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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

N,N'-bis(2-mercaptoethyl)isophthalamide for the treatment of mercury toxicity

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Disclaimer Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.	

On 11 January 2012, orphan designation (EU/3/11/944) was granted by the European Commission to CTI Science Limited, Ireland, for N,N'-bis(2-mercaptoethyl)isophthalamide for the treatment of mercury toxicity.

What is mercury toxicity?

Mercury toxicity can occur when a patient has been exposed to mercury. The level of toxicity depends on the chemical form of the mercury and how the patient was exposed to it. Exposure may occur through certain foods (such as fish), from mercury-containing dental amalgams (a substance used in some dental fillings) or through contact with materials in factories where mercury-containing products are used or manufactured.

Mercury toxicity can lead to symptoms affecting several body systems such as the nervous, gastrointestinal (gut including the liver), and the renal (kidney) systems. Acute toxicity can result in shortness of breath, chest pain, chills, nausea and vomiting, joint swelling and rash, while long-term exposure to mercury commonly results in mouth lesions, tremor, poor coordination and psychiatric problems among others.

Mercury toxicity is life threatening due to the damage it can cause to the nervous, renal, endocrine (hormonal) and gastrointestinal systems.

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

At the time of designation, mercury toxicity affected less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 51,000 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 designation, medicines authorised in EU countries for mercury toxicity included dimercaptoprol, D-pencillamine, 2,3-dimercaptosuccinic acid (DMSA), and 2,3-dimercapto-1-propane sulfonic acid (DMPS). These medicines are 'chelating' agents: they work by attaching to mercury to form a compound that can be more easily excreted from the body.

The sponsor has provided sufficient information to show that N,N'-bis(2-mercaptoethyl)isophthalamide might be of significant benefit for patients with mercury toxicity because it works in a partially different way to existing treatments and early studies indicate that it might improve the treatment of patients with this condition. 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?

Like other medicines for mercury toxicity, N,N-bis-(2mercaptoethyl)isophthalamide is a chelating agent. However, while other medicines are 'hydrophilic', which means that they attach to the mercury found in water but not in fat, this medicine is 'lipophilic' and is expected to be able to reach the mercury in fatty tissues in the body. When the medicine is taken by mouth, it is expected to attach to the mercury in fatty tissues such as the brain, forming a compound which the body is then able to excrete.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

At the time of submission, no clinical trials with the medicine in patients with mercury toxicity had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for mercury toxicity or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 9 November 2011 recommending the granting of this designation.

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union (EU 27), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 509,000,000 (Eurostat 2012).

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	N,N'-bis(2-mercaptoethyl)isophthalamide	Treatment of mercury toxicity
Bulgarian	N,N'-бис (2-меркаптоетил)изофталамид	Лечение на живачна токсичност
Czech	N,N'-bis(2-mercaptoethyl)isophthalamide	Léčba toxicity rtuti
Danish	N,N'-bis(2-mercaptoethyl)isophthalamid	Behandling af kviksølv toksicitet
Dutch	N,N'-bis(2-mercaptoethyl)isophthalamide	Behandeling van kwikvergiftiging
Estonian	N,N'-bis(2-merkaptoetüüll)isoftalamiid	Elavhõbeda toksilisuse ravi
Finnish	N,N'-bis(2-merkaptoetyyli)isoftalamidi	Elohopeamyrkytyksen hoito
French	N,N'-bis(2-mercaptoéthyle)isophthalamide	Traitement de la toxicité au mercure
German	N,N'-Bis(2-mercaptoethyl)Isophthalamid	Behandlung einer Quecksilbervergiftung
Greek	N,N'-δις(2-μερκαπτοαιθυλ)ισοφθαλαμίδη	Θεραπεία της τοξικότητας υδραργύρου
Hungarian	N,N'-bisz(2-merkaptoetil)isophthalamide	Higanymérgezés kezelése
Italian	N,N'-bis(2-mercaptoetil)isofthalamide	Trattamento di tossicità del mercurio
Latvian	N,N'-bis(2-merkaptoetil)izoftalamīds	Dzīvsudraba toksicitātes ārstēšana
Lithuanian	N,N'-bis(2-merkaptoetil)izoftalamidas	Gyvsidabrio toksiškumo gydymas
Maltese	N,N'-bis(2-mercaptoethyl)isophthalamide	Kura ta' tossiċità bil-merkurju
Polish	N,N'-bis(2-merkaptoetylo)izoftalamid	Leczenie zatruć rtęcią
Portuguese	N,N'-bis (2-mercaptoetilo)isoftalamida	Tratamento da intoxicação pelo mercúrio
Romanian	N,N'-bis(2-mercaptoetil)izoftalamidă	Tratamentul intoxicaţiei cu mercur
Slovak	N,N'-bis(2-merkaptoetyl) izoftalamid	Liečba otravy ortuťou
Slovenian	N,N'-bis(2-merkaptoetil)izoftalamid	Zdravljenje zastrupitev z živim srebrom
Spanish	N,N'-bis(2-mercaptoetilo)isophthalamide	El tratamiento de la toxicidad por mercurio
Swedish	N,N'-bis(2-merkaptoetyl)isophthalamide	Behandling av kvicksilverförgiftning
Norwegian	N,N'-bis(2-merkaptoetyl)isofthalamid	Behandling av kvikksølvforgiftning
Icelandic	N,N'-bis(2-mercaptóethýl)ísóphthalamíð	Meðferð kvikasilfurs eitrunar

[1] At the time of designation