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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Maribavir for the prevention of cytomegalovirus (CMV) disease in patients with impaired cell mediated immunity deemed at risk

On 18 December 2007, orphan designation (EU/3/07/519) was granted by the European Commission to ViroPharma Limited, United Kingdom, for maribavir for the prevention of cytomegalovirus (CMV) disease in patients with impaired cell mediated immunity deemed at risk.

The sponsorship was transferred to ViroPharma SPRL, Belgium, in February 2009.

What is cytomegalovirus (CMV) disease in patients with impaired cell mediated immunity deemed at risk?

Cytomegalovirus (CMV) is a virus that infects many people worldwide. In the majority of cases the virus is latent (inactive) and causes neither disease nor any symptoms of any kind in man. Usually, the virus is only activated in patients who, for some reason, have a weaker immune system (natural defence system against pathogens such as bacteria and virus) than normal. That is called "impaired immunity". Impaired immunity is seen, for example, in organ transplanted patients who are receiving the necessary medicines to suppress the immune system and in patients with acquired immunodeficiency disease, e.g. due to human immunodeficiency virus (HIV) and who subsequently develop acquired immunodeficiency syndrome (AIDS). The risk of activation of latent CMV is particularly high if the cellular component of the immune system is weakened (the "cell mediated immunity"). CMV disease can affect several organs in the body, such as the eyes, lungs and the gastrointestinal tract (the stomach and intestines) and cause organ failure. CMV disease is chronically debilitating and life-threatening.

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 deemed at risk of cytomegalovirus (CMV) disease was estimated to be less than 4 people in 10,000 in the European Union (EU) *. This is equivalent to a total of fewer than 200,000 people, which is below the

*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 498,000,000 (Eurostat 2006).



threshold 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?

Several medicinal products were authorised for the prevention of CMV disease in the Community at the time of orphan drug application. Current methods of prevention aim to decrease the production of virus particles (virions) by inhibiting (blocking) a viral enzyme (a protein that speeds up the conversion of certain substances into other substances) called CMV DNA polymerase. Satisfactory argumentation has been submitted by the sponsor to justify the assumption that maribavir might be of potential significant benefit for the prevention of cytomegalovirus (CMV) disease in patients with impaired cell mediated immunity deemed at risk, mainly because it has a new mechanism of action, may be used in combination with other treatments and may potentially work in patients where other methods of prevention are unsuccessful. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

Maribavir is designed to bind to and inhibit (block) a viral enzyme called UL97 that is necessary for the virus for many processes. According to the sponsor, maribavir will inhibit this enzyme and thus prevent viral activation from latency in immunocompromised patients.

What is the stage of development of this medicine?

The effects of maribavir were evaluated in experimental models. At the time of submission of the application for orphan designation, clinical trials in patients with impaired cell mediated immunity were ongoing.

Maribavir was not authorised anywhere worldwide for the prevention of cytomegalovirus (CMV) disease in patients with impaired cell mediated immunity deemed at risk, at the time of submission. Orphan designation of maribavir was granted in the United States for prevention of cytomegalovirus viremia and disease in the population at risk.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 November 2007 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 European Union) 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 languages¹, Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Maribavir	Prevention of cytomegalovirus (CMV) disease in patients with impaired cell mediated immunity deemed at risk
Bulgarian	Марибавир	Превенция на цитомегаловирусно (CMV) заболяване при пациенти с увреден клетъчно-медиран имунитет считани за рискови
Czech	Maribavir	Prevence cytomegalovirové (CMV) choroby u pacientů s poruchou buněčné imunity se zvýšeným rizikem
Danish	Maribavir	Forebyggelse af cytomegalovirus (CMV)-sygdom hos risikopatienter med svækket cellemedieret immunitet
Dutch	Maribavir	Preventie van cytomegalievirusinfectie bij risicopatiënten met verzwakte cellulaire immunitet
Estonian	Marivabir	Tsütomegaloviiruse (CMV)-haiguse ennetamine patsientidel, kellel on suurenenud risk rakulise immunsuse häireks.
Finnish	Maribaviiri	Sytomegalovirussairauden ehkäisy riskipotilailla, joiden soluvälitteinen immunitaetti on heikentynyt
French	Maribavir	Prévention de la maladie due au CMV chez les patients à risque présentant une altération de l'immunité cellulaire
German	Maribavir	Prävention der CMV-Erkrankung bei gefährdeten Patienten mit gestörter zellvermittelter Immunität
Greek	Maribavir	Προφύλαξη από τον μεγαλοκυτταροϊό (CMV) σε ασθενείς υψηλού ρίσκου, με διαταραχή της κυτταροεξαρτώμενης ανοσίας
Hungarian	Maribavir	Citomegalovírus (CMV) betegség megelőzése csökkent celluláris immunitá rizikója esetén
Italian	Maribavir	Prevenzione delle malattie da citomegalovirus (CMV) nei pazienti a rischio, con deficit dell'immunità cellulo-mediata
Latvian	Maribavirs	Citomegalovīrusa (CMV) infekcijas profilakse riska grupas slimniekiem ar šūnu imunitātes traucējumiem
Lithuanian	Maribaviras	Citomegalo viruso (CMV) sukeltos ligos prevencija pacientams su susilpnėjusiu netiesioginiu ląsteliniu imunitetu
Maltese	Maribavir	Prevenzjoni ta' mard ikkawżat mill-citomegalovirus (CMV) f'pazienti b'riskju li għandhom dgħjufija ta' l-immunità permezz taċ-ċelloli
Polish	Maribawir	Zapobieganie cytomegalii (CMV) u chorych zwiększonego ryzyka z obniżoną odpornością typu komórkowego
Portuguese	Maribavir	Prevenção da doença por citomegalovírus (CMV) em doentes com alteração da imunidade mediada por células .
Romanian	Maribavir	Prevenirea bolii produse de citomegalovirus (CMV) la pacienții cu imunitate mediată celular deficitară considerați cu risc

¹ At the time of designation

Language	Active Ingredient	Indication
Slovak	Maribavir	Prevenencia cytomegalovírusovej choroby (CMV) u pacientov s rizikom porušenej bunkovej imunity
Slovenian	Maribavir	Preprečitev okužbe s citomegalovirusom (CMV) pri bolnikih s sumom zvečanega tveganja zaradi oslABLJENE celične imunosti
Spanish	Maribavir	Prevención de la enfermedad por citomegalovirus (CMV) en pacientes con deterioro de la inmunidad mediada por células considerados de riesgo
Swedish	Maribavir	Förebyggande av cytomegalovirus (CMV) sjukdom hos riskpatienter med nedsatt cellmediert immunitet
Norwegian	Maribavir	Forebygging av cytomegalovirus (CMV)-sykdom hos pasienter med nedsatt cellemediert immunitet og som har antatt øket risiko
Icelandic	Maribavir	Fyrirbyggjandi meðferð við cýtómegalóveiru (CMV) sjúkdómi hjá sjúklingum með skert frumubundið ónæmi og teljast í áhættu