



European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of cysteamine hydrochloride for the treatment of cystinosis

On 7 November 2008, orphan designation (EU/3/08/578) was granted by the European Commission to Orphan Europe SARL, France, for cysteamine hydrochloride for the treatment of cystinosis.

What is cystinosis?

Cystinosis is an inherited disorder characterized by the defect of cystinosisin, a protein present in the membrane of the lysosomes of the cells, that normally removes excess cystine. When cystinosisin's function is impaired, cystinosis (accumulation of cystine) occurs; free cystine builds up continuously and it forms intracellular crystal deposits throughout the body. These crystals negatively affect many systems in the body, especially the kidneys and eyes.

There are three types of cystinosis, each with slightly different symptoms: nephropathic cystinosis, intermediate cystinosis, and non-nephropathic or ocular cystinosis. Infants affected by nephropathic cystinosis initially show poor growth and kidney problems. Kidney problems lead to the loss of important minerals, salts, fluids, and other nutrients. The loss of nutrients impairs growth and results in soft, bowed bones (hypophosphatemic rickets). The nutrient imbalances in the body lead to increased urination, thirst, dehydration, and abnormally acidic blood. Cystinosis can affect patients' cornea leading to photophobia (intolerance of light), keratopathy (lesions in the cornea) and loss of visual acuity. Systemic cystinosis can lead to renal insufficiency after long term renal disease, with end stage renal failure occurring between the age of 6 and 12 years old. Patients affected by cystinosis also develop other long term complications, such as hypothyroidism and pulmonary dysfunction. Cystinosis is a life threatening condition.

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

At the time of designation cystinosis affected approximately 0.1 in 10,000 people in the European Union (EU) *. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP). This is below the threshold for orphan designation which is 5 in 10,000. This is equivalent to a total of around 5,000 people.

What treatments are available?

At the time of application for orphan designation, oral cysteamine (cysteamine bitartrate) was available in all Member States as a centrally authorised medicinal product. Ophthalmic (eye) formulations of cysteamine were not authorised in EU, but were used for the management of ocular cystinosis.

*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 (EU 27), Norway, Iceland and Lichtenstein. This represents a population of 502,282,000 (Eurostat 2008).

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that cysteamine hydrochloride might be of potential significant benefit for the treatment of cystinosis mainly because ocular symptoms of cystinosis are not adequately treated with oral cysteamine and the ocular formulation is expected to improve overall outcome in patients with ocular forms of cystinosis. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

Cysteamine hydrochloride reacts with cystine to form other substances that are able to leave the lysosome using the specific lysine cellular transport systems. By doing this cysteamine is expected to prevent cystine accumulation in lysosomes and this way rescue the cell damage that occurs because of cysteamine deficiency.

What is the stage of development of this medicine?

The effects of cysteamine hydrochloride were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with cystinosis were ongoing.

Cysteamine hydrochloride was not authorised anywhere worldwide for cystinosis or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 10 September 2008 a positive opinion recommending the grant of the above-mentioned 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 Community) 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.

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**Translations of the active ingredient and indication in all EU languages
and Norwegian and Icelandic**

Language	Active ingredient	Indication
English	Cysteamine hydrochloride	Treatment of cystinosis
Bulgarian	Цистеамин хидрохлорид	Лечение на цистинозата
Czech	Mercaptaminum hydrochloridum	Léčba cystinózy
Danish	Cysteamin hydroklorid	Behandling af cystinose
Dutch	Cysteaminehydrochloride	Behandeling van cystinose
Estonian	Tsüsteamiin- vesinikkloriid	Tsüstinoosi ravi
Finnish	Kysteamiinihydrokloridi	Kystinoosin hoito
French	Chlorhydrate de cystéamine	Traitement de la cystinose
German	Cysteaminhydrochlorid	Behandlung der Zystinose
Greek	Υδροχλωρική κυστεαμίνη	Θεραπεία της κυστίνωσης
Hungarian	Cisztamin hidroklorid	Cystinosis kezelése
Italian	Cisteamina cloridrato	Trattamento della cistinosi
Latvian	Cisteamīna hidrohlorīds	Cistinozes ārstēšana
Lithuanian	Cisteamino hidrochloridas	Cistinozės gydymas
Maltese	Cysteamine hydrochloride	Kura taċ-ċistinożi
Polish	Chlorowodorek cysteaminy	Leczenie cystynozy
Portuguese	Cloridrato de cisteamina	Tratamento da cistinose
Romanian	Clorhidrat de cisteamină	Tratamentul cistinozei
Slovak	Cysteamíniumchlorid	Liečba cystinózy
Slovenian	Cisteaminijev klorid	Zdravljenje cistinoze
Spanish	Cisteamina clorhidrato	Tratamiento de la cistinosis
Swedish	Cysteaminhydroklorid	Behandling av cystinos
Norwegian	Cysteaminhydroklorid	Behandling av cystinose
Icelandic	Cysteamín hýdróklóríð	Meðferð cystíngeymdarkvilla.