EMA recommends revocation of authorisation for sickle cell disease medicine Adakveo

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Information on Adakveo

- Adakveo is a medicine for preventing painful crises in patients aged 16 years and older with sickle cell disease, a genetic condition in which the red blood cells become rigid and sticky and change from being disc-shaped to being crescent-shaped (like a sickle).
- More information about the medicine can be found on the EMA website.

The following product is authorised via centralised procedure.

Active Ingredients	Product Name	Pharmaceutical Form	Classif-cation	Authorisation Number	MAH/license holder
Crizanlizumab	Adakveo	Concentrate for solution for infusion	POM	EMEA/H/C/004874	Novartis Europharm Limited

Information from the EMA about the safety concern

- EMA's human medicines committee (CHMP) has recommended revoking the marketing authorisation for Adakveo (crizanlizumab), a medicine for preventing painful crises (called vaso-occlusive crises) in patients aged 16 years and older with sickle cell disease.
- This follows a review by the CHMP, which concluded that the benefits of the medicine did not outweigh its risks. The review looked at results of the STAND study, which compared the effectiveness and safety of Adakveo with placebo (a dummy treatment) in patients who had previously had painful crises leading to a healthcare visit.
- The study showed that Adakveo did not reduce the number of painful crises leading to a healthcare visit. Patients treated with Adakveo had on average 2.5 painful crises with a subsequent healthcare visit over the first year of treatment, compared with 2.3 crises in the placebo group.
- In addition, the average number of crises requiring a healthcare visit or treatment at home was 4.7 with Adakveo compared with 3.9 with placebo.
- In its review, the CHMP also looked at data from other studies, a managed access program and real-world data. However, the studies had several limitations, such as the lack of a comparator, and could not be used to show the effect of Adakveo or counterbalance the negative results of the STAND study.

- In terms of safety, the STAND study did not raise new concerns but showed a higher rate of severe and serious treatment-related side effects for Adakveo compared with placebo. The CHMP therefore concluded that its benefits do not outweigh the risks.
- At the time of marketing authorisation, data showed that Adakveo was effective at reducing the number of painful crises in patients with sickle cell disease. However, the data were limited and there was some uncertainty about the size of the medicine's effect.
- EMA therefore requested the STAND study as a condition for the marketing authorisation of Adakveo, which was granted in October 2020. As the STAND study results do not confirm the benefits previously seen with Adakveo, the CHMP has now concluded that the benefits do not outweigh the risks and recommended the revocation of its authorisation in the EU.
- Following the CHMP's recommendation, the European Commission issued a legally binding decision on 3 August 2023. Patients who have any questions should speak to their doctor, nurse or pharmacist.

Information about the procedure

- The review of Adakveo has been initiated at the request of the European Commission, under Article 20 of Regulation (EC) No 726/2004.
- The review has been carried out by the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which has adopted