23 September 2014
EMA/COMP/443070/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Sodium ascorbate and menadione sodium bisulfite for the treatment of autosomal dominant polycystic liver disease

On 22 August 2014, orphan designation (EU/3/14/1308) was granted by the European Commission to JJGConsultancy Ltd, United Kingdom, for sodium ascorbate and menadione sodium bisulfite for the treatment of autosomal dominant polycystic liver disease.

What is autosomal dominant polycystic liver disease?

Autosomal dominant polycystic liver disease (ADPLD) is an inherited condition in which cells in the lining of the bile ducts (the network of channels in the liver through which bile is secreted) grow and develop abnormally, forming numerous cysts (fluid-filled sacs) in the tissue of the liver.

Women are affected more than men and tend to have larger cysts. About 20% of patients with the condition develop symptoms due to the growth of these cysts, which can gradually enlarge the liver so that it presses on other organs, causing pain and preventing both the liver and the other organs from working properly. Cysts may also become twisted under pressure (torsion) leading to tissue damage or rupture, and complications due to infection or bleeding into the centre of the cyst may occur. The condition is 'autosomal dominant', which means that it is caused by gene mutations (defects) that are 'dominant' because a person can have the disease even if they have inherited a defective gene from only one parent.

ADPLD is a chronically debilitating and life-threatening condition due to failure of organs around the enlarged liver and the complications of infection, torsion and bleeding into the cyst.

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

At the time of designation, ADPLD affected approximately 0.02 in 10,000 people in the European Union (EU). This was equivalent to a total of around 1,000 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).

[*]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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What treatments are available?

At the time of designation, no satisfactory methods were authorised in the EU for the treatment of ADPLD. Patients with symptoms were treated with supportive care and surgery to relieve the effects of cyst growth. Patients without symptoms did not require treatment.

How is this medicine expected to work?

The medicine combines a form of vitamin C, sodium ascorbate, with a form of vitamin K, menadione sodium bisulfite, both of which have been available for many years in the EU. When given together, these vitamins can interfere with the cycle of growth and development of abnormal cells, preventing them from growing. In patients with ADPLD this action of both vitamins is expected to reduce the growth of cysts and so stop enlargement of the liver and development of symptoms and complications.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with this medicine in patients with ADPLD had been started.

At the time of submission, the combination of sodium ascorbate and menadione sodium bisulfite was not authorised anywhere in the EU for ADPLD. Orphan designation of the medicine had been granted in the United States for ADPLD and the related condition, autosomal dominant polycystic kidney disease.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 10 July 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	Sodium ascorbate and menadione sodium bisulfite	Treatment of autosomal dominant polycystic liver disease
Bulgarian	Натриев аскорбат и менадион натриев бисулфит	Лечение на автозомно-доминантна поликистозна чернодробна болест.
Croatian	Natrijev askorbat i natrijev menadionbisulfit	Liječenje autosomno dominantne policistične bolesti jetre
Czech	Askorbát sodný a bisulfát menadion sodný	Léčba autosomálně dominantní polycystózy jaterní
Danish	Natrium ascorbat og menadion natrium bisulfit	Behandling af autosomal polycystisk leversygdom
Dutch	Natriumascorbaat en menadionenatriumbisulfiet	Behandeling van autosomal dominant polycystisch
Estonian	Naatriumaskorbaadi ja naatriummenadiooni bisulfit	Autosoom-dominantse polütsüstilise maksahaiguse ravi
Finnish	Natrium askorbaatti ja menadioni natrium bisulfiitti	Autosomaalisen dominantin polykystisen maksasairauden hoito
French	Ascorbate de sodium et bisulfite sodique de ménadione	Traitement de la maladie polykystique automosale dominante du foie
German	Natriumascorbat und Menadion-natriumbisulfit	Behandlung einer autosomal-dominanten Polyzystischen Lebererkrankung
Greek	Ασκορβικό νάτριο και μεναδιόνη θειώδους νατρίου	Θεραπεία της αυτοσωματικής επικρατούς πολυκυστικής νόσου του ήπατος
Hungarian	Nátrium aszkorbát és menadion nátrium biszulfit	Autoszomális domináns policisztás májbetegség kezelése
Italian	Sodio ascorbato e menadione sodio bisolfito	Trattamento della malattia epatica policistica autosomica dominante
Latvian	Nātrija askorbāts un menadiona nātrija bisulfīts	Autosomālās dominantās policistiskās aknu slimības ārstēšana
Lithuanian	Natrio askorbatas ir menadiono natrio bisulfitas	Autosominės dominantinės policistinės kepenų ligos gydymas
Maltese	Sodium ascorbate u menadione sodium bisulfite	Kura tal-marda poliċistika tal-fwied awtosomali dominanti
Polish	Askorbinian sodu i wodorosiarczyn sodowy menandionu	Leczenie autosomalnego dominującego zwyrodnienia wielotorbielowatego wątroby
Portuguese	Ascorbato de sódio e bissulfito sódico de menadiona	Tratamento da doença poliquística autosómica dominante do fígado
Romanian	Ascorbat de sodiu şi bisulfit sodic de menadionă	Tratamentul bolii polichistice hepatice autosomal dominante
Slovak	Askorbát sodný a menadión bisulfit sodný	Liečba autozomálne dominantnej polycystickej choroby pečene

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	Natrijev askorbat in menadion natrijev bisulfit	Zdravljenje akutne autosomno dominantne bolezni policističnih jeter
Spanish	Ascorbato de sódio y bissulfito sódico de menadiona	Tratamento de la enfermdad policistica autosómica dominante del hígado
Swedish	Natriumaskorbat och menadionnatriumbisulfit	Behandling av autosomal dominant polycystisk leversjukdom
Norwegian	Natriumaskorbat og menadionnatriumbisulfitt	Behandling av autosomal dominant polycystisk leversykdom
Icelandic	Natríum ascorbat og menadíón natríum bísúlfít	Meðferð autosomal ráðandi fjölblöðru lifrarsjúkdómi