



COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

**PUBLIC SUMMARY OF
POSITIVE OPINION FOR ORPHAN DESIGNATION
OF**

**recombinant human hepatitis C monoclonal antibody against C4 region of E1
for the prevention of
recurrent hepatitis C virus induced liver disease in liver transplant recipients**

On 6 December 2007, orphan designation (EU/3/07/503) was granted by the European Commission to GENimmune, N.V., Belgium, for recombinant human hepatitis C monoclonal antibody against C4 region of E1 for the prevention of recurrent hepatitis C virus induced liver disease in liver transplant recipients.

What is recurrent hepatitis C virus induced liver disease in liver transplant recipients?

Hepatitis is a general term that means inflammation of the liver. Hepatitis C is an infectious disease that affects the liver, caused by the hepatitis C virus. This viral infection does not always cause symptoms in the patient, and thus some people infected with the virus will not look or feel ill; others might have mild flu-like symptoms, or can become very ill.

Most patients fully recover spontaneously while others remain infected, initially without any sign or symptom of the disease. They are called hepatitis C virus carriers and they are at risk of serious liver disease, such as cirrhosis (liver scarring) and liver cancer. In these cases, liver transplantation (getting a liver from a donor) could become a necessity. However, since the virus is found also in other organs of the body of hepatitis C virus carriers, the transplanted liver might become infected on its turn and the liver disease could start again in the transplanted liver. Recurrent hepatitis C virus induced liver disease in liver transplant recipients is chronically debilitating and life-threatening.

What are the methods of prevention available?

No satisfactory methods were authorised at the time of application.

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

Based on the information provided by the sponsor and previous knowledge of the Committee, recurrent hepatitis C virus induced liver disease in liver transplant recipients was considered to affect approximately 0.1 in 10,000 persons in the European Union, which, at the time of designation, corresponded to about 5000 persons.

How is this medicinal product expected to act?

Antibodies are proteins, which specifically recognise and attach themselves to certain structures, such as proteins found on the surface of viruses or bacteria. Recombinant human hepatitis C monoclonal antibody against C4 region of E1 is an antibody that recognises and neutralises (prevents from being harmful) a specific structure found on hepatitis C virus particles. The sponsor has suggested that recombinant human hepatitis C monoclonal antibody against C4 region of E1 would prevent recurrent

* 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.

hepatitis C virus induced liver disease through this mechanism. Thus, if administered after liver transplantation, it could potentially protect the new liver from becoming infected by hepatitis C virus.

What is the stage of development of this medicinal product?

The evaluation of the effects of recombinant human hepatitis C monoclonal antibody against C4 region of E1 in experimental models was ongoing. At the time of submission of the application for orphan designation, no clinical trials in patients with recurrent hepatitis C virus induced liver disease in liver transplant recipients were initiated.

