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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

betaine anhydrous for the treatment of homocystinuria

On 9 July 2001, orphan designation (EU/3/01/045) was granted by the European Commission to Orphan Europe, France, for betaine anhydrous for the treatment of homocystinuria.

What is homocystinuria?

Homocystinuria is a genetic disorder. People who are born with homocystinuria are unable to properly break down methionine, an amino acid found in food. Methionine is used by the body for growth and repair. The remaining methionine is normally broken down through chemical reactions to a compound known as homocysteine and then to cysteine. Excess homocysteine is reversed back to methionine and vitamins assist in these processes. Most people with homocystinuria are missing cystathionine B-synthetase, an enzyme (protein that speeds up chemical reactions) that converts homocysteine into cysteine in the liver. With untreated homocystinuria, this balance is disturbed. There is an excess of homocysteine and methionine and a lack of cysteine. The imbalance can lead to mental retardation, severe bone problems, osteoporosis, or thinning of the bones, dislocated lenses of the eyes, blood clots and heart disease. Homocystinuria is chronically debilitating and life threatening.

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

At the time of designation, homocystinuria affected 0.165 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 6,200 people, and is below the threshold 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?

Several medicinal products were authorised for homocystinuria in the Community at the time of submission of the application for orphan drug designation. The available medicines were for symptomatic treatment.

*Disclaimer: The number of patients affected by the condition is estimated and assessed for the purpose of the designation, for a European Community population of 377,000,000 (Eurostat 2001) and may differ from the true number of patients affected by the condition.

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Betaine anhydrous could be of potential significant benefit for the treatment of homocystinuria. This is because it may be more effective than the existing medicinal products. 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?

Betaine anhydrous is a naturally occurring substance. This enzyme can work alone in the conversion of homocysteine to methionine. As a result of the administration of high doses of betaine anhydrous blood levels of homocysteine could be reduced below the toxic level.

What is the stage of development of this medicine?

The effects of betaine anhydrous have been evaluated in experimental models.

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

At the time of submission, betaine anhydrous was not authorised anywhere in the world for the treatment of homocystinuria. Orphan designation of betaine anhydrous had been granted in the United States for the treatment of homocystinuria.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 23 May 2001 recommending the granting of this designation.

Update: Betaine anhydrous (Cystadane) has been authorised in the EU since 17 February 2007 for adjunctive treatment of homocystinuria, involving deficiencies or defects in:

- cystathionine beta-synthase (CBS),
- 5,10-methylene-tetrahydrofolate reductase (MTHFR),
- cobalamin cofactor metabolism (cbl).

Cystadane should be used as supplement to other therapies such as vitamin B6 (pyridoxine), vitamin B12 (cobalamin), folate and a specific diet.

More information on Cystadane can be found in the European public assessment report (EPAR) on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports

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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	Betaine anhydrous	Treatment of Homocystinuria
Danish	Vandfri betain	Behandling af homocysteinuri
Dutch	Betaïne anhydraat	Behandeling van homocystinurie
Finnish	Anhydridinen betaiiini	Homokystinurian hoito
French	Bétaïne anhydre	Traitement de l'homocystinurie
German	Betainanhydrat	Behandlung der Homocysteinurie
Greek	Άνυδρος βεταΐνη	Θεραπεία της ομοκυστινουρίας
Italian	Betaina anidra	Trattamento dell'omocistinuria
Potuguese	Betaína anidra	Tratamento da homocistinúria
Spanish	Betaína anhidra	Tratamiento de la homocistinuria
Swedish	Betain dehydat	Behandling för homocystinuri

[1] At the time of designation