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EMA/COMP/797338/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Tenofovir disoproxil fumarate for the treatment of Aicardi-Goutières syndrome

On 15 January 2015, orphan designation (EU/3/14/1419) was granted by the European Commission to Dr Yanick Crow, France, for tenofovir disoproxil fumarate for the treatment of Aicardi-Goutières syndrome.

What is Aicardi-Goutières syndrome?

Aicardi-Goutières syndrome is a hereditary disorder that mainly affects the brain and skin. Most patients do not have symptoms at birth, but develop symptoms within the first year of life, such as irritability and feeding difficulties, and sometimes seizures (fits). Most children with Aicardi-Goutieres syndrome have severe intellectual disability, and around 40% have painful, itchy skin lesions, usually on the fingers, toes and ears.

Aicardi-Goutières syndrome is a long-term debilitating and life-threatening disease due to the severe brain dysfunction, which in most cases results in death during childhood.

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

At the time of designation, Aicardi-Goutières syndrome affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 51,000 people*, and 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 designation, no satisfactory methods were authorised in the EU for the treatment of Aicardi-Goutières syndrome. Patients received symptomatic treatment such as managing feeding problems and, if present, epilepsy.

*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 28), Norway, Iceland and Liechtenstein. This represents a population of 511,100,000 (Eurostat 2014).

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How is this medicine expected to work?

Aicardi-Goutières syndrome is caused by mutations (defects) in any of 7 genes that are responsible for making certain enzymes which break up unneeded molecules of DNA. As a result, unneeded molecules of DNA accumulate inside cells. These DNA molecules are mistaken by the body's immune system for those of viruses, triggering an immune response against the body's own DNA that results in severe brain dysfunction and the other symptoms of Aicardi-Goutières syndrome.

Tenofovir disoproxil fumarate is a type of antiviral medicine, called a 'nucleotide reverse transcriptase inhibitor' and already authorised for the treatment of human immunodeficiency (HIV-1). In the body, tenofovir disoproxil fumarate is converted to its active form, tenofovir. Tenovofir is expected to work in Aicardi-Goutières syndrome by blocking an enzyme called 'reverse transcriptase' that is involved in the production of some types of unneeded DNA molecules, thereby decreasing their accumulation within cells. This is expected to prevent the triggering of an immune response against the body own DNA, thus improving the symptoms of Aicardi-Goutières syndrome.

What is the stage of development of this medicine?

The effects of tenofovir disoproxil fumarate have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with the medicine in patients with Aicardi-Goutières syndrome had been started.

Tenofovir has been authorised worldwide for many years for the treatment of HIV-1 infections. At the time of submission, tenofovir disoproxil fumarate was not authorised anywhere in the EU for Aicardi-Goutières syndrome or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 11 December 2014 recommending the granting of this designation.

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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

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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	Tenofovir disoproxil fumarate	Treatment of Aicardi-Goutières syndrome
Bulgarian	Тенофовир дизопроксил фумарат	Лечение на синдрома на Aicardi-Goutières
Croatian	Tenofovirdizoproksilfumarata	Liječenje sindroma Aicardi-Goutières
Czech	Tenofovir disoproxil fumarat	Léčba syndromu Aicardi-Goutières
Danish	Tenofovirdisoproxil fumarat	Behandling af syndrom Aicardi-Goutières
Dutch	Tenofovirdisoproxilfumaraat	Behandeling van het syndroom Aicardi-Goutières
Estonian	Tenofoviirdisoproksiil-fumaraat	Aicardi-Goutières'I sündroomi ravi
Finnish	Tenofoviiridisoproksiili fumaraatti	Aicardi-Goutières syndrooman hoito
French	Fumarate de ténofovir disoproxil	Traitement du syndrome d'Aicardi-Goutières
German	Tenofovir Disoproxil Fumarat	Behandlung des Aicardi-Goutières Syndroms
Greek	φουμαρική τενοφοβίρη δισοπροξίλη	Θεραπεία του συνδρόμου Aicardi-Goutières
Hungarian	Tenofovir-dizoproxil fumarát	Aicardi-Goutières szindróma kezelése
Italian	Tenofovir disoproxil fumarato	Trattamento della sindrome Aicardi-Goutières
Latvian	Tenofovīra dizoproksil fumarāts	*Aicardi-Goutières* sindroma ārstēšana
Lithuanian	Tenofoviro dizoproksilio fumaratasfumarate	*Aicardi-Goutières* sindromo gydymas
Maltese	Tenofovir disoproxil fumarate	Kura tas-sindrome ta' Aicardi-Goutières
Polish	Fumaran dizoproksylu tenofowiru	Leczenie zespołu Aicardi-Goutières
Portuguese	Tenofovir disoproxil fumarato	Tratamento de síndrome Aicardi-Goutières
Romanian	Tenofovir disoproxil fumarat	Tratamentul sindromului Aicardi-Goutières
Slovak	Tenofovir disoproxil fumarát	Liečba syndrómu Aicardi-Goutières
Slovenian	Tenofovirdizoproksil fumarat	Zdravljenje sindroma Aicardi-Goutières
Spanish	Tenofovir disoproxilo fumarato	Tratamiento del síndrome de Aicardi-Goutières
Swedish	Tenofovirdisoproxil fumarat	Behandling av syndromet Aicardi-Goutières
Norwegian	Tenofovirdisoproksilfumaratfumarate	Behandling av Aicardi-Goutières syndrom
Icelandic	Tenófóvírtvísóproxíl fúmarat	Meðferð á heilkenni Aicardi-Goutières

[1] At the time of designation