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Refusal of the marketing authorisation for Kizfizo (temozolomide)

Re-examination confirms refusal

After re-examining its initial opinion, the European Medicines Agency has confirmed its recommendation to refuse marketing authorisation for the medicine Kizfizo. The medicine was intended for the treatment of children with neuroblastoma, a cancer of nerve cells.

The Agency issued its opinion after re-examination on 27 February 2025. The Agency had issued its initial opinion on14 November 2024. The company that applied for authorisation of Kizfizo is Orphelia Pharma.

What is Kizfizo and what was it intended for?

Kizfizo was developed as a cancer medicine for treating children over the age of 1 year with high-risk neuroblastoma. It was meant to be used in combination with another cancer medicine, either irinotecan or topotecan, in:

- children whose neuroblastoma had not improved with chemotherapy (other medicines used to treat cancer);
- children whose disease has come back and is worsening after they had previously received chemotherapy and stem cell transplantation (a procedure where a patient's blood-producing cells are replaced).

Kizfizo contains the active substance temozolomide and was developed as a 'hybrid' medicine. This means that it is similar to a reference medicine containing the same active substance, but there are certain differences between the two.

While the reference medicine, Temodal, is available as capsules or a powder to make a solution for infusion (drip) into a vein, Kizfizo is a liquid to be taken by mouth or through a tube running from the nose to the stomach.

Kizfizo was designated an 'orphan medicine' (a medicine used in rare diseases) on 21 August 2019 for neuroblastoma. Further information on the orphan designation can be found on the Agency's website.

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How does Kizfizo work?

The active substance in Kizfizo, temozolomide, is an alkylating agent. In the body, it changes into another compound called MTIC. MTIC modifies the DNA in a way that stops cells from dividing, causing them to die. By doing so, temozolomide is expected to slow down the growth of neuroblastoma.

What did the company present to support its application?

The reference medicine, Temodal, is authorised for another cancer (glioblastoma) but has been used to treat neuroblastoma. The company carried out a study to investigate whether Kizfizo is 'bioequivalent' to Temodal. Two medicines are bioequivalent when they produce the same levels of the active substance in the body and are therefore expected to have the same effect.

The company also provided the results of a clinical study involving 102 patients aged up to 21 years old with neuroblastoma who were given temozolomide alone and in combination with irinotecan or topotecan. The main measure of effectiveness was the response to treatment. The company supported these findings with results from an observational study that included children with neuroblastoma treated with temozolomide.

What were the main reasons for refusing the marketing authorisation?

The Agency noted that in both the clinical and observational studies (which did not compare temozolomide with any other treatment) the proportion of patients who responded to the combination of temozolomide plus irinotecan or topotecan was too modest to show that it is beneficial to patients. Furthermore, it was not possible to determine the effect of temozolomide on the basis of the data from these studies.

Therefore, the Agency's opinion was that the balance of benefits and risks of Kizfizo in the treatment of children with neuroblastoma could not be established.

Following a request from the company, the CHMP re-examined the available data and also sought the advice of a group of experts who were asked to address several questions about the medicine's benefits. As the Committee's concerns were not resolved, the initial refusal was confirmed after re-examination.

Does this refusal affect patients in clinical trials?

The company informed the Agency that there are no consequences for patients in clinical trials with Kizfizo.

If you are in a clinical trial and need more information about your treatment, speak with your clinical trial doctor.