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Refusal of the marketing authorisation for Sohonos (palovarotene)

Re-examination confirms refusal

After re-examining its initial opinion, the European Medicines Agency has confirmed its recommendation to refuse marketing authorisation for Sohonos, a medicine intended for the treatment of fibrodysplasia ossificans progressiva (FOP). FOP is a rare genetic disease that causes extra bone to form in places outside the skeleton (a process called heterotopic ossification) such as in joints, muscles, tendons and ligaments, leading to progressively decreasing mobility and other severe impairments.

The Agency issued its opinion after re-examination on 25 May 2023. The Agency had issued its initial opinion on 26 January 2023. The company that applied for authorisation of Sohonos, Ipsen Pharma, had requested a re-examination of EMA's initial opinion.

What is Sohonos and what was it intended for?

Sohonos was intended to reduce the abnormal formation of bone in joints, muscles, tendons and ligaments in adults and children (over 8 years of age in girls and over 10 years of age in boys) with FOP. It contains the active substance palovarotene and was to be available as capsules to be taken by mouth every day.

Sohonos was designated an 'orphan medicine' (a medicine used in rare diseases) on 19 November 2014 for the treatment of FOP. Further information on the orphan designation can be found on the Agency's website: ema.europa.eu/medicines/human/orphan-designations/eu3-14-1368.

How does Sohonos work?

The active substance in Sohonos, palovarotene, belongs to a class of medicines known as retinoids. It attaches to the retinoic acid receptor (gamma), which is present in cells that are involved in bone formation. By attaching to these receptors, the medicine switches on processes that reduce bone formation. This was expected to relieve the symptoms of the condition.

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What did the company present to support its application?

The company provided results from one main study involving 107 adults and children with FOP. All study participants were given Sohonos and the study results were compared with those of a second study involving 114 patients with FOP who received no treatment.

The main measure of effectiveness in the main study was the change in the amount of newly developed heterotopic ossifications in patients.

What were the main reasons for refusing the marketing authorisation?

At the time of the initial evaluation, the Agency considered that no firm conclusions could be drawn on the benefits of the medicine, as the applicant's conclusion was based on a post-hoc analysis which was neither scientifically nor clinically justified and pre-specified study objectives were not met. In addition, results from other studies and the limited long-term clinical data available did not support efficacy. Regarding safety, the risk of premature physeal closure (a disruption to the areas of new bone growth in the end of long bones, which keeps them from growing normally), which is a known risk with retinoid treatment in growing patients, could not adequately be mitigated with the risk minimisation measures proposed by the company. In addition, the Agency considered that some questions regarding the quality of the active substance had not been resolved.

These concerns did not change after re-examination of the data provided, and the Agency's opinion therefore remained that the quality, safety and efficacy of Sohonos had not been sufficiently demonstrated. The Agency therefore considered that the benefits of Sohonos did not outweigh its risks and it recommended refusing marketing authorisation.

Does this refusal affect patients in clinical trials or compassionate use programmes?

The company informed the Agency that there are no consequences for patients in clinical trials or in compassionate use programmes with Sohonos.

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