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Public summary of opinion on orphan designation

Adeno-associated virus serotype HSC15 expressing human arylsulfatase A gene for the treatment of metachromatic leukodystrophy

On 26 June 2020, orphan designation EU/3/20/2297 was granted by the European Commission to YES Pharmaceutical Development Services GmbH, Germany, for adeno-associated virus serotype HSC15 expressing human arylsulfatase A gene (also known as HMI-202) for the treatment of metachromatic leukodystrophy.

What is metachromatic leukodystrophy?

Metachromatic leukodystrophy is a hereditary disease caused by the lack of an enzyme called arylsulfatase A. This enzyme is needed to break down substances in the body called sulfatides. Therefore, in patients with the disease, sulfatides gradually build up in the cells of the nervous system and destroy the covering around the nerves called myelin. This causes symptoms such as muscle wasting and paralysis, progressive loss of vision, seizures (fits) and dementia (loss of intellectual function).

Metachromatic leukodystrophy is a seriously debilitating and life-threatening disease because the symptoms get worse over time, leading to severe disability and death usually in adolescence.

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

At the time of designation, metachromatic leukodystrophy affected less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 52,000 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 metachromatic leukodystrophy. Patients received supportive treatment to temporarily relieve the symptoms of the disease, such as physiotherapy and antiepileptic medicines.

*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, Iceland, Liechtenstein, Norway and the United Kingdom. This represents a population of 519,200,000 (Eurostat 2020).

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How is this medicine expected to work?

The medicine is made of a virus that has been modified to contain genetic material responsible for producing the missing enzyme, arylsulfatase A. The virus is able to cross over from the blood into the brain also from blood into nerve cells. The genetic material is expected to be incorporated into cells in the patient's body. A single dose of the medicine into a vein is expected to help cells produce arylsulfatase A continually and so reduce symptoms of the disease for a long time.

The type of virus used in this medicine (adeno-associated virus) does not cause disease in humans.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

At the time of submission of the application for orphan designation, no clinical trials with the medicine in patients with metachromatic leukodystrophy had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of metachromatic leukodystrophy or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 20 May 2020, 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

Contact details of the current sponsor for this orphan designation can be found on [EMA website](#).

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	Adeno-associated virus serotype HSC15 expressing human arylsulfatase A gene	Treatment of metachromatic leukodystrophy
Bulgarian	Адено-асоцииран вирус серотип HSC15 експресиращ човешка арилсулфатаза А	Лечение на метахроматична левкодистрофия
Croatian	Adeno-povezani virus serotipa HSC15 koji izražava ljudsku arilsulfatazu A	Liječenje metakromatske leukodistrofije
Czech	Adeno-asociovaný virus sérotypu HSC15 exprimující lidský gen proou arylsulfatázu A	Léčba metachromatické leukodystrofie
Danish	Adenoassocieret virusserotype HSC15 udtrykkende human arylsulfatase A	Behandling af metakromatisk leukodystrofi
Dutch	Adeno-geassocieerd virus serotype HSC15 dat humaan arylsulfatase A tot expressie brengt	Behandeling van metachromatische leukodystrofie
Estonian	Inimese arüülsulfataas A geeni ekspresseeriv adeno-assotsieerunud viirusvektori serotüüp HSC15	Metakromaatilise leukodüstroofia ravi
Finnish	Adenoassosioituneen viruksen serotyypin HSC15 joka ilmentää ihmisen arylisulfataasi A:ta	Metakromaattisen leukodystrofian hoito
French	Virus adéno-associé de sérotype HSC15 exprimant le gène de l'arylsulfatase A humaine	Traitement de la leucodystrophie métachromatique
German	Adeno-assoziiertes Virus-Serotyp HSC15 der menschlichen Aryl-Sulfatase A	Behandlung der metachromatischen Leukodystrophie
Greek	Αδενο-σχετιζόμενος ιός οροτύπου HSC15 που εκφράζει το γονίδιο της ανθρώπινης αρυλοσουλφάτασης Α	Θεραπεία της μεταχρωματικής λευκοδυστροφίας
Hungarian	Humán arilsulfatáz A-t expresszáló adenoasszociált vírus HSC15 szerotípusa	Metakromatikus leukodisztrófia kezelésére
Italian	Virus adeno-associato sierotipo HSC15 che esprime l'arilsolfatasi umana A	Trattamento della leucodistrofia metacromatica
Latvian	Adenoasociētā vīrusa serotips HSC15 kas ekspresē cilvēka arilsulfatāzes A gēnu	Metahromatiskās leikodistrofijas ārstēšana

¹ At the time of designation

Language	Active ingredient	Indication
Lithuanian	Adeno-asocijuoto viruso HSC15 serotipas, ekspresuojantis žmogaus arilsulfatazės A geną	Metachrominės leukodistrofijos gydymas
Maltese	Serotip HSC15 ta' virus adeno-assoċjat li jesprimi l-ġene tal-bniedem arilsulfatazi A	Kura ta' lewkodistrofija metakromatika
Polish	Wirus związany z adenowirusami serotypu HSC15 eksprymujący gen ludzkiej arylsulfatazy A	Leczenie leukodystrofii metachromatycznej
Portuguese	Vírus adeno-associado de serotipo HSC15 expressando a arilsulfatase A humana	Tratamento da leucodistrofia metacromática
Romanian	Virus adeno-asociat de serotip HSC15 care exprimă gena arilsulfatază A umană	Tratamentul leucodistrofiei metacromatice
Slovak	Adeno-asociovaný vírus sérotypu HSC15 exprimujúci ľudskú arylsulfatázu A	Liečba metachromatickej leukodystrofie
Slovenian	Adeno-asociran-virus serotipa HSC15 ki izraža humano arilsulfatazo A	Zdravljenje metakromatske levkodistrofije
Spanish	Virus adeno-asociado del serotipo HSC15 que expresa arilsulfatasa A humana	Tratamiento de la leucodistrofia metacromática
Swedish	Adenoassocierat virus serotyp HSC15 som uttrycker humant arylsulfatas A	Behandling av metakromatisk leukodystrofi
Norwegian	Adenoassosiert virus serotype HSC15 som uttrykker genet for human arylsulfatase A	Behandling av metakromatisk leukodystrofi
Icelandic	Adenótengd veirufurja af sermisgerð HSC15 sem tjáir arýlsúlfatasa A úr mönnum	Meðferð við hvítkyrningafæðsúlfatíðhvítukyrkingi