



31 March 2016
EMA/COMP/72050/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

2-Ethylbutyl (2S)-2-[[[(S)-{[(2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-5-cyano-3,4-dihydroxytetrahydrofuran-2-yl]methoxy}(phenoxy)phosphoryl]amino}propanoate for the treatment of Ebola virus disease

On 17 February 2016, orphan designation (EU/3/16/1615) was granted by the European Commission to Gilead Sciences International Ltd, United Kingdom, for 2-ethylbutyl (2S)-2-[[[(S)-{[(2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-5-cyano-3,4-dihydroxytetrahydrofuran-2-yl]methoxy}(phenoxy)phosphoryl]amino}propanoate for the treatment of Ebola virus disease.

What is Ebola virus disease?

Ebola virus disease is a severe disease caused by infection with viruses known as ebolaviruses. There are 5 known species of ebolavirus, 4 of which are known to cause the disease in humans. Zaire ebolavirus, sometimes referred to simply as 'ebola virus' or EBOV, is the cause of the largest outbreaks of the disease to date and has led to the most deaths.

Infection is caused by contact with the body fluids of an infected person. After infection there is an incubation period of between 2 to 21 days, following which the newly infected person starts to experience symptoms. The first symptoms typically are fever, headache, fatigue, muscle pain and sore throat. These are followed by other symptoms such as diarrhoea, vomiting, rash, kidney and liver problems and, in some cases, internal bleeding and bleeding from the gums, eyes, nose and ears. Patients are infectious once they start to develop symptoms.

Ebola virus disease is a life-threatening condition that is frequently fatal due to fluid loss and severe bleeding.

What is the estimated number of patients affected by the condition?

At the time of designation, Ebola virus disease affected less than 0.01 in 10,000 people in the European Union (EU). This 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 treatments are available?

At the time of application for orphan designation, there were no satisfactory treatments authorised in the EU for treating Ebola virus disease. Different treatments were used to relieve the symptoms of the disease, such as providing fluids by a drip into a vein and balancing electrolytes (body salts), maintaining oxygen supply to the body and blood pressure, and treating other infections if they develop.

How is this medicine expected to work?

Ebolaviruses contain RNA (a type of genetic material). In order for ebolaviruses to multiply and cause disease, copies of the RNA must be made by a virus enzyme called RNA polymerase. This medicine is expected to block the RNA polymerase of the Ebola virus and so to prevent ebolaviruses from multiplying.

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, a clinical trial with the medicine in healthy volunteers was ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for Ebola virus disease. Orphan designation of the medicine had been granted in the United States for Ebola virus disease.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 21 January 2016 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

Sponsor's contact details:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's [rare disease designations page](#).

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	2-ethylbutyl (2S)-2-{{(S)-{[(2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-5-cyano-3,4-dihydroxytetrahydrofuran-2-yl]methoxy} (phenoxy)phosphoryl]amino} propanoate	Treatment of Ebola virus disease
Bulgarian	2-етилбутил (2S)-2-{{(S)-{[(2R,3S,4R,5R)-5-(4-аминопироло [2,1-f][1,2,4]триазин-7-ил)-5-циано-3,4-дихидрокситетрахидрофуран-2-ил]метокси} (фенокси)фосфорил]амино} пропаноат	Лечение на Ебола вирусно заболяване
Croatian	2-etilbutil (2S)-2-{{(S)-{[(2R,3S,4R,5R)-5-(4-aminopirolo[2,1-f][1,2,4]triazin-7-il)-5-cijano-3,4-dihidroksitetrahidrofuran-2-il]metoksi} (fenoksi)fosforil]amino} propanoat	Liječenje Ebola virusne bolesti
Czech	2-ethylbutyl (2S)-2-{{(S)-{[(2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-5-cyano-3,4-dihydroxytetrahydrofuran-2-yl]methoxy} (fenoxy)fosforyl]amino} propanoát	Léčba Ebola virové choroby
Danish	2-ethylbutyl (2S)-2-{{(S)-{[(2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-5-cyano-3,4-dihydroxytetrahydrofuran-2-yl]methoxy} (phenoxy)phosphoryl]amino} propanoat	Behandling af Ebola virus-sygdom
Dutch	2-ethylbutyl-(2S)-2-{{(S)-{[(2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazine-7-yl)-5-cyano-3,4-dihydroxytetrahydrofuran-2-yl]methoxy} (fenoxy)fosforyl]amino} propanoaat	Behandeling van Ebola virusziekte
Estonian	2-etüülibutüül (2S)-2-{{(S)-{[(2R,3S,4R,5R)-5-(4-aminopürrool[2,1-f][1,2,4]triasiin-7-üül)-5-tsüano-3,4-dihüdrosütetrahüdrofuraan-2-üül]metoksü} (fenoksü)fosforüül]amino} propanoaat	Ebola viiruse haiguse ravi
Finnish	2-etyylibutyyli (2S)-2-{{(S)-{[(2R,3S,4R,5R)-5-(4-aminopyrroli[2,1-f][1,2,4]triatsiini-7-yyli)-5-syaani-3,4-dihydroksitetrahydrofuraani-2-yyli]metoksi} (fenoksi)fosforyyli]amino} propanoatti	Ebola-viruksen aiheuttaman taudin hoito
French	2-éthylbutyl (2S)-2-{{(S)-{[(2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazine-7-yl)-5-cyano-3,4-dihydroxy-tétrahydrofurane-2-yl]méthoxy} (phénoxy)phosphoryl]amino} propanoate	Traitement de la maladie à virus Ebola
German	2-Ethylbutyl-(2S)-2-{{(S)-{[(2R,3S,4R,5R)-5-(4-Aminopyrrolo [2,1-f][1,2,4]Triazin-7-yl)-5-Cyano-3,4-Dihydroxytetrahydrofuran-2-yl]Methoxy} (Phenoxy)Phosphoryl]amino} Propanoat	Behandlung der Ebola-Viruskrankheit

