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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Letermovir for the treatment of cytomegalovirus disease in patients with impaired cell mediated immunity

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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.

On 6 June 2012, orphan designation (EU/3/12/999) was granted by the European Commission to AiCuris GmbH & Co. KG, Germany, for letermovir for the treatment of cytomegalovirus disease in patients with impaired cell mediated immunity.

The sponsorship was transferred to Merck Sharp & Dohme Limited, United Kingdom, in March 2013.

What is cytomegalovirus disease?

Cytomegalovirus is a common virus that usually only causes 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 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 inflammation 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 affected by the condition?

At the time of designation, cytomegalovirus disease in patients with impaired cell mediated immunity affected approximately 2.1 people in 10,000 per year in the European Union (EU). This is equivalent to a total of around 106,000 people* per year, which was considered to be below the ceiling for orphan designation. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

At the time of designation, several antiviral medicines were authorised in the EU for the treatment of cytomegalovirus disease in patients with impaired cell mediated immunity (ganciclovir, valganciclovir, valaciclovir, foscarnet and cidofovir).

The sponsor has provided sufficient information to show that letermovir might be of significant benefit for the treatment of cytomegalovirus disease in patients with impaired cell mediated immunity because early studies show that it works in a different way to existing medicines and might improve effectiveness against strains of cytomegalovirus resistant to existing antiviral medicines. This assumption 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?

When cytomegalovirus multiply during an infection, its genetic material (DNA) is replicated and packaged into small protein shells, giving rise to newly formed viruses that can proceed to infect other cells. This medicine is thought to block the action of an enzyme of the virus called 'terminase', which is involved in packaging the correct length DNA in the protein shells. By blocking the enzyme, the medicine is expected to prevent viruses from reaching maturity, so that no new infectious viruses can be produced.

What is the stage of development of this medicine?

The effects of letermovir have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with letermovir in the prevention of cytomegalovirus disease in patients with impaired cell mediated immunity were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for cytomegalovirus disease in patients with impaired cell mediated immunity. Orphan designation of letermovir had been granted in the EU for the prevention of cytomegalovirus disease in patients with impaired cell mediated immunity deemed at risk and in the United States of America for the prevention of human cytomegalovirus viraemia and disease in patients at risk.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 April 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.

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	Letermovir	Treatment of cytomegalovirus disease in patients with impaired cell mediated immunity
Bulgarian	Летермовир	Лечение на цитомегаловирусна (CMV) болест при пациенти с увреден клетъчно-медииран имунитет
Czech	Letermovir	Léčba cytomegalovirové choroby u pacientů s poruchou buněčné imunity
Danish	Letermovir	Behandling af cytomegalovirus -sygdom hos patienter med svækket cellemedieret immunitet
Dutch	Letermovir	Behandeling van cytomegalievirusinfectie bij patiënten met verzwakte cellulaire immuniteit
Estonian	Letermovir	Tsütomegaloviiruse haiguse ravi patsientidel, kellel on rakuvahendatud immunsuse häire
Finnish	Letermoviiri	Sytomegalovirussairauden hoito, kun potilaan soluvälitteinen immuniteetti on heikentynyt
French	Letermovir	Traitement de la maladie due au CMV chez les patients présentant une altération de l'immunité cellulaire
German	Letermovir	Behandlung der CMV-Erkrankung bei Patienten mit gestörter zellvermittelter Immunität
Greek	Λετερμοβίρη	Θεραπεία της λοίμωξης από μεγαλοκυτταροϊό (CMV) σε ασθενείς με διαταραχή της κυτταροεξαρτώμενης ανοσίας
Hungarian	Letermovir	Cytomegalovirus (CMV) okozta betegség kezelése csökkent celluláris immunitással rendelkező betegeknél
Italian	Letermovir	Trattamento della malattia da citomegalovirus (CMV) nei pazienti con deficit dell'immunità cellulo-mediata
Latvian	Letermovirs	Citomegalovīrusa (CMV) infekcijas ārstēšana pacientiem ar šūnu imunitātes traucējumiem
Lithuanian	Letermoviras	Citomegaloviruso (CMV) sukeltos ligos gydymas, pacientams su sutrikusiu ląsteliniu imunitetu
Maltese	Letermovir	Kura ta' mard ikkawżat minn ċitomegalovirus (CMV) f'pazjenti b'dgħjufija fl-immunità medjata miċ-ċelluli
Polish	Letermowir	Leczenie choroby wywołanej przez wirusa cytomegalii (CMV) u pacjentów z zaburzeniami odporności komórkowej
Portuguese	Letermovir	Tratamento da doença por citomegalovírus (CMV) em doentes com alteração da imunidade celular
Romanian	Letermovir	Tratamentul bolii produsă de citomegalovirus (CMV) la pacienţii cu imunitate mediată celular deficitară
Slovak	Letermovir	Liečba cytomegalovírusovej choroby u pacientov s poruchou bunkami sprostredkovanej imunity
Slovenian	Letermovir	Zdravljenje citomegalovirusne (CMV) okužbe pri bolnikih z oslabljeno celično imunsko odportnostjo
Spanish	Letermovir	Tratamiento de la enfermedad por citomegalovirus (CMV) en pacientes con deterioro de la inmunidad mediada por células

[1] At the time of designation

Language	Active ingredient	Indication
Swedish	Letermovir	Behandling av cytomegalovirus (CMV) sjukdom hos patienter med nedsatt cellmedierad immunitet
Norwegian	Letermovir	Behandling av cytomegalovirus (CMV)-sykdom hos pasienter med nedsatt cellemediert immunitet
Icelandic	Letermovir	Til meðferðar við cýtómegalóveiru (CMV) sjúkdómi hjá sjúklingum með skert frumubundið ónæmi