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EMA/COMP/642562/2010
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Silibinin-C-2',3-dihydrogensuccinate, disodium salt for the prevention of recurrent hepatitis C in liver transplant recipients

On 17 December 2010, orphan designation (EU/3/10/828) was granted by the European Commission to Rottapharm S.p.A., Italy, for silibinin-C-2',3-dihydrogensuccinate, disodium salt for the prevention of recurrent hepatitis C in liver transplant recipients.

What is recurrent hepatitis C in liver transplant recipients?

Hepatitis C is an infection of the liver due to the hepatitis C virus. Patients with chronic (long-term) infection are at risk of liver damage and may develop serious liver diseases such as cirrhosis (liver scarring) and liver cancer, which require liver transplantation. However, because the hepatitis C virus remains in the body, the transplanted liver is also at risk of becoming infected, and therefore of developing cirrhosis and cancer.

Recurrent (repeated) hepatitis C in liver transplant recipients is a debilitating and life-threatening condition because of the serious complications that can develop in the transplanted liver.

What is the estimated number of patients at risk of developing the condition?

At the time of designation, the number of liver transplant recipients at risk of developing recurrent hepatitis C was estimated to be less than 1 person in 10,000 in the European Union (EU)*. This is equivalent to a total of fewer than 51,000 people, which 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 27), Norway, Iceland and Liechtenstein. This represents a population of 506,500,000 (Eurostat 2010).

What methods of prevention are available?

At the time of designation, there were no satisfactory treatments authorised for the prevention of recurrent hepatitis C in liver transplant recipients. Patients at risk were treated using the 'standard of care' for hepatitis C (pegylated interferon and ribavirin).

How is this medicine expected to work?

Silibinin-C-2',3-dihydrogensuccinate, disodium salt is made from a substance extracted from milk thistle fruits. It has been used since the mid-1980s as an antidote to poisoning with the fungus *Amanita phalloides*.

In the prevention of hepatitis C recurrence in liver transplant recipients, it is expected to work as an antiviral medicine by stopping the hepatitis C virus from multiplying. When given at the time of liver transplantation, this is expected to rid the body of the virus, therefore preventing the transplanted liver from becoming infected at a later date.

What is the stage of development of this medicine?

The effects of silibinin-C-2',3-dihydrogensuccinate, disodium salt have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine in liver transplant recipients at risk of developing recurrent hepatitis C were ongoing.

At the time of submission, the medicine was authorised in 15 countries in the EU for the treatment of liver intoxication due to *Amanita phalloides* under the trade name Legalon SIL. The medicine was not authorised anywhere in the EU for the prevention of recurrent hepatitis C in liver transplant recipients nor 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 7 October 2010 recommending the granting of this designation.

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

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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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Silibinin-C-2',3-dihydrogensuccinate, disodium salt	Prevention of recurrent hepatitis C in liver transplant recipients
Bulgarian	Силибинин-С-2',3-дихидрогенсуксинат, двунатриева сол	Превенция на рекурентен Хепатит С при пациенти, получили чернодробни транспланти
Czech	Disodná sůl silibinin-C-2',3-dihydrogensukcinátu	Léčba pravostranného srdečního selhání po kardiotoronii
Danish	Silibinin-C-2',3-dihydrogensuccinat, dinatriumsalt	Forebyggelse af tilbagevendende hepatitis C i levertransplantatmodtagere
Dutch	Silibinine-C-2',3-diwaterstofsuccinaat, dinatriumzout	Preventie van recurrenthe hepatitis C in levertransplantatrecipiënten
Estonian	Silibiniin-C-2',3-divesiniksuktsinaadi dinaatriumsool	Retsidiivse C-hepatiidi ärahoidmine maksatransplantaadi retsiipientidel.
Finnish	Silibiniini-C-2',3-divetyasukkinaatti, dinatriumsuola	Toistuvan hepatiitti C:n esto maksansiirtojen vastaanottajissa
French	Silibiline-C-2',3-dihydroxysuccinate, sel disodique	Prévention des recurrences de l'hépatite virale C chez les transplantés hépatiques
German	Dinatrium(silibinin-C-2',3-disuccinat)	Prävention rezidivierender Hepatitis C-Infektionen bei Lebertransplantatempfängern
Greek	Σιλιβινίνη-С-2',3-δισώξινη ηλεκτρική, δινάτριο άλας	Πρόληψη ηποτροπιάζουσας Ηπατίτιδας C σε λήπτες μοσχεύματος ήπατος
Hungarian	Szilibinin-C-2',3-dihidrogén-szukcinát dinátrium sója	Májtranszplantációt követő visszatérő Hepatitis –C megelőzése
Italian	Silibinina-C-2',3-diidrogenosuccinato, sale disodico	Prevenzione delle recidive dell'epatite C in pazienti sottoposti a trapianto di fegato
Latvian	Silibinīna-C-2',3-dihidrogēnsukcināta dinātrija sāls	C hepatīta recidīva profilakse aknu transplantāta recipientiēm
Lithuanian	Silibinino-C-2',3-dihidrogensukcinatas, dinatrio druska	Pakartotinio hepatito C viruso kepenyse prevencija, kepenų transplantato recipientams
Maltese	Silibinin-C-2',3-dihydrogensuccinate, disodium salt	Prevenzjoni tal-epatite tat-tip Ċ rikorrenti f'pazjenti li kellhom trapijant tal-fwied
Polish	Sylibino-C-2',3-dwuodorobursztynian, sól dwusodowa	Zapobieganie nawracającemu zapaleniu wątroby typu C u biorców przeszczepu wątroby
Portuguese	Silibinina-C-2',3-di-hidrogenossuccinato, sal dissódico	Prevenção da hepatite C recorrente em receptores de transplante hepático
Romanian	Silibină-C-2',3-dihidrogen succinat, sare disodică	Profilaxia hepatitei C recurente la pacienții cu transplant hepatic
Slovak	Dvojsodná soľ silibinín-C-2',3-dihydrogénsukcinátu	Prevencia rekurentnej hepatitídy C u pacientov po transplantácii pečene

¹ At the time of designation

Slovenian	Silibinin-C-2',3-dihidrogensukcinat, dinatrijeva sol	Preprečevanje rekurentnega hepatitisa C pri bolnikih z jetrnim poresadkom
Spanish	Silibinina-C-2',3-dihidrógeno-succinato, sal disódica	Prevención de la recurrencia de la hepatitis C en recipientes de transplante de hígado
Swedish	Silibinin-C-2',3-divätesuccinat, dinatriumsalt	Profylax av återkommande hepatit C hos levertransplantat mottagare
Norwegian	Silibinin-C-2',3-dihydrogensuksinat, dinatriumsalt	Forebygging av hepatitt C residiv hos mottagere av levertransplantat
Icelandic	Silibinin-C-2',3-tvíhýdrógen súkkínat, tvínatríum salt	Fyrirbyggjandi gegn endurvakinni lífrabólgu C lífrarsjúkdómi hjá lífrarígræðsluþegum