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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Fomepizole for the treatment of methanol poisoning

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in April 2003 on request from the sponsor.

On 30 May 2001, orphan designation (EU/3/01/040) was granted by the European Commission to IDIS Ltd, United Kingdom, for fomepizole for the treatment of methanol poisoning.

What is methanol poisoning?

Poisoning by methanol leads to a severe metabolic acidosis (a disorder of the acid-base balance where the blood pH is abnormally low) causing blindness and liver and kidney damages. The toxicity of methanol poisoning is due to a chemical substance called formic acid, which is produced during the break down of methanol in the body. The process of methanol breakdown has many steps and the first step involves an enzyme (a specialised protein) called alcohol dehydrogenase. Alcohol dehydrogenase speeds up breaking down of alcohol. Methanol poisoning, depending on the levels of toxic metabolites, can lead to irreversible blindness, and even death. Methanol poisoning is a chronically debilitating and life-threatening condition.

What is the estimated number of patients affected by the condition?

At the time of designation, methanol poisoning affected approximately 0.16 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 6,000 people, and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

At the time of submission of the application for orphan designation there were no authorised treatments in the Community for methanol poisoning. However, ethanol was used as an antidote against methanol poisoning to prevent organ toxicity and the formation of the toxic substance formic

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union. This represents a population of 377,000,000 (Eurostat 2001).

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acid. Ethanol therapy is used for the treatment of the condition because alcohol dehydrogenase favours binding to ethanol rather than methanol. Therefore, the presence of ethanol occupies alcohol dehydrogenase and prevents the breakdown of methanol, eventually stopping the production of the toxic metabolites. Satisfactory argumentation has been submitted by the sponsor to justify that fomepizole might be of significant benefit because if might improve the overall outcome of patients due to its new mechanism of action. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

Fomepizole can block the activity of alcohol dehydrogenase. As the inhibition of alcohol dehydrogenase is a key step in treating methanol poisoning, it is thought that fomepizole could prevent formation of the toxic formic acid and thus prevent the damages to various organs.

What is the stage of development of this medicine?

The effects of fomepizole were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with methanol poisoning were completed.

At the time of the submission, orphan drug designation was granted fomepizole in the United States for the treatment of methanol and ethylene glycol poisoning.

Fomepizole was approved in the United States for the treatment of methanol or suspected methanol poisoning in December 2000.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 10 April 2001 recommending the granting of this designation.

Opinions on orphan medicinal product designations are based on the following three criteria:

- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the EU) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

For more information

Sponsor's contact details:

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For contact details of patients' organisations whose activities are targeted at rare diseases see:

- Orphanet, a database containing information on rare diseases which includes a directory of patients' organisations registered in Europe.
- European Organisation for Rare Diseases (EURORDIS), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Fomepizole	Treatment of methanol poisoning
Danish	Fomepizol	Behandling af methanolforgiftning
Dutch	Fomepizol	Behandeling van methanol vergiftiging
Finnish	Fomepitsoli	Metanolimyrkytyksen hoito.
French	Fomépizole	Traitement des intoxications au méthanol
German	Fomepizole	Behandlung von Methanolvergiftungen
Greek	Φομεπιζόλη	Θεραπεία της δηλητηρίασης με μεθανόλη
Italian	Fomepizolo	Trattamento dell'intossicazione da metanolo
Portuguese	Fomepizol	Tratamento das intoxicaçaoes com metanol.
Spanish	Fomepizol	Tratamiento de las intoxicaciones con metanol.
Swedish	Fomepizol	Behandling av methanolförgiftning

[1] At the time of designation