26 March 2013
EMA/COMP/105680/2013
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant human heat shock protein 70 for the treatment of Niemann-Pick's disease, type C

On 12 March 2013, orphan designation (EU/3/13/1110) was granted by the European Commission to Orphazyme ApS, Denmark, for recombinant human heat shock protein 70 for the treatment of Niemann-Pick's disease, type C.

What is Niemann-Pick's disease type C?

Niemann-Pick disease is a group of inherited disorders belonging to the larger family of metabolic disorders called 'lysosomal storage diseases', in which fats accumulate within lysosomes (part of the body's cells which break down nutrients and other materials).

In Niemann-Pick disease type C, transporter proteins needed to move fatty substances in the cells are abnormal, leading to the build-up of fats such as cholesterol within cells in the brain and elsewhere in the body (such as the spleen and liver). This causes a wide range of symptoms, including behavioural problems, learning disabilities and difficulty moving and speaking.

Niemann-Pick disease type C is chronically debilitating and life threatening since the build-up of fatty substances can cause brain damage and swelling of the spleen and the liver.

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

At the time of designation, Niemann-Pick disease type C affected approximately 0.1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 5,000 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, Zavesca (miglustat) was authorised in the EU to treat Niemann-Pick disease type C. The sponsor has provided sufficient information to show that this medicine might be of

*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 509,000,000 (Eurostat 2013).

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

significant benefit for patients with the disease because of its novel mechanism of action which involves stabilising the lysosomes within the cells and was shown to results in improved effects in experimental models compared with current treatment. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

This medicine is a 'heat shock protein', a type of protein in the body that is involved in protecting cells by stabilising proteins and folding back proteins that have been damaged by stresses such as high temperatures (heat shock).

In Niemann-Pick disease type C, the medicine is expected to protect cells by stabilising the membranes of the lysosomes. This stabilisation involves activating sphingomyelinase, a protein involved in the processing of fats within the lysosomes, thereby reducing the accumulation of fats within lysosomes.

The medicine is to be delivered by injection into a vein and is expected to be able to cross the barrier which separates the blood from the brain tissue (the blood-brain barrier), thereby reaching the brain, as well as the other organs affected by the condition.

The heat shock protein is produced by a method known as 'recombinant DNA technology': it is made by cells that have received a gene (DNA), which makes them able to produce the protein.

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 medicinal product in experimental models was ongoing.

At the time of submission of the application for orphan designation, no clinical trials with the medicinal product in patients with Niemann-Pick disease type C had been started.

At the time of submission, the medicinal product was not authorised anywhere in the EU for Niemann-Pick disease type C 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 6 February 2013 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:

Orphazyme ApS
Ole Maaløes Vej 3
2200 Copenhagen
Denmark
Telephone: +45 293 464 30
E-mail: pl@orphazyme.com

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	Recombinant human heat shock protein 70	Treatment of Niemann-Pick disease, type C
Bulgarian	Рекомбинантен човешки топлинен шок протеин 70	Лечение на болест на Нийман-Пик, тип С
Czech	Rekombinantní lidský protein teplotního šoku 70	Léčba Niemann-Pickovy choroby, typ C
Danish	Rekombinant human heat-shock-protein 70	Behandling af Niemann-Picks sygdom, type C
Dutch	Recombinant humaan hitteschok-protëine 70	Behandeling van de ziekte van Niemann-Pick, type C
Estonian	Rekombinantne inimese kuumashoki valgk 70	C tüüpi Niemann-Pick'i tõve ravi
Finnish	Rekombinantti ihmisen lämpösokkiproteiini 70	Niemann-Pick'n taudin tyyppi C:n hoito
French	Protéine recombinante humaine du choc thermique 70	Traitement de la maladie de Niemann-Pick de type C
German	Rekombinantes humanes Hitzeschock-Protein 70	Behandlung des Morbus Niemann-Pick Typ C
Greek	Ανασυνδυασμένη ανθρώπινη πρωτεΐνη θερμικού σοκ 70	Θεραπεία της Νόσου Niemann-Pick τύπου C
Hungarian	Rekombináns emberi 70 kDa-os hősokkfehérje (Hsp 70)	C típusú Niemann-Pick betegség kezelése
Italian	Proteina dello shock termico 70 umanaricombinante	Trattamento della Malattia di Niemann-Pick, tipo C
Latvian	Rekombinants cilvēka karstumšoka olbaltumviela 70	C tipa Nīmaņa-Pika slimības ārstēšanai
Lithuanian	Rekombinantinis žmogaus šiluminio šoko baltymas 70	C tipo Niemann-Picko ligos gydymas
Maltese	Proteina b'xokk termiku 70 umana rikombinanti	Kura tal-marda ta' Niemann-Pick tat-tip Ċ
Polish	Rekombinowane ludzkie białko szoku cieplnego 70	Leczenie choroby Niemanna-Picka typu C
Portuguese	Proteína 70 de choque térmico humana recombinante	Tratamento da Doença de Niemann-Pick, tipo C
Romanian	Proteină de şoc termic 70 umană recombinantă	Tratamentul bolii Niemann-Pick tip C
Slovak	Rekombinantný ľudský protein tepelného šoku 70	Liečba NiemannPick, typ C
Slovenian	Rekombinantni človeški toplotni šokovni protein 70	Zdravljenje Niemann-Pickove bolezni, tipa C

[1] At the time of designation

Language	Active ingredient	Indication
Spanish	Proteína 70 del shock térmicorecombinante humana	Tratamiento de la Enfermedad de Niemann-Pick, tipo C
Swedish	Rekombinant mänskligt heat shock protein 70	Behandling av Niemann-Picks sjukdom, typ C
Norwegian	Rekombinant human varmesjokkprotein 70	Behandling av Niemann-Picks sykdom, type C
Icelandic	Raðbrigða manna hitalostsmyndað prótín 70	Til meðferðar á Niemann-Pick sjúkdómi, gerð C