The European Agency for the Evaluation of Medicinal Products
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 trientine dihydrochloride for the treatment of Wilson's disease

On 24 October 2003, orphan designation (EU/3/03/172) was granted by the European Commission to Univar Limited, United Kingdom, for trientine dihydrochloride for the treatment of Wilson's disease.

What is Wilson's disease?
Wilson's disease is a genetic disorder that causes excessive copper accumulation in the liver or brain. The liver of a person who has Wilson's disease does not release copper into the bile, as it should. Bile is a liquid produced by the liver that helps with digestion. In Wilson disease, the copper absorbed from the food by the intestines builds up in the liver and injures liver tissue. Eventually, the damage causes the liver to release the copper directly into the bloodstream, which carries the copper throughout the body. The copper accumulated and transported by the bloodstream can then cause damage in other organs like the kidneys, brain, and eyes. If not treated, Wilson's disease can be chronically debilitating and life threatening.

What are the methods of treatment available?
Treatment of Wilson's disease generally consists of anti-copper agents to remove excess copper from the body and to prevent it from re-accumulating. Several medicinal products were authorised for Wilson's disease in the Community at the time of submission of the application for orphan drug designation.
Trientine dihydrochloride could be of potential significant benefit for the treatment of Wilson's disease, by making it available over the whole Community. In addition, trientine dihydrochloride may have a different safety profile for the treatment of the condition from that of medicinal products authorised today. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

What is the estimated number of patients affected by the condition*?
According to the information provided by the sponsor, Wilson's disease was considered to affect about 22,500 persons in the European Union.

How is this medicinal product expected to act?
Trientine dihydrochloride binds to the free copper in blood and increases copper excretion in the urine. It might also act by blocking intestinal copper absorption, but this possible mechanism remains to be fully demonstrated.

What is the stage of development of this medicinal product?

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 75 23 70 40
E-mail: orphandrugs@emea.eu.int www.emea.eu.int

The active substance, trientine dihydrochloride is authorised in the United Kingdom, in Wilson's patients who are intolerant of penicillamine therapy. The product authorised in the United Kingdom is exported to Germany, France, Greece, Norway, Switzerland, Austria and Ireland, however supply is restricted to named patients only.

Trientine dihydrochloride has been granted marketing authorisation in the United States for treatment of Wilson's disease in patients who are intolerant of penicillamine.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 10 September 2003 a positive opinion recommending the grant of the above-mentioned designation.

Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products which were considered for designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of the quality, safety and efficacy will be necessary before this product can be granted a marketing authorisation.

For more information:
Sponsor's contact details:
Univar Limited
International House, Zenith
Paycocke Road
Basildon,
Essex SS14 3DW
United Kingdom
Telephone: (44-1268) 59 44 00
Telefax: (44-1268) 59 44 81
E-mail: trientine@univareurope.com

Patients' associations contact points:

Asociación Española de Familiares y Enfermos de Wilson
c/ Juan de Valladolid, 4, 1º D
E-47014 Valladolid
Spain
Telephone: (34-983) 372 150
E-mail: wilsons@terra.es

*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 385,000,000 (Eurostat 2002) and may differ from the true number of patients affected by the condition. This estimate is based on available information and calculations presented by the sponsor at the time of the application.

COMETA A.S.M.M.E. Associazione Studio Malattie Metaboliche Ereditarie ONLUS
Via Vittorio Veneto 12a
35020 Legnaro (PD)
I-Italy
Telephone: +39 049 9903303
Telefax: +39 178 220 3410
E-mail: info@cometaasmme.org

Morbus Wilson e.V.
Meraner Str. 17
D-83024 Rosenheim
Telephone: 0049-8031-249230
Telefax: 0049-8031-43876
info@morbus-wilson.de

Translations of the active ingredient and indication in all EU languages

Language	**Active Ingredient**	**Indication**
English	Trientine dihydrochloride	Treatment of Wilson’s disease
Danish	Trientine dihydrochlorid	Behandling af Wilson's sygdom
Dutch	Trientine dihydrochloride	Behandeling van de ziekte van Wilson
Finnish	Trientiini dihydrokloridi	Wilsonin taudin hoito
French	Dichlorhydrate de trientine	Traitement de la maladie de Wilson
German	Trientine dihydrochloride	Behandlung der Wilson Krankheit
Greek	Διυδροχλωρική Τριεντίνη	Θεραπεία της νόσου του Wilson
Italian	Trientine diidrocloruro	Trattamento della malattia di Wilson
Portuguese	Di-hidrocloreto de trientina	Tratamento da doença de Wilson
Spanish	Dihidrocloruro de trientina	Tratamiento de la enfermedad de Wilson
Swedish	Trientindihydroklorid	Behandling av Wilsons sjukdom