European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of recombinant human heparan-N-sulfatase for the treatment of mucopolysaccharidosis III, type A (Sanfilippo A syndrome)

On 7 November 2008, orphan designation (EU/3/08/582) was granted by the European Commission to Shire Pharmaceutical Development Limited, United Kingdom, for recombinant human heparan-N-sulfatase for the treatment of mucopolysaccharidosis III, type A (Sanfilippo A syndrome).

What is mucopolysaccharidosis III, type A (Sanfilippo A syndrome)?
The mucopolysaccharidoses are a group of rare, inherited lysosomal storage disorders caused by the deficiency or absence of specific lysosomal enzymes. The absence of these enzymes (molecule that speeds up chemical reactions in the body) results in the accumulation of complex sugar molecules in the cells and tissues, and in cellular organelles, called lysosomes. In the presence of normal lysosomal enzymes these sugars would be transformed into other substances and used by the body. These complex sugars are known as mucopolysaccharides or glycosaminoglycans (GAGs) and serve as the building blocks for connective tissues in the body. Patients affected by mucopolysaccharidosis III, type A have mutations in the gene coding for heparan-N-sulfatase, resulting in a deficiency or absence of this enzyme. Thus one type of GAG called heparan sulphate is not degraded as it should and accumulates.
MPS III, or Sanfilippo syndrome results from the lack of four different enzymes necessary to degrade the GAG. Each enzyme deficiency defines a different form of Sanfilippo syndrome: type IIIA (Sanfilippo A), type IIIB (Sanfilippo B), type IIIC (Sanfilippo C), and type IIID (Sanfilippo D). Symptoms of MPS IIIA (Sanfilippo A) usually arise between 2 to 6 years of age, although in some cases diagnosis is made as late as at 13 years of age. The clinical symptoms of the condition present different degrees of severity. The central nervous system is the most severely affected system in patients with MPS IIIA. Problems in language development, motor skills, and intellectual development characterise the condition. In addition, there is hyperactivity (excess motor activity) that contributes to disturbances in sleep. Overall, individuals with MPS IIIA have a marked developmental delay and the long-term survival is poor. The condition is chronically debilitating and life-threatening.

What is the estimated number of patients affected by the condition?
At the time of designation mucopolysaccharidosis III, type A (Sanfilippo A syndrome) affected approximately 0.03 in 10,000 people in the European Union (EU) [*]. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP). This is below the threshold for orphan designation which is 5 in 10,000. This is equivalent to a total of around 1,500 people.

What are the methods of treatment available?

[*]Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 27), Norway, Iceland and Lichtenstein. This represents a population of 502,282,000 (Eurostat 2008).

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There are no authorised products for the condition in the Community. Bone marrow transplant has been used in an attempt to slow disease progression.

How is this medicine expected to work?
Patients affected by mucopolysaccharidosis IIIA have genetic mutations that result in a deficiency or absence of the enzyme heparan-N-sulphatase. This medicinal product is an enzyme identical to the normal human heparan-N-sulfatase synthesized in the laboratory using a method called recombinant DNA technology. The product does not carry the mutations/alterations that cause the condition and it is expected to replace the non-functional heparan-N-sulphatase and degrade the GAG heparan sulfate that has accumulated, thus decreasing the symptoms of Sanfilippo A.

What is the stage of development of this medicine?
The evaluation of the effects of recombinant human heparan-N-sulfatase in experimental models was ongoing.

At the time of submission of the application for orphan designation, no clinical trials in patients with Mucopolysaccharidosis, type III A (Sanfilippo A syndrome) were initiated.

The product was not authorised in any country inside or outside the EU at the time of submission of the application.
In the United States orphan drug status was granted on 22 May 2008 for treatment of Sanfilippo syndrome.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 10 September 2008 a positive opinion recommending the grant of the above-mentioned designation.

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Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products which were considered for designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of the quality, safety and efficacy will be necessary before this product can be granted a marketing authorisation.

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Translations of the active ingredient and indication in all EU languages and Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Recombinant human heparan N-sulfatase	Treatment of mucopolysaccharidosis, type IIIA (Sanfilippo A syndrome)
Bulgarian	Рекомбинантна човешка хепаран N-сулфатаза	Лечение на мукополизахаридоза, тип IIIA (синдром на Санфилипо А)
Czech	Rekombinantní lidská heparan N-sulfatáza	Léčba mukopolysacharidozy typu IIIA (syndrom Sanfilippo A) rekombinantní lidskou heparan N-sulfatázou
Danish	Rekombinant human heparan N-sulfatase	Behandling af mucopolysaccharidose type III (Sanfilippo syndrom)
Dutch	Recombinant humaan heparan N-sulfatase	Behandeling van mucopolysacharidose, type IIIA (Sanfilippo-A-syndroom)
Estonian	Rekombinantne inimese heparaani N-sulfataas	IIIA-tüüpi mukopolüsahharidoosi (A-tüüpi Sanfilippo sündroomi) ravi
Finnish	Rekombinantti humaani heparaani N-sulfataasi	Tyypin IIIA (Sanfilippo A) mukopolysakkaridoosin hoito
French	Héparan N-sulfatase humain recombinant	Traitement de la mucopolysaccharidose de type IIIA (maladie de Sanfilippo A)
German	Rekombinante menschliche Heparan-N-Sulfatase	Behandlung der Mukopolysaccharidose Typ IIIA (Sanfilippo-Syndrom Typ A)
Greek	Ανασυνδυασμένη ανθρώπινη ηπαράνη Ν-σουλφατάση	Θεραπεία βλεννοπολυσακχαρίδωσης, τύπου IIIA (σύνδρομο Sanfilippo A)
Hungarian	Rekombináns humán heparán N-szulfatáz	IIIA típusú mucopolisacharidosis (Sanfilippo A szindróma) kezelése
Italian	Eparan N-solfatasi umana ricombinante	Trattamento della mucopolisaccaridosi di tipo IIIA (sindrome di Sanfilippo A)
Latvian	Rekombinantā cilvēka heparāna N-sulfatāze	IIIA tipa mukopolisaharidozes (Sanfilipo A sindroms) ārstēšana
Lithuanian	Rekombinantinė žmogaus heparan-N-sulfatazė	Mukopolisacharidozės, IIIA tipo gydymas, (Sanfilippo A sindromas)
Maltese	*Heparan N-sulfatase* uman rikombinanti	Kura tal-mukopolisakkaridożi tat-tip IIIA (sindrome ta' Sanfilippo tat-tip A)
Polish	Ludzka rekombinowana N-sulfataza heparanu	Leczenie mukopolisacharydozy, typ III A (zespół Sanfilippo A)
Portuguese	Heparano N-sulfatase humana recombinante	Tratamento da mucopolissacaridose, tipo IIIA (síndrome de Sanfilippo de tipo A)
Romanian	Heparan N-sulfatază umană recombinantă	Tratamentul mucopolizaharidozei de tip IIIA (sindromul Sanfilippo tip A)
Slovak	Rekombinantná ľudská heparán-N-sulfatáza	Liečba mukopolysacharidózy typu III.A (Sanfilippo syndróm)
Slovenian	Rekombinantna humana heparan N-sulfataza	Zdravljenje mukopolisaharidoze vrste IIIA (sindroma Sanfilippo A)
Spanish	Heparán N-sulfatasa humana recombinante	Tratamiento de la mucopolisacaridosis tipo IIIA (síndrome de Sanfilippo A)
Swedish	Rekombinant humant heparan-N-sulfatas	Behandling av mukopolysackaridos, typ IIIA (Sanfilippos syndrom, typ A)