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COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF ammonium tetrathiomolybdate for the treatment of Wilson's disease

On 1 April 2008, orphan designation (EU/3/08/539) was granted by the European Commission to JJGConsultancy Ltd, United Kingdom, for ammonium tetrathiomolybdate 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 body, typically in the liver and 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's disease, the copper that is normally 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 medicinal products to remove excess copper from the body and to prevent it from re-accumulating in different parts of the body by trapping copper. Several medicinal products were authorised for Wilson's disease in the Community at the time of submission of the application for orphan drug designation.

Ammonium tetrathiomolybdate might be of potential significant benefit for the treatment of Wilson's disease, because it is expected to be beneficial for the patients with Wilson's disease who suffer from neurological symptoms. 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 with Wilson's disease*?

Based on the information provided by the sponsor and previous knowledge of the Committee, Wilson's disease was considered to affect not more than 0.6 in 10,000 persons in the European Union which, at the time of designation, corresponded to about 30,000 persons.

How is this medicinal product expected to act?

Ammonium tetrathiomolybdate binds to copper and to a protein called albumin in the bloodstream. Once bound to ammonium tetrathiomolybdate and albumin, copper cannot be taken up by the organs and the damaging effects of copper are expected to decrease. Ammonium tetrathiomolybdate also acts

* Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 27), Norway, Iceland and Lichtenstein. This represents a population of 498,000,000 (Eurostat 2006). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

in the intestine, by blocking the absorption of copper into the bloodstream, then decreasing copper uptake.

What is the stage of development of this medicinal product?

The effects of ammonium tetrathiomolybdate were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with Wilson's disease were ongoing.

Ammonium tetrathiomolybdate was not authorised anywhere worldwide for Wilson's disease, at the time of submission. Orphan designation of ammonium tetrathiomolybdate was granted in the United States for the treatment of Wilson's disease.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 6 February 2008 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.

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**Translations of the active ingredient and indication in all EU languages
and Norwegian and Icelandic**

Language	Active Ingredient	Indication
English	Ammonium tetrathiomolybdate	Treatment of Wilson's disease
Bulgarian	Амониев тетра тиомолибдат	Лечение на болест на Уилсон
Czech	Amonium terathiomolybdat	Léčba Wilsonovy choroby
Danish	Ammonium tetrathiomolybdat	Behandling af Wilson's sygdom
Dutch	Ammonium tetrathiomolybdaat	Behandeling van de ziekte van Wilson
Estonian	Ammoonium-tetratiomolübdaat	Wilsoni haiguse ravi
Finnish	Ammoniumtetratiomolybdaatti	Wilsonin taudin hoito
French	Tétrathiomolybdate d'ammonium	Traitement de la maladie de Wilson
German	Ammonium tetrathiomolybdat	Behandlung des Morbus Wilson
Greek	Τετραθειούχο μολυβδένο αμμώνιο	Θεραπεία της νόσου του Wilson
Hungarian	Ammónium tetrathiomolybdát	Wilson-betegség kezelése
Italian	Tetratiomolibdato di ammonio	Trattamento della malattia di Wilson
Latvian	Amonija tetratiomolibdāts	Vilsons slimības ārstēšana
Lithuanian	Amonio tetratiomolibdatas	Vilsono ligos gydymas
Maltese	Ammonium tetrathiomolybdate	Kura tal-marda ta' Wilson
Polish	Tetrathiomolybdate amonowy	Leczenie choroby Wilsona
Portuguese	Tetratiomolibdato de amónio	Tratamento da doença de Wilson
Romanian	Tetratiomolibdat de amoniu	Tratamentul bolii Wilson
Slovak	Tetratiomolybdénan amónny	Liečba Wilsonovej choroby
Slovenian	Amonijev tetratiomolibdat	Zdravljenje Wilsonove bolezni
Spanish	Tetratiomolibdato de amonio	Tratamiento de la enfermedad de Wilson
Swedish	ammonium tetratiomolybdat	Behandling av Wilsons sjukdom
Norwegian	Ammoniumtetratiomolybdat	Behandling av Wilsons sykdom
Icelandic	Ammóníak tetrátíómólýbdat	Meðferð við Wilsons sjúkdómi