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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Covalently closed DNA plasmids coding for *cytomegalovirus phosphoprotein 65* and *glycoprotein B* genes for the prevention of cytomegalovirus disease in patients with impaired cell mediated immunity deemed at risk

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Disclaimer

Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.

Withdrawn

On 9 August 2012, orphan designation (EU/3/12/1042) was granted by the European Commission to Astellas Pharma Europe B.V., the Netherlands, for covalently closed DNA plasmids coding for *cytomegalovirus phosphoprotein 65* and *glycoprotein B* genes for the prevention of cytomegalovirus disease in patients with impaired cell mediated immunity deemed at risk.

What is cytomegalovirus disease?

Cytomegalovirus is a common virus that can cause mild infection such as a sore throat. Most people get infected at some stage during their lifetime but are very often unaware of it. After infection, the virus remains in the body in a 'latent' (inactive) state and only becomes active again if the body's immunity, specifically its cell-mediated immunity, is weakened.

Cell-mediated immunity is a defence mechanism where specialised cells called T-lymphocytes directly neutralise viruses. In people with weakened cell-mediated immunity, such as patients with HIV infection or transplant patients receiving immunosuppressant treatment (medicines that reduce the activity of the immune system), cytomegalovirus can become active again and, this time, cause severe infection.

Cytomegalovirus disease in patients with impaired cell-mediated immunity is long-term debilitating and life threatening because of the complications it causes, such as infection of the lungs, liver and digestive tract, as well as reduced graft survival in transplanted patients.

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

At the time of designation, the number of patients with impaired cell-mediated immunity at risk of cytomegalovirus disease was estimated to be less than 3 people in 10,000 in the European Union (EU). This is equivalent to a total of fewer than 153,000 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).

What methods of prevention are available?

At the time of orphan designation, several antiviral medicines (aciclovir, ganciclovir, valaciclovir and valganciclovir) were approved in the EU for the prevention of cytomegalovirus disease in transplant recipients. Patients at risk were also closely monitored to detect signs of cytomegalovirus infection as early as possible.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients at risk of cytomegalovirus disease because it works in a different way to existing treatments, and is expected to stimulate both cell-mediated immunity (which involves cells directly attacking the virus) and humoral immunity (which involves the use of specialised proteins called antibodies to attack the virus). In addition, it may reduce the need for antiviral treatment which can have several side effects. These assumptions will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

This medicine contains the genes (DNA) responsible for making two proteins of the CMV virus (phosphoprotein 65 and glycoprotein B). When given to the patient, the genes are expected to produce the two proteins, which are in turn expected to stimulate an immune response against the cytomegalovirus. The immune system is then expected to be able to produce a more effective response when it is exposed to the virus again.

The two proteins in the medicine have been chosen because they are expected to be able to stimulate cell-mediated immunity and humoral immunity.

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, clinical trials with the medicine in transplant recipients were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for prevention of cytomegalovirus disease. Orphan designation of the medicine had been granted in the United States of America for prevention of cytomegalovirus disease and associated complications.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 11 July 2012 recommending the granting of this designation.

*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.
At the time of designation, this represented a population of 509,000,000 (Eurostat 2012).

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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.

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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	Covalently closed DNA plasmids coding for cytomegalovirus *phosphoprotein 65* and *glycoprotein B* genes	Prevention of cytomegalovirus disease in patients with impaired cell mediated immunity deemed at risk
Bulgarian	Ковалентно свързани ДНК плазмиди, кодиращи цитомегаловирусните *фосфолипопротеин 65* и *гликопротеин B* гени	Превенция на цитомегаловирусна болест при рискови пациенти с увреден клетъчен имунитет
Czech	DNA vakcína proti cytomegaloviru (CMV) s plazmidy nesoucími geny *fosfoprotein 65* (pp65) a *glykoprotein B* (gB).	Prevence cytomegalovirového onemocnění u rizikových pacientů s poruchou buněčné imunity
Danish	Kovalent lukkede DNA plasmider indeholdende gener, somudtrykker cytomegalovirus *phosphoprotein 65* (pp65) og *glykoprotein B* (gB).	Forebyggelse af cytomegalovirus (CMV)-sygdom hos risikopatienter med svækket cellemedieret immunitet.
Dutch	Covalent gesloten DNA plasmiden coderend voor cytomegalovirus *fosfoproteïne 65* en *glycoproteïne B* genen	Preventie van cytomegalovirusziekte bij risicopatiënten met verzwakte cellulaire immuniteit
Estonian	Kovalentse sidemega ühendatud DNA plasmiidid, mis kodeerivad tsütomegaloviiruse *fosfoproteiin 65* ja *glükoproteiin B* geene.	Tsütomegaloviiruse haiguse ennetamine patsientidel, kellel on kõrgenenud risk rakulise immunsuse häirele.
Finnish	Sytomegalovirus (CMV) DNA-rokote, joka sisältää *fosfoproteiini 65*- (pp65) ja *glykoproteiini B* (gB) -geenejä ilmentäviä plasmideja.	CMV-viremioiden ja/tai sytomegalovirussairauden ehkäisy potilailla, joiden soluvälitteinen immuniteetti on heikentynyt siirron vuoksi.
French	Vaccin ADN contre le cytomégalovirus (CMV), contenant des plasmides exprimant les gènes de la *phosphoprotéine 65* (pp65) et de la *glycoprotéine B* (gB).	Prévention des maladies à cytomégalovirus chez des patients à risque présentant une altération de l'immunité cellulaire.
German	Kovalent geschlossene DNA Plasmide, die für die CMV Gene "*Phosphoprotein 65*" und "*Glycoprotein B*" kodieren	Prävention einer CMV Erkrankung in Risikopatienten mit gestörterter zellvermittelter Immunität