Recombinant human hepatitis C monoclonal antibody against C4 region of E1 was not authorised anywhere worldwide for the prevention of recurrent hepatitis C virus induced liver disease in liver transplant recipients or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 10 October 2007 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	Recombinant human hepatitis C monoclonal antibody against C4 region of E1	Prevention of recurrent hepatitis C virus induced liver disease in liver transplant recipients
Bulgarian	Рекомбинантно човешко хепатит С моноклонално антитяло срещу фрагмент С4 на Е1	Предотвратяване на рецидиви на чернодробно заболяване, причинено от вируса на хепатит С, при чернодробно трансплантирани пациенти
Czech	Rekombinantní humánní monoklonální protilátka hepatitidy C proti C4 E1	Prevence recidivy jaterního onemocnění indukovaného virem hepatitidy C u nemocných po transplantaci jater
Danish	Rekombinant monoklonalt humant C4 region fra E1 antistof mod hepatitis C	Forebyggelse mod tilbagevendende hepatitis C virus induceret leversygdom i levertransplantatmodtagere
Dutch	Recombinant humaan monoklonaal hepatitis C antilichaam gericht tegen C4 regio van E1	Preventie van wederkerende hepatitis C virus geïnduceerde leveraandoening in levertransplant recipiënten
Estonian	Rekombinantne inimese C-hepatiidi monoklonaalne antikeha E1 C4 regiooni vastu	Retsidiivse C-hepatiidi tingitud maksahaiguste ärahoidmine maksatransplantaadi retsipientidel.
Finnish	Rekombinantti humaani monoklonaalinen Hepatiitti C vasta-aine E1 C4-alueella kohtaan	Toistuvan hepitiitti C -viruksen aiheuttaman maksasairauden estäminen maksansiirtojen vastaanottajissa
French	Anticorps recombinant monoclonal humain anti-hépatite C dirigé contre la région C4 de E1	Prévention des manifestations hépatiques récurrentes causées par le virus de l'hépatite C chez les transplantés hépatiques
German	Humaner monoklonaler rekombinanter Hepatitis C Antikörper gegen Region C4 von E1	Schutz vor Wiederauftreten der Hepatitis C-Infektion bei Lebertransplantatempfängern
Greek	Ανθρώπινο μονοκλωνικό αντίσωμα ενάντια της περιοχής C4 της πρωτεΐνης E1 του ιού της ηπατίτιδας Γ	Πρόληψη από υποτροπιάζουσα ηπατική νόσο προερχόμενη από τον ιό της Ηπατίτιδας C σε λήπτες μοσχεύματος ήπατος
Hungarian	E1 burokfehérje C4 régiója ellenes rekombináns humán Hepatitis C monoklonális antitest	Májtranszplantációt követő visszatérő Hepatitis –C virus fertőzés megelőzése
Italian	Anticorpo monoclonale umano ricombinante anti HCV, diretto contro la regione C4 di E1	Prevenzione delle malattie epatiche ricorrenti indotte dal virus dell'epatite C in pazienti sottoposti a trapianto di fegato
Latvian	Rekombinēta cilvēka C hepatīta monoklonālas antivielas pret E1 hepatīta C4 vīrusu	Atkārtotas hepatīta C izraisītas aknu slimības profilaksei aknu transplantāta recipientiem
Lithuanian	Rekombinantinis žmogaus hepatito C monokloninis antikūnas prieš C4 sritį iš E1	Kepenų ligos, nulemtos pakartotinio hepatito C viruso, prevencija kepenų transplantato recipientams
Maltese	Anti-korp monoklonali uman	Prevenzjoni ta' mard tal-fwied rikorrenti

	rikombinanti ta' l-epatite tat-tip C kontra r-regjun C ta' l-E1	ikkawzat mill-virus ta' l-epatite tat-tip C f' pazjenti li kellhom trapjant tal-fwied
Polish	Rekombinowane ludzkie przeciwcialo monoklonalne przeciw fragmentowi C4 bialka E1 wirusowego zapalenia watroby typu C	Zapobieganie nawracajacemu zapaleniu watroby wywołanemu przez wirus typu C u biorców przeszczepu watroby
Portuguese	Anticorpo monoclonal recombinante humano da região C4 da proteina E1 do vírus da Hepatite C	Prevenção da doença hepática recorrente induzida pelo vírus da hepatite C em recipientes de transplante hepático
Romanian	Anticorp monoclonal uman recombinant pentru regiunea C4 a proteinei E1 a virusului hepatitic C	Prevenirea recurenței afecțiunilor hepatice induse de virusul hepatitic C, la pacienții cu transplant hepatic
Slovak	Rekombinantná ľudská monoklónna protilátka hepatitídy C (proti C4 E1)	Prevenia rekurentnej hepatitídy C u príjemcov transplantátov pečene s vírusmi indukovanými ochoreniami pečene
Slovenian	Humano monoklonsko rekombinantno protitelo proti regiji C4 proteina E1 virusa hepatitisa C	Preprečevanje ponovne jetrne okvare, povzročene s HCV, pri prejemniku jetrnega transplantata
Spanish	Anticuerpo monoclonal recombinante contra la región C4 de la proteína E1 del virus de la hepatitis C	Prevenición de la recurrencia de la enfermedad hepática inducida por el virus de la hepatitis C en receptores transplante de hígado
Swedish	Rekombinant human hepatit C monoklonal antikropp mot C4 region av E1	Profylax av återkommande hepatit C virusinducerad lever sjukdom hos levertransplantat mottagare
Norwegian	Rekombinant humant monoklonalt antistoff mot hepatitt C, C4 region av E1	Forebygging av tilbakevendende hepatitt C virus-indusert leversykdom hos levertransplanterte pasienter
Icelandic	Manna einstofna mótefni gegn C4 svæði E1próteini lifrabólgu C veiru.	Fyrirbyggjandi gegn endurteknum lifrabólgu C tengdum lifrarsjúkdómi hjá lifrarígræðsluþegum