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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Melphalan flufenamide for the treatment of plasma cell myeloma

On 19 March 2015, orphan designation (EU/3/15/1463) was granted by the European Commission to Oncopeptides AB, Sweden, for melphalan flufenamide for the treatment of plasma cell myeloma.

What is plasma cell myeloma?

Plasma cell myeloma (also called multiple myeloma) is a cancer of a type of white blood cell called plasma cells. Plasma cells originate in the bone marrow, the spongy tissue inside the large bones of the body. In plasma cell myeloma the division of plasma cells becomes out of control, resulting in abnormal, immature plasma cells multiplying and filling up the bone marrow. These immature cells interfere with the production of normal white blood cells, red blood cells and platelets (components that help the blood to clot), leading to complications such as anaemia (low red blood cell counts), bone pain and fractures, raised blood calcium levels and kidney disease.

Plasma cell myeloma is a debilitating and life-threatening disease particularly because it disrupts the normal functioning of the bone marrow, damages the bones and causes kidney failure.

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

At the time of designation, plasma cell myeloma affected approximately 3.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 185,000 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, several medicines were authorised for plasma cell myeloma in the EU. The main treatment for plasma cell myeloma was chemotherapy (medicines to treat cancer) usually combined with corticosteroids to reduce the activity of the immune system, the body's natural defences. Where chemotherapy did not work, some patients received an allogeneic stem-cell transplant (a complex procedure where the patient receives stem cells from a matched donor to help

*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 512,900,000 (Eurostat 2015).

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restore the bone marrow). Radiotherapy (using radiation to kill cancer cells) was used to treat pain due to bone damage and prevent further damage. Interferon alfa was sometimes used in combination with chemotherapy.

The sponsor has provided sufficient information to show that melphalan flufenamide might be of significant benefit to patients with plasma cell myeloma because early studies showed a response to treatment in patients whose disease had come back or was not responding to previous treatments. 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?

Melphalan flufenamide is a type of chemotherapy medicine known as an alkylating agent. It works by adding a small chemical group called alkyl group to the DNA in cells, altering the DNA and interfering with its function in cell division and growth. As a result, the cells cannot divide and grow and they ultimately die. The medicine acts mainly against fast growing cells, such as cancer cells.

Melphalan flufenamide consists of melphalan (a cancer medicine already authorised to treat plasma cell myeloma) attached to another molecule, flufenamide, which enables it to enter cells more easily. Once inside, free melphalan is released by certain enzymes that are present in higher levels in cancer cells, enabling it to act on their DNA and kill the cell.

What is the stage of development of this medicine?

The effects of melphalan flufenamide have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with melphalan flufenamide in patients with plasma cell myeloma were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for plasma cell myeloma 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 12 February 2015 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:

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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	Melphalan flufenamide	Treatment of plasma cell myeloma
Bulgarian	мелфалан флуфенамид	Лечение на плазмоцитен миелом
Croatian	Melfalanflufenamid	Liječenje multiplog mijeloma
Czech	Melfalan flufenamid	Léčba myelomu
Danish	Melphalan-flufenamid	Behandling af plasmacellemyelom
Dutch	Melfalan flufenamide	Behandeling van plasmacel myeloom
Estonian	Melfalaanflufenamiid	Plasmarakulise müeloomi ravi
Finnish	Melfalaaniflufenamidi	Plasmasolumyelooman hoito
French	Melphalan flufénamide	Traitement du myélome des cellules plasmatiques
German	Melphalan flufenamid	Behandlung des Plasmazell Myeloms
Greek	μελφαλάνη-φλουφεναμίδη	Θεραπεία του πλασματοκυτταρικού μυελώματος
Hungarian	Melfalán-flufenamid	Plasma sejtes myeloma kezelése
Italian	Melfalan-flufenamide	Trattamento del Mieloma Plasmacellulare
Latvian	Melfalāna flufenamīds	Plazmas šūnu mielomas ārstēšana
Lithuanian	Melfalano flufenamidas	Plazminių ląstelių mielomos gydymas
Maltese	Melphalan flufenamide	Kura tal-mjeloma taċ-ċelluli tal-plasma
Polish	Melfalanu flufenamid	Leczenie szpiczaka mnogiego
Portuguese	Melfalan flufenamida	Tratamento do mieloma de células plasmáticas
Romanian	Melfalan flufenamidă	Tratamentul mielomului plasmocitar
Slovak	Melfalan flufenamid	Liečba myelómu z plazmatických buniek
Slovenian	Melfalan flufenamid	Zdravljenje plazmocitoma
Spanish	Melfalán flufenamida	Tratamiento del mieloma de células plasmáticas
Swedish	Melfalan flufenamid	Behandling av plasmacellsmyelom
Norwegian	Melfalanflufenamid	Behandling av plasmacellemyelom
Icelandic	Melfalan flúfenamíð	Meðferð á plasmafrumumýelómi

[1] At the time of designation