13 September 2016
EMA/COMP/455724/2016
Committee for Orphan Medicinal Products

Recommendation for maintenance of orphan designation at the time of marketing authorisation

Zalmoxis (allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2)) for the adjunctive treatment of haematopoietic stem cell transplantation

On 28 June 2016, the Committee for Orphan Medicinal Products (COMP) completed its review of the designation EU/3/03/168 for Zalmoxis (allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2))[1] as an orphan medicinal product for the adjunctive treatment of haematopoietic stem cell transplantation. The COMP assessed whether, at the time of marketing authorisation, the medicinal product still met the criteria for orphan designation. The Committee looked at the seriousness and prevalence of the condition, and the existence of other methods of treatment. As other methods of treatment are authorised in the European Union (EU), the COMP also considered whether the medicine is of significant benefit to patients undergoing haematopoietic stem cell transplantation. The COMP recommended that the orphan designation of the medicine be maintained[2].

Life-threatening or long-term debilitating nature of the condition

The Committee for Medicinal Products for Human Use (CHMP) recommended the authorisation of Zalmoxis for: 'adjunctive treatment in haploidentical haematopoietic stem cell transplantation of adult patients with high-risk haematological malignancies'.

This falls within the scope of the product's designated orphan indication, which is 'adjunctive treatment of haematopoietic stem cell transplantation'.

[1] Previously known as 'herpes simplex 1 virus-thymidine kinase and truncated low affinity nerve growth factor receptor transfected donor lymphocytes'.
[2] The maintenance of the orphan designation at time of marketing authorisation would, except in specific situations, give an orphan medicinal product 10 years of market exclusivity in the EU. This means that in the 10 years after its authorisation similar products with the same therapeutic indication cannot be placed on the market.

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The COMP concluded that there had been no change in the seriousness of the condition since the orphan designation in 2003. Haematopoietic stem cell transplantation remains long-term debilitating and life threatening because it makes the patient more susceptible to severe infections and may lead to graft-versus-host disease (when transplanted cells attack the body).

Prevalence of the condition

The sponsor provided updated information on the prevalence of haematopoietic stem cell transplantation based on data from the annual activity survey of the European Society of Blood and Marrow Transplantation.

On the basis of the information provided by the sponsor and the knowledge of the COMP, the COMP concluded that the prevalence of haematopoietic stem cell transplantation remains below the ceiling for orphan designation. At the time of the review of the orphan designation, it was estimated that 0.32 people in 10,000 per year undergo haematopoietic stem cell transplantation. This is equivalent to a total of around 16,000 people per year in the EU.

Existence of other methods of treatment

At the time of the review of the orphan designation, other treatments were authorised in the EU for use in haematopoietic stem cell transplantation. These included medicines to reduce the risk of infections and to help restore the immune system, such as antiviral medicines, antifungal medicines, immunoglobulins (blood proteins that have been extracted from donor plasma), growth factors and vaccines. Medicines that suppress the immune system, such as ciclosporin, were used for the treatment of graft-versus-host disease.

Significant benefit of Zalmoxis

The COMP concluded that the claim of a significant benefit of Zalmoxis in haematopoietic stem cell transplantation is justified because Zalmoxis was shown to improve survival and reduce the number of patients who developed graft-versus-host disease after haematopoietic stem cell transplantation, compared with data from databases of previous patients who received the best standard care after transplantation.

Therefore, although other methods for the treatment of this condition have been authorised in the EU, the COMP concluded that Zalmoxis is of significant benefit to patients undergoing haematopoietic stem cell transplantation.

Conclusions

Based on the data submitted and the scientific discussion within the COMP, the COMP considered that Zalmoxis still meets the criteria for designation as an orphan medicinal product and that it should remain in the Community Register of Orphan Medicinal Products.

Further information on the current regulatory status of Zalmoxis can be found in the European public assessment report (EPAR) on the Agency's website ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports.