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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Cholic acid for the treatment of inborn errors in primary bile acid synthesis responsive to treatment with cholic acid

First publication	16 November 2009
Rev.1: transfer of sponsorship	22 December 2011
Rev.2: information about Marketing Authorisation	24 April 2014
Rev.3: transfer of sponsorship and administrative update	4 March 2015
Rev.4: transfer of sponsorship	22 May 2015
Rev.5: removal of information about Marketing Authorisation following the annulment on 11 June 2015	28 September 2015
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 28 October 2009, orphan designation (EU/3/09/683) was granted by the European Commission to Special Products Ltd, United Kingdom, for cholic acid for the treatment of inborn errors in primary bile acid synthesis responsive to treatment with cholic acid.

The sponsorship was transferred to FGK Representative Service GmbH, Germany, in December 2011 to ASK Pharmaceuticals GmbH, Germany, in November 2014 and finally to Retrophin Europe Limited, Ireland, in May 2015.

What are inborn errors in primary bile acid synthesis?

Inborn errors in primary bile acid synthesis are a group of diseases in which the liver does not produce ('synthesise') enough 'primary bile acids'. These acids are the main components of the bile, a fluid that helps digestion, and include cholic acid and chenodeoxycholic acid. The lack of bile acids is caused by inborn genetic abnormalities.

Patients lacking primary bile acids produce abnormal bile acids instead. These acids can damage the liver. In some cases, this can lead to liver failure. Not all errors in primary bile acid synthesis can be

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treated with cholic acid. Therefore, patients with these conditions can be divided into two groups, depending on whether they are responsive to treatment with cholic acid or not.

Inborn errors in primary bile acid synthesis responsive to treatment with cholic acid are a group of long-term debilitating and life-threatening diseases because they can severely damage the liver.

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

At the time of designation, inborn errors in primary bile acid synthesis responsive to treatment with cholic acid affected approximately 0.07 in 10,000 people in the European Union (EU). This was equivalent to a total of around 3,500 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, no satisfactory methods were authorised in the EU for the treatment of inborn errors in primary bile acid synthesis responsive to treatment with cholic acid. Patients with severe liver disease may need a liver transplant. Chenodeoxycholic acid and another bile acid called ursodeoxycholic acid, although authorised for other conditions, were used to treat inborn errors in primary bile acid synthesis.

How is this medicine expected to work?

Cholic acid is expected to work by replacing some of the missing bile acids in patients with inborn errors in primary bile acid synthesis. This is expected to decrease the production of abnormal bile acids and contribute to the normal activity of bile acids, therefore relieving the symptoms of these diseases.

What is the stage of development of this medicine?

The sponsor of this application has not conducted any studies with cholic acid. However, it provided the results of studies on the effects of cholic acid in experimental models and of clinical trials from the published literature to support its application for orphan designation.

At the time of submission, cholic acid was not authorised anywhere in the EU for inborn errors in primary bile acid synthesis responsive to treatment with cholic acid. Orphan designation of cholic acid had been granted in the EU and the United States of America for inborn errors in primary bile acid synthesis.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 2 September 2009 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 504,800,000 (Eurostat 2009).

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	Cholic acid	Treatment of inborn errors of primary bile acid synthesis responsive to treatment with cholic acid
Bulgarian	Холиева киселина	Лечение на вродени дефекти в първичната синтеза на жлъчна киселина, реагиращи на лечение с холиева киселина
Croatian	Kolatna kiselina	Liječenje prirođenih pogrešaka primarne sinteze žučne kiseline koje odgovaraju na liječenje kolatnom kiselinom
Czech	Kyselina cholová	Léčba vrozené primární poruchy syntézy žlučových kyselin odpovídající na terapii kyselinou cholovou
Danish	Cholsyre	Behandling af medfødt mangel på syntese af primære galdesyrer som responderer på behandling med cholsyre
Dutch	Cholinezuur	Behandeling van aangeboren deficiëntie in de primaire galzuursynthese, beantwoordend aan behandeling met cholinezuur
Estonian	Koliinhape	Sünnipärase primaarse sapphappe sünteesi häire, mis allub koliinhappe ravile, ravi
Finnish	Koolihappo	Primaarisen sappihapposynteesin synnynnäisen, koolihapolle reagoivan vajauksen hoito
French	Acide cholique	Traitement des déficits congénitaux de synthèse des acides biliaires primaires qui repondent au traitement par l'acide cholique
German	Cholsäure	Therapie von mit Cholsäure behandelbaren, angeborenen Störungen der primären Gallensäuresynthese
Greek	Χολικό Οξύ	Θεραπεία σύμφυτης ελαττωματικής σύνθεσης πρωτογενών χολικών οξέων που ανταποκρίνεται σε θεραπεία με χολικό οξύ
Hungarian	Cholsav	Cholsav kezelésre reagáló veleszületett primér epesav szintézis rendellenesség kezelése
Italian	Acido colico	Trattamento degli errori congeniti di sintesi degli acidi biliari primari, che rispondono al trattamento con acido colico
Latvian	Holskābe	Iedzimtu primāru žultsskābes sintēzes traucējumu ārstēšanai, kas padodas ārstēšanai ar holskābi
Lithuanian	Cholio rūgštis	Įgimtų pirminių tulžies rūgščių sintezės sutrikimų, turinčių atsaką į cholio rūgštį, gydymas
Maltese	Cholic acid	Kura ta' żbalji mit-twelid fis-sintesi ta' l-aċidu biljari primarju li jirrispondu għall-kura bil-cholic acid
Polish	Kwas cholowy	Leczenie wrodzonych zaburzeń pierwotnej syntezy kwasów żółciowych reagujące na leczenie kwasem cholowym
Portuguese	Ácido cólico	Tratamento das alterações congénitas da síntese de ácidos biliares primários que respondem ao tratamento com ácido cólico

[1] At the time of transfer of sponsorship

Language	Active ingredient	Indication
Romanian	Acid colic	Tratamentul anomaliilor congenitale ale sintezei de acizi biliari primari care răspund la tratamentul cu acid colic
Slovak	Kyselina cholová	Liečba vrodených porúch primárnej syntézy žlčovej kyseliny, citlivých na liečbu žlčovou kyselinou
Slovenian	Holinska kislina	Zdravljenje vrojenih motenj sinteze primarnih žolčnih kislin, ki se odzivajo na holinsko kislino
Spanish	Ácido cólico	Tratamiento de la deficiencia congénita de síntesis de los ácidos biliares primarios que responde al tratamiento con ácido cólico
Swedish	Cholsyra	Behandling av medfödd oförmåga att syntetisera primära gallsyror mottaglig till cholsyra behandling
Norwegian	Kolsyre	Behandling av medfødt defekt i syntese av primære gallesyrer, som responderer på kolsyre-behandling
Icelandic	Gallsýra	Meðferð við arfgengum göllum á gallsýrumyndun sem svara meðferð með gallsýru