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Public summary of opinion on orphan designation

Pevonedistat for the treatment of myelodysplastic syndromes

On 14 December 2018, orphan designation (EU/3/18/2120) was granted by the European Commission to Takeda Pharma A/S, Denmark, for pevonedistat for the treatment of myelodysplastic syndromes.

What are myelodysplastic syndromes?

Myelodysplastic syndromes are a group of disorders in which the red blood cells, white blood cells and platelets produced by the bone marrow (the spongy tissue inside large bones) do not mature normally. Patients with myelodysplastic syndromes can develop several symptoms including tiredness or weakness due to anaemia (low red blood cell counts), infections due to low white blood cell counts, and bruising or abnormal bleeding due to low platelet counts.

Myelodysplastic syndromes are long-term debilitating and life-threatening diseases because they can lead to severe anaemia, infections or bleeding, and can result in leukaemia (cancer of the white blood cells).

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

At the time of designation, myelodysplastic syndromes affected less than 2 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 103,000 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, some medicines were authorised in the EU for the treatment of myelodysplastic syndromes. The choice of treatment depended on a number of factors, including the type and the extent of the disease, whether it had been treated before, and the patient's age, symptoms and general state of health. The main treatments included medicines that stimulate production of blood cells, chemotherapy (medicines to treat cancer), blood transfusions and stem cell transplantation. Stem cell transplantation is a procedure where the patient's bone marrow is cleared 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 517,400,000 (Eurostat 2018).

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cells and replaced with stem cells from a donor to form new bone marrow that produces healthy blood cells.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with myelodysplastic syndromes. Early data in patients showed that they had longer time without their disease getting worse following treatment with the medicine in combination with azacitidine (a medicine for myelodysplastic syndromes), when compared with azacitidine taken alone.

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?

Pevonedistat blocks the activity of an enzyme in the body called NEDD8-activating enzyme (NAE). NAE is involved in the growth and spread of cancer cells. By blocking NAE in patients with myelodysplastic syndromes, pevonedistat is expected to prevent development and worsening of cancer.

What is the stage of development of this medicine?

The effects of pevonedistat have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with pevonedistat in patients with myelodysplastic syndromes were ongoing.

At the time of submission, pevonedistat was not authorised anywhere in the EU for myelodysplastic syndromes. Orphan designation of pevonedistat had been granted in the United States for these conditions.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 November 2018 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:

Contact details of the current sponsor for this orphan designation can be found on the 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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Pevonedistat	Treatment of myelodysplastic syndromes
Bulgarian	Певонедистат	Лечение на миелодиспластичен синдром
Croatian	Pevonedistat	Liječenje mijelodisplastičnih sindroma
Czech	Pevonedistat	Léčba myelodysplastického syndromu
Danish	Pevonedistat	Behandling af myelodysplastiske syndromer
Dutch	Pevonedistat	Behandeling van myelodysplastische syndromen
Estonian	Pevonedistaat	Müelodüsplastiliste sündroomide ravi
Finnish	Pevonedistaatti	Myelodysplastisten syndroomien hoito
French	Pevonedistat	Traitement des syndromes myélodysplasiques
German	Pevonedistat	Behandlung der myelodysplastischen Syndrome
Greek	Πεβονεδιστάτη	Θεραπεία των μυελοδυσπλαστικών συνδρόμων
Hungarian	Pevonedistat	Myelodysplasias syndroma kezelése
Italian	Pevonedistat	Trattamento delle sindromi mielodisplastiche
Latvian	Pevonedistats	Mielodisplastisko sindromu ārstēšana
Lithuanian	Pevonedistatas	Mielodisplastinių sindromų gydymas
Maltese	Pevonedistat	Kura tas-sindromi mjelodisplastiċi
Polish	pewonedistat	Leczenie zespołów mielodysplastycznych
Portuguese	Pevonedistate	Tratamento dos síndromes mielodisplásicos
Romanian	Pevonedistat	Tratamentul sindromului mielodisplazic
Slovak	Pevonedistat	Liečba myelodysplastického syndrómu
Slovenian	Pevonedistat	Zdravljenje mielodisplastičnega sindroma
Spanish	Pevonedistat	Tratamiento de los síndromes mielodisplásicos
Swedish	Pevonedistat	Behandling av myelodysplastiska syndrom
Norwegian	Pevonedistat	Behandling av myelodysplastisk syndrom
Icelandic	Pevónedistat	Til meðferðar við mergmisþroskaheilkenni

[1] At the time of designation