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EMA/COMP/322667/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Norursodeoxycholic acid for the treatment of primary sclerosing cholangitis

On 4 July 2014, orphan designation (EU/3/14/1288) was granted by the European Commission to Dr Falk Pharma GmbH, Germany, for norursodeoxycholic acid for the treatment of primary sclerosing cholangitis.

What is primary sclerosing cholangitis?

Primary sclerosing cholangitis is a condition in which there is long-term inflammation and scarring (fibrosis) of the bile ducts in the liver. These ducts are tubes through which bile, a liquid produced by the liver to help digest fats, flows to the intestine. As a result of the damage to the ducts, bile acids, essential components of bile, build up in the liver and damage the liver tissue. Early symptoms of the disease include tiredness and itching. The disease is more common in middle-aged men.

Primary sclerosing cholangitis is a long-term debilitating and life-threatening disease because, when the disease progresses, it may lead to portal hypertension (high blood pressure in the vessels connecting the liver and the gut), liver cirrhosis (scarring of the liver) and liver failure, and may increase the risk of liver cancer.

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

At the time of designation, primary sclerosing cholangitis affected less than 1.6 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 82,000 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 containing ursodeoxycholic acid were authorised in some EU countries to treat primary sclerosing cholangitis. In advanced cases, the patient may need a liver transplant.

*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 28), Norway, Iceland and Liechtenstein. This represents a population of 511,100,000 (Eurostat 2014).

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The sponsor has provided sufficient information to show that norursodeoxycholic acid might be of significant benefit for patients with the condition because early studies in experimental models show that the medicine may have an improved beneficial effect on liver function compared with the authorised treatment. 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?

Norursodeoxycholic acid is a modified form of ursodeoxycholic acid, a bile acid found in small amount in human bile and which is already authorised for the treatment of primary sclerosing cholangitis.

Norursodeoxycholic acid, once taken by the patient, is thought to enter repeated cycles in which it is secreted by the liver cells, partially re-absorbed by the cells of the bile ducts, and then re-enters the liver cells. These cycles are thought to 'flush' the bile ducts. By 'flushing' the biliary system, this medicine is expected to prevent the build-up of bile acids in the liver and therefore the damage to the liver tissue.

What is the stage of development of this medicine?

The effects of norursodeoxycholic acid have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients with primary sclerosing cholangitis were ongoing.

At the time of submission, norursodeoxycholic acid was not authorised anywhere in the EU for primary sclerosing cholangitis 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 14 May 2014 recommending the granting of this designation.

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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	Norursodeoxycholic acid	Treatment of primary sclerosing cholangitis
Bulgarian	Норурсодезоксихолева киселина	Лечение на първичен склерозиращ холангит
Croatian	Norursodeoksikolatna kiselina	Liječenje primarnog sklerozirajućeg kolangitisa
Czech	Kyselina nor-ursodeoxycholová	Léčba primární sklerotizující cholangoitidy
Danish	Norursodeoxycholsyre	Behandling af primær skleroserende cholangitis
Dutch	Nor-ursodeoxycholzuur	Behandeling van primaire scleroserende cholangitis
Estonian	Norursodeoksükoolhape	Primaarse skleroseeriva kolangiidi ravi
Finnish	Norursodeoksikoolihappo	Primaarisen sklerosoivan kolangiitin hoito
French	Acide norursodésoxycholique	Traitement de la cholangite sclérosante primitive
German	Norursodesoxycholsäure	Behandlung der primär sklerosierenden Cholangitis
Greek	Νορ-ουρσοδεοξυχολικό οξύ	Θεραπεία της πρωτοπαθούς σκληρυντικής χολαγγειίτιδας
Hungarian	Nor-urzodezoxikólsav	Primer sclerotizáló cholangitis kezelése
Italian	Acido nor-ursodesossicolico	Trattamento della colangite sclerosante primitiva
Latvian	Norursodeoksiholskābe	Primārā sklerozējošā holangīta ārstēšana
Lithuanian	Norursodeoksicholio rūgštis	Pirminio sklerozuojančio cholangito gydymas
Maltese	Norursodeoxycholic acid	Kura tal-kolanġite sklerosanti primarja
Polish	Kwas norursodeoksycholowy	Leczenie pierwotnego stwardniającego zapalenia dróg żółciowych
Portuguese	Ácido nor-ursodesoxicólico	Tratamento da colangite esclerosante primária
Romanian	Acid norursodeoxicolic	Tratamentul colangitei sclerozante primare
Slovak	kyselina norursodeoxycholová	Liečba primárnej sklerotizujúcej cholangitídy
Slovenian	Norursodeoksiholna kislina	Zdravljenje primarnega sklerozirajočega holangitisa
Spanish	Ácido norursodesoxicólico	Tratamiento de colangitis esclerosante primaria
Swedish	Norursodeoxykolsyra	Behandling av primär skleroserande kolangit
Norwegian	Norursodeoksykolsyre	Behandling av primær skleroserende cholangitt
Icelandic	Norúrsódeoxýkólínsýra	Meðferð við frumkominni herslisgallrásarbólgu

[1] At the time of designation