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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Ornithine phenylacetate for the treatment of acute liver failure

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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/3/11/945) was granted by the European Commission to Dr Ulrich Granzer, Germany, for ornithine phenylacetate for the treatment of acute liver failure.

The sponsorship was transferred to Voisin Consulting S.A.R.L., France, in September 2014.

What is acute liver failure?

Acute liver failure is the sudden loss of normal liver functions in a patient with a previously normal liver and without evidence of chronic (long-term) liver disease. The most common first sign of liver failure is yellowing of the skin (jaundice). Acute liver failure brings serious complications such as bruising and bleeding due to impaired blood clotting, cerebral oedema (swelling around the brain), convulsions (fits) and coma. The most common causes of acute liver failure in the European Union (EU) are toxic damage (for example due to consumption of large amounts of alcohol or overdose of medicines such as paracetamol) or viral hepatitis (an infectious disease that affects the liver).

Acute liver failure is a long-term debilitating and life-threatening disease because of its damaging effects on the brain and other organs.

What is the estimated number of patients?

At the time of designation, acute liver failure affected approximately 0.06 in 10,000 people in the EU. This is equivalent to a total of around 3,000 people*, and is below the ceiling for orphan 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).

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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, the main treatment option for acute liver failure was liver transplantation. Patients with acute liver failure caused by paracetamol overdose were treated with N-acetylcysteine.

The sponsor has provided sufficient information to show that ornithine phenylacetate might be of significant benefit for patients with acute liver failure because early studies in experimental models show that it may 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?

Ornithine phenylacetate is expected to reduce the high levels of ammonia seen in the blood of patients with acute liver failure. Ammonia is a substance naturally produced by the body which may cause harm if it is not processed normally. One function of the liver is to transform this substance into urea which is then harmlessly eliminated in the urine. When the liver fails, it cannot transform ammonia into urea. The ammonia then accumulates in the blood and the brain causing many of the symptoms of acute liver failure.

Ornithine phenylacetate is made of two substances, ornithine and phenylacetate. Ornithine is used by muscle cells to produce glutamine, an amino acid. Production of glutamine from ornithine requires ammonia, which is taken up from excess ammonia circulating in the blood. Phenylacetate is then expected to attach to glutamine forming a substance that is eliminated in the urine.

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 ornithine phenylacetate in experimental models was ongoing.

At the time of submission, no clinical trials with ornithine phenylacetate in patients with acute liver failure had been started.

At the time of submission, ornithine phenylacetate was not authorised anywhere in the EU for acute liver failure 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.

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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	Ornithine phenylacetate	Treatment of acute liver failure
Bulgarian	Орнитин фенилацетат	Лечение на остра чернодробна недостатъчност
Croatian	Ornitin fenilacetat	Liječenje akutnog zatajenja jetre
Czech	Ornitin-fenylacetát	Léčba Akutní jaterní insuficience
Danish	Ornithin phenylacetat	Behandling af akut leversvigt
Dutch	Ornithinefenylacetaat	Behandeling van acuut leverfalen
Estonian	Ornitiin fenüülatsetaat	Akuutse maksapuudulikkuse ravi
Finnish	Ornitiinifenyyliasetaatti	Akuutin maksan vajaatoiminnan hoito
French	Phénylacétate d'ornithine	Traitement de l'insuffisance hépatique aiguë
German	Ornithinphenylacetat	Behandlung des akuten Leberversagens
Greek	Φαινυλοξική ορνιθίνη	Θεραπεία της οξείας ηπατικής ανεπάρκειας
Hungarian	Ornitin-fenil-acetát	Akut májelégtelenség kezelése
Italian	Ornitina fenilacetato	Trattamento della insufficienza epatica acuta
Latvian	Ornitīna fenilacetāts	Akūtas aknu mazspējas ārstēšana
Lithuanian	Ornitino fenilacetatas	Ūmaus kepenų nepakankamumo gydymas
Maltese	Ornithine phenylacetate	Kura ta' insuffiċjenza akuta tal-fwied
Polish	Fenylooctan ornityny	Leczenie ostrej niewydolności wątroby
Portuguese	fenil acetato de ornitina	Tratamento da insuficiência hepática aguda
Romanian	Fenilacetat de ornitină	Tratamentul insuficienţei hepatice acute
Slovak	Fenylacetát ornitínu	Liečba akútneho zlyhania pečene
Slovenian	Ornitin fenilacetat	Zdravljenje akutne jetrne odpovedi
Spanish	Fenilacetato de ornitina	Tratamiento de la insuficiencia hepática aguda
Swedish	Ornitinfenylacetat	Behandling av akut leversvikt
Norwegian	Ornitinfenylacetat	Behandling av akutt leversvikt
Icelandic	Ornitínfenýlasetat	Meðferð bráðrar lifrarbilunar

[1] At the time of transfer of sponsorship