EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

21 December 2016
EMA/700601/2016
Committee for Orphan Medicinal Products

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

Venclyxto (venetoclax) for the treatment of chronic lymphocytic leukaemia

On 14 October 2016, the Committee for Orphan Medicinal Products (COMP) completed the review of the designation EU/3/12/1080 for Venclyxto (venetoclax[1]) as an orphan medicinal product for the treatment of chronic lymphocytic leukaemia. 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 with chronic lymphocytic leukaemia. 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 Venclyxto with the following indication:

> 'Venclyxto monotherapy is indicated for the treatment of chronic lymphocytic leukaemia (CLL) in the presence of 17p deletion or TP53 mutation in adult patients who are unsuitable for or have failed a B cell receptor pathway inhibitor.
>
> Venclyxto monotherapy is indicated for the treatment of CLL in the absence of 17p deletion or TP53 mutation in adult patients who have failed both chemoimmunotherapy and a B cell receptor pathway inhibitor.'

This falls within the scope of the product's designated orphan indication, which is: 'treatment of chronic lymphocytic leukaemia'.

[1] Previously known as 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide.
[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.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

The COMP concluded that there had been no change in the seriousness of the condition since the orphan designation in 2012. Chronic lymphocytic leukaemia remains a condition that is debilitating in the long-term and life threatening, particularly due to the risk of reduced blood cells, enlarged livers and spleens and severe infection.

Prevalence of the condition

The sponsor provided updated information on the prevalence of chronic lymphocytic leukaemia based on data from registries.

On the basis of the information provided by the sponsor and the knowledge of the COMP, the COMP concluded that the prevalence of CLL remains below the ceiling for orphan designation, which is 5 people in 10,000. At the time of the review of the orphan designation, the prevalence was estimated to be approximately 4.8 people in 10,000. This is equivalent to a total of around 250,000 people in the EU.

Existence of other methods of treatment

At the time of the review of the orphan designation, several chemotherapy or immunotherapy medicines (treatments that stimulate the immune system to kill cancer cells) were authorised in the EU for the treatment of chronic lymphocytic leukaemia, including bendamustine, chlorambucil, cyclophosphamide, fludarabine, obinutuzumab, ofatumumab and rituximab.

Medicines known as B cell receptor pathway inhibitors such as ibrutinib and idelalisib were also used, including in patients with 17p deletion or TP53 mutation. These genetic changes make patients unsuitable for treatment with a combination of chemotherapy and immunotherapy medicines.

Significant benefit of Venclyxto

The COMP concluded that the claim of a significant benefit of Venclyxto is justified because the medicine has been shown to improve symptoms in patients with few treatment options, such as patients with 17p deletion or TP53 mutation who had not responded well to B cell receptor pathway inhibitors, and patients without these mutations who had not responded either to such treatments or to chemotherapy and immunotherapy medicines.

In one main study, Venclyxto led to a treatment response in the majority of patients with 17p deletion or a TP53 mutation. In another study, Venclyxto produced a response in more than half of patients with or without 17p deletion or a TP53 mutation but whose CLL had failed to respond to treatments with B-cell receptor pathway inhibitors.

Therefore, although other methods for the treatment of this condition have been authorised in the EU, the COMP concluded that Venclyxto is of significant benefit to patients affected by chronic lymphocytic leukaemia.

Conclusions

Based on the data submitted and the scientific discussion within the COMP, the COMP considered that Venclyxto 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 Venclyxto 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.