¹ At the time of designation

Language	Active ingredient	Indication
Greek	(2S)-2-[[[(S)-{[(2R,3S,4R,5R)-5-(4-αμινοπυρρολό [2,1-f][1,2,4]τριαζινο-7-υλο)-5-κυανο-3,4-διυδροξυτετραϋδροφουρανο-2-υλο]μεθοξυ} (φαινοξυ)φωσφορυλο]αμινο}προπανοϊκό 2-αιθυλοβουτύλιο	Θεραπεία της νόσου από τον ιό Έμπολα
Hungarian	2-etylbutil (2S)-2-[[[(S)-{[(2R,3S,4R,5R)-5-(4-aminopirrolo[2,1-f][1,2,4]triazin-7-il)-5-ciano-3,4-dihidroxitetrahidrofurán-2-il]metoxi} (fenoxi)foszforil]amino}propanoát	Ebola vírus fertőzés kezelése
Italian	2-Etilbutil (2S)-2-[[[(S)-{[(2R,3S,4R,5R)-5-(4-amminopirrolo [2,1-f][1,2,4]triazin-7-il)-5-ciano-3,4-diidrossitetraidrofurano-2-il]metossi} (fenossi)fosforil]ammino}propanoato	Trattamento della malattia da virus Ebola
Latvian	2-etylbutil (2S)-2-[[[(S)-{[(2R,3S,4R,5R)-5-(4-aminopirolo[2,1-f][1,2,4]triazīn-7-il)-5-ciān-3,4-dihidroksitetrahidrofurān-2-il]metoksi} (fenoksi)fosforil]amino}propanoāts	Ebolas vīrusa slimības ārstēšana
Lithuanian	2-etylbutil (2S)-2-[[[(S)-{[(2R,3S,4R,5R)-5-(4-aminopirolo[2,1-f][1,2,4]triazin-7-il)-5-ciano-3,4-dihidroksitetrahidrofuran-2-il]metoksi} (fenoksi)fosforil]amino}propanoatas	<i>Ebola</i> viruso sukeltos ligos gydymas
Maltese	2-ethylbutyl (2S)-2-[[[(S)-{[(2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-5-cyano-3,4-dihydroxytetrahydrofuran-2-yl]methoxy} (phenoxy)phosphoryl]amino}propanoate	Kura tal-marda mill-virus Ebola
Polish	2-etylobutylo (2S)-2-[[[(S)-{[(2R,3S,4R,5R)-5-(4-aminopirolo[2,1-f][1,2,4]triazyn-7-yl)-5-cyjano-3,4-dihydroksytetrahydrofuran-2-yl]metoksy} (fenoksy)fosforyl]amino}propionian	Leczenie choroby wywołanej przez wirus Ebola
Portuguese	Propanoato de 2-etylbutil (2S)-2-[[[(S)-{[(2R,3S,4R,5R)-5-(4-aminopirrolo[2,1-f][1,2,4]triazina-7-il)-5-ciano-3,4-dihidroxitetrahidrofurano-2-il]metoxi} (fenoxi)fosforil]amino}	Tratamento da doença por vírus Ébola
Romanian	2-etylbutil (2S)-2-[[[(S)-{[(2R,3S,4R,5R)-5-(4-aminopirolo[2,1-f][1,2,4]triazin-7-il)-5-ciano-3,4-dihidroxitetrahidrofuran-2-il]metoxi} (fenoxi)fosforil]amino}propanoat	Tratamentul bolii virale Ebola
Slovak	2-etylbutyl (2S)-2-[[[(S)-{[(2R,3S,4R,5R)-5-(4-aminopyrolo[2,1-f][1,2,4]triazín-7-yl)-5-cyano-3,4-dihydroxytetrahydrofurán-2-yl]metoxy} (fenoxy)fosforyl]amino}propanoát	Liečba Ebola vírusového ochorenia
Slovenian	2-etylbutil (2S)-2-[[[(S)-{[(2R,3S,4R,5R)-5-(4-aminopirolo[2,1-f][1,2,4]triazin-7-il)-5-ciano-3,4-dihidroksitetrahidrofuran-2-il]metoksi} (fenoksi)fosforil] amino}propanoat	Zdravljenje Ebola virusne bolezni

Language	Active ingredient	Indication
Spanish	(2S)-2-{{(S)-{[(2R,3S,4R,5R)-5-(4-aminopirroló [2,1-f][1,2,4]triazin-7-il)-5-ciano-3,4-dihidroxitetrahidrofurano-2-il]metoxi}(fenoxi)fosforil]amino}propanoato de 2-etilbutilo	Tratamiento de la enfermedad viral de Ébola
Swedish	2-Etylbutyl (2S)-2-{{(S)-{[(2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-5-cyano-3,4-dihydroxitetrahydrofuran-2-yl]metoxi}(fenoxi)fosforyl]amino}propanoat	Behandling av Ebolavirussjukdom
Norwegian	2-Etylbutyl (2S)-2-{{(S)-{[(2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-5-cyano-3,4-dihydroksytetrahydrofuran-2-yl]metoksy}(fenoksy)fosforyl]amino}propanoat	Behandling av ebolavirussykdom
Icelandic	2-etylbutýl (2S)-2-{{(S)-{[(2R,3S,4R,5R)-5-(4-amínópýrróló[2,1-f][1,2,4]tríazín-7-ýl)-5-cýanó-3,4-dihýdroxýtetrahýdrófúran-2-ýl]metoxý}(fenoxý)fosfóryl] amínó}própanóat	Meðferð Ebóluveiru sjúkdóms