14 December 2023
EMA/CHMP/506425/2023
Committee for Medicinal Products for Human Use (CHMP)

Summary of opinion[1] (initial authorisation)

Casgevy

exagamglogene autotemcel

On 14 December 2023, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a conditional[2] marketing authorisation for the medicinal product Casgevy[3], intended for the treatment of transfusion-dependent β-thalassemia (TDT) and sickle cell disease (SCD). As Casgevy is an advanced therapy medicinal product, the CHMP positive opinion is based on an assessment by the Committee for Advanced Therapies.

The applicant for this medicinal product is Vertex Pharmaceuticals (Ireland) Limited.

Casgevy will be available as a 4-13 x 10^6 cells/ml dispersion for infusion and is intended for one-time administration. The active substance of Casgevy is exagamglogene autotemcel, a haematological agent (ATC code: B06AX05). Exagamglogene autotemcel is a cellular therapy consisting of autologous CD34+ haematopoietic stem cells (HSCs) edited *ex vivo* by CRISPR/Cas9 technology at the erythroid-specific enhancer region of the *BCL11A* gene. When the edited cells are transplanted back into the patients, BCL11A expression in erythroid cells is reduced, increasing γ-globin expression and foetal haemoglobin (HbF) production. This addresses the absent haemoglobin A in patients with TDT and the aberrant haemoglobin S in patients with SCD.

The benefits of Casgevy are its ability to eliminate dependence on chronic red blood cell transfusions in patients with TDT and its ability to reduce the number of vaso-occlusive crises in patients with SCD. The most common side effects are low white blood cell counts including febrile neutropenia, low level of platelets, liver disease, nausea, vomiting, headache and mouth sores. These events are due to the medicines required for the modified blood cells to engraft and replace the unmodified stem cells.

[1] Summaries of positive opinion are published without prejudice to the Commission decision, which will normally be issued 67 days from adoption of the opinion
[2] A conditional marketing authorisation is granted to a medicinal product that fulfils an unmet medical need when the benefit to public health of immediate availability outweighs the risk inherent in the fact that additional data are still required. The marketing authorisation holder is expected to provide comprehensive clinical data at a later stage.
[3] This product was designated as an orphan medicine during its development. EMA will now review the information available to date to determine if the orphan designation can be maintained

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The full indication is:

> β-thalassemia
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> Casgevy is indicated for the treatment of transfusion-dependent β-thalassemia (TDT) in patients 12 years of age and older for whom haematopoietic stem cell (HSC) transplantation is appropriate and a human leukocyte antigen (HLA)-matched related HSC donor is not available.
>
> Sickle cell disease
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> Casgevy is indicated for the treatment of severe sickle cell disease (SCD) in patients 12 years of age and older with recurrent vaso-occlusive crises (VOCs) for whom haematopoietic stem cell (HSC) transplantation is appropriate and a human leukocyte antigen (HLA)-matched related HSC donor is not available.

Casgevy should be administered in an authorised treatment centre by physicians experienced in HSC transplantation and in the treatment of patients with haemoglobinopathies.

Detailed recommendations for the use of this product will be described in the summary of product characteristics (SmPC), which will be published in the European public assessment report (EPAR) and made available in all official European Union languages after the marketing authorisation has been granted by the European Commission.