[1] At the time of designation

Language	Active ingredient	Indication
Greek	Ομοιπολικά κλεισμένα πλασμίδια DNA που κωδικοποιούν για τα γονίδια της *φωσφοπρωτεΐνης 65* (pp65) και της *γλυκοπρωτεΐνης B* (GB) του κυτταρομεγαλοϊού.	Προφύλαξη από τον μεγαλοκυτταροϊό (CMV) σε ασθενείς υψηλού ρίσκου, με διαταραχή της κυτταροεξαρτώμενης ανοσίας
Hungarian	Citomegalovírus (CMV) elleni DNS-vakcina, *foszfoprotein 65* (pp65) és *glikoprotein B* (gB) gént expresszáló plazmidokkal.	Citomegalovírus betegség megelőzése csökkent celluláris immunitású, kockázatnak kitett betegek esetén.
Italian	Plasmidi covalentemente chiusi codificanti per i geni della *fosfoproteina 65* (pp65) e della *glicoproteina B* (gB).	Prevenzione della malattia da citomegalovirus nei pazienti con deficit dell'immunità cellulo-mediata considerati a rischio
Latvian	Citomegalovīrusa (CMV) DNS vakcīna ar plazmīdiem, kas izsaka *fosfoproteīna 65* (pp65) un *glikoproteīna B* (gB) gēnus.	Citomegalovīrusa virēmijas un/vai saslimšanas profilakse riska grupas slimniekiem ar šūnu imunitātes traucējumiem transplantācijas dēļ.
Lithuanian	Kovalentiškai artimos DNR plazmidės, koduojančios citomegalo viruso (CMV) *fosfoproteino 65* ir *glikoproteino B* genus	Citomegalo viruso sukeltos infekcijos prevencija dėl galimos rizikos pacientams su susilpnėjusiu netiesioginiu ląsteliniu imunitetu
Maltese	*Plasmids* ta' DNA magħluqin premezz ta' rabta kovalenti li jikkodifikaw għal ġeni ta' *phosphoprotein 65* u *glycoprotein B* ta' ċitomegalovirus	Prevenzjoni ta' mard ikkawżat mill-ċitomegalovirus f'pazjenti b'riskju li għandhom dgħjufija tal-immunità permezz taċ-ċelloli
Polish	Kowalentnie zamknięte plazmidy DNA zawierające geny kodujące *fosfoproteinę 65* i *glikoproteinę B* wirusa cytomegalii.	Zapobieganie choroby wywołanej przez wirusa cytomegalii u pacjentów z zaburzeniami odporności komórkowej zagrożonych zakażeniem
Portuguese	Vacina com ADN de citomegalovírus (CMV) com plasmídeos que expressam genes de *fosfoproteína 65* (pp65) e de *glicoproteína B* (gB).	Prevenção de viremia e/ou doença causada por citomegalovírus em doentes com alteração da imunidade mediada por células devido a transplante.
Romanian	Plasmide ADN covalent închis codante pentru genele *fosfoproteinei 65* şi *glicoproteinei B* ale virusului citomegalic	Profilaxia bolii produse de citomegalovirus la pacienţii cu imunitate celulară deficitară consideraţi la risc.
Slovak	Kovalentne uzavreté DNA plazmidy kódujúce gény cytomegalovírusu pre *fosfoproteín 65* a *glykoproteín B*.	Prevencia cytomegalovírusového ochorenia u rizikových pacientov s poruchou bunkovej imunity.

Language	Active ingredient	Indication
Slovenian	Cepivo proti virusu citomegalije (CMV), DNA s plazmidi, ki izražajo gena *fosfoprotein 65* (pp65) in *glikoprotein B* (gB).	Preprečevanje citomegalovirusne viremije in/ali bolezni pri bolnikih z oslabljeno celično imunostjo po presaditvi.
Spanish	Plásmidos ADN cerrados de forma covlente que codifican los genes *fosfoproteína 65* (pp65) y *glucoproteína B* (gB) del citomegalovirus.	Prevención de la enfermedad por citomegalovirus en pacientes con deterioro de la inmunidad mediada por células considerados de riesgo.
Swedish	Kovalent slutna DNA-plasmider som uttrycker cytomegalovirus *fosfoprotein 65*- (pp65) och *glykoprotein B*- (gB) gener.	Förebyggande av cytomegalovirus sjukdom hos patienter med nedsatt cellmedierad immunitet och med ökad risk.
Norwegian	Kovalent lukket DNA-plasmider som koder for *fosfoprotein 65* (pp65) og *glykoprotein B* (gB) gener.	Forebygging av cytomegalovirussykdom hos pasienter med nedsatt cellemediert immunitet og med økt risiko..
Icelandic	Samtengt lokuð DNA plasmíð sem kóða fyrir cýtómegalóveiru *fosfópróteini 65* og *glýkópróteini B* genum	Fyrirbyggjandi meðferð gegn cýtómegalóveiru sjúkdómi hjá sjúklingum með skert frumubundið ónæmi sem eru metnir í aukinni áhættu

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