20 June 2016
EMA/COMP/313647/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Vemurafenib for treatment of Langerhans' cell histiocytosis

On 30 May 2016, orphan designation (EU/3/16/1670) was granted by the European Commission to Groupe d'étude des histiocytoses, Hôpital Trousseau, France, for vemurafenib for treatment of Langerhans' cell histiocytosis.

What is Langerhans' cell histiocytosis?

Langerhans' cell histiocytosis is a disease in which immune cells known as Langerhans' cells grow quickly and accumulate in various tissues in the body including in bone, skin, liver, spleen, lungs, pituitary gland (gland located at the base of the brain) and the central nervous system (brain and spinal cord).

Langerhans' cell histiocytosis occurs mainly in childhood and the features vary depending on the parts of the body affected. Common features include bone pain and swelling, skin rash, breathing problems, liver problems and reduced blood cells.

Langerhans' cell histiocytosis is a life-threatening and debilitating condition that can lead to various serious complications depending on the organ affected.

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

At the time of designation, Langerhans' cell histiocytosis affected less than 0.5 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 26,000 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 orphan designation, the main treatment for Langerhans' cell histiocytosis was chemotherapy which usually included vinblastine (authorised to treat histiocytosis, a group 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 28), Norway, Iceland and Liechtenstein. This represents a population of 513,700,000 (Eurostat 2016).

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conditions that includes Langerhans' cell histiocytosis). Treatment guidelines also recommended the use of other medicines although not authorised for this condition.

The sponsor has provided sufficient information to show that vemurafenib might be of significant benefit for patients with Langerhans' cell histiocytosis. Published clinical data have shown vemurafenib successfully treating patients whose condition did not improve with standard 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?

Around half of the cases of Langerhans' cell histiocytosis are due to a mutation (change) in the *BRAF* gene, called the BRAF V600E mutation. This mutation results in the production of an abnormal BRAF protein which makes Langerhans' cells grow and divide quickly. Vemurafenib is expected to work by attaching to and blocking the abnormal BRAF protein thereby slowing down the growth and spread of the Langerhans cells.

What is the stage of development of this medicine?

The effects of vemurafenib have been evaluated in experimental models.

At the time of submission of the application for orphan designation, the sponsor had not started clinical trials with vemurafenib in patients with Langerhans' cell histiocytosis.

At the time of submission, vemurafenib was authorised in the EU for unresectable or metastatic melanoma (a skin cancer) in patients with the BRAF V600E mutation.

At the time of submission, vemurafenib was not authorised anywhere in the EU for Langerhans' cell histiocytosis 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 21 April 2016 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

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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Vemurafenib	Treatment of Langerhans' cell histiocytosis
Bulgarian	Вемурафениб	Лечение на хистоцитоза на Лангерхансовите клетки
Croatian	Vemurafenib	Liječenje histiocitoze Langerhansovih stanica
Czech	Vemurafenib	Léčba histiocytózy z Langerhansových buněk
Danish	Vemurafenib	Behandling af Langerhans-celle histiocytose
Dutch	Vemurafenib	Behandeling van langerhanscelhistiocytose
Estonian	Vemurafeniib	Langerhansi rakkude histiotsütoosi ravi
Finnish	Vemurafenib	Langerhansin solujen histiosytoosin hoito
French	Vemurafenib	Traitement de l' histiocytose à cellules de Langerhans
German	Vemurafenib	Behandlung der Langerhans-Zell-Histiozytose
Greek	Βεμουραφενίμπη	Θεραπεία των κυττάρων Langerhans ιστιοκύτωση
Hungarian	Vemurafenib	Langerhans-sejt hisztiocitózis kezelése
Italian	Vemurafenib	Trattamento dell'istiocitosi acellule di Langherans
Latvian	Vemurafenib	Langerhansa šūnu histiocitozes ārstēšana
Lithuanian	Vemurafenibas	Langerhanso ląstelių histiocitozėsgydymas
Maltese	Vemurafenib	Kura tal-istjoċitosi taċ-ċelluli ta' Langerhans
Polish	Wemurafenib	Leczenie histiocytozy z komórek Langerhansa
Portuguese	Vemurafenib	Tratamento de histiocitose de células de Langerhans
Romanian	Vemurafenib	Tratamentul histiocitozei cu celule Langerhans
Slovak	Vemurafenib	Liečba histiocytózy Langerhansových buniek
Slovenian	Vemurafenib	Zdravljenje histiocitoze Langerhansovih celic
Spanish	Vemurafenib	Tratamiento de la histiocitosis de células de Langerhans
Swedish	Vemurafenib	Behandling av Langerhans cell histiocytosis
Norwegian	Vemurafenib	Behandling av Langerhans celle histiocytose
Icelandic	Vemúrafeníb	Meðferð Langerhans frumul histíócýtósis

[1] At the time of designation