduction of residual risk of cardiovascular events in adult patients with type-2 diabetes mellitus as add on to statin therapy.

This medicine is expected to lower the lipid (fat) levels in blood in order to prevent cardiovascular events resulting from the narrowed blood vessels.

What was the proposal from the applicant?

For children, the applicant proposed:

Not to do any study in children (from birth to less than 18 years of age), because they claimed that cardiovascular complications in diabetic patients do not occur in paediatric patients, i.e. before the age of 18 years. Therefore, the applicant requested an exemption (waiver*) from the obligation to study the medicine in any children, in the condition reduction of residual cardiovascular events in patients with diabetes.

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Is there a need to treat children affected by residual CV events in patients with diabetes?

Based on existing knowledge, and on data submitted by the applicant, the Paediatric Committee concluded that the scope of the PIP should not be limited to the condition proposed by the applicant, because the actual aim of this product's administration to diabetic patients is the treatment of elevated lipid levels in the blood. The expected reduction of the cardiovascular complications is just a consequence of this treatment. The Committee concluded that the condition, discussed in the applicant's proposal, should be treatment of elevated lipid levels, which does affect children, and the product could potentially address a paediatric need in this condition.

What did the Paediatric Committee conclude on the potential use of this medicine in children?

The Committee disagreed with the request of the applicant to be exempt from performing studies in children, since the medicinal product may be useful in a paediatric indication for treatment, prevention or diagnosis.

The Committee considered that because there is a need for safe and effective lipid-lowering drugs for children in Europe, and this product has a clear potential to meet that need in diabetic and non-diabetic patients alike. Also, it is important to find out whether a lipid-lowering treatment started early in childhood would reduce the cardiovascular risk that may lead to events in adulthood only.

Consequently, the applicant was invited to propose a paediatric investigation plan in the future, and the PDCO adopted an opinion refusing the request of a product-specific waiver.

What happens next?

The applicant has now received the EMA Decision (P/0222/2014)* on this medicine. A positive Decision is necessary for the applicant to request in the future a marketing authorisation* for this medicine in adults and/or in children.

As the Paediatric Committee disagreed with the request, the applicant will need to make a new proposal to the Committee, if they still intend to proceed with the development of the medicine.

*Definitions:

Applicant	The pharmaceutical company or person proposing the Paediatric Investigation Plan or requesting the Product-Specific Waiver
Children	All children, from birth to the day of the 18th birthday.
Paediatric investigation plan (PIP)	Set of studies and measures, usually including clinical studies in children, to evaluate the benefits and the risks of the use of a medicine in children, for a given disease or condition. A PIP may include "partial" waivers (for example, for younger children) and/or a deferral (see below).
Waiver	An exemption from conducting studies in children, for a given disease or condition. This can be granted for all children (product-specific waiver), or in specific subsets (partial waiver): for example, in boys or in children below a given age.
Deferral	The possibility to request marketing authorisation for the use of the medicine in adults, before completing one or more of the studies /measures included in a PIP. The Paediatric Committee may grant a deferral to avoid a delay in the availability of the medicine for adults.
Opinion	The result of the evaluation by the Paediatric Committee of the European Medicines Agency. The opinion may grant a product-specific waiver, or agree a PIP.
Decision	The legal act issued by the European Medicines Agency, which puts into effect the Opinion of the Paediatric Committee.
Pharmaceutical form	The physical aspect of the medicine (the form in which it is presented), for example: a tablet, capsule, powder, solution for injection, etc. A medicine can have more than one pharmaceutical form.
Placebo	A substance that has no therapeutic effect, used as a control in testing new drugs.
Active control	A medicine with therapeutic effect, used as a control in testing new drugs.
Historical control	A group of patients with the same disease, treated in the past and used in a comparison with the patients treated with the new drug.
Route of administration	How a medicine is given to the patient. For example: for oral use, for intramuscular use, for intravenous use, etc. The same medicine, or the same pharmaceutical form, may be given through more than one route of administration.
Patent	A form of protection of intellectual property rights. If a medicinal product is protected by a patent, the patent holder has the sole right to make, use, and sell the product, for a limited period. In certain circumstances, a patent for a medicinal product may be extended for a variable period by a Supplementary Protection Certificate.
Marketing Authorisation	When a Marketing Authorisation is granted, the pharmaceutical company may start selling the medicine in the relevant country (in the whole European Union, if the procedure was a centralised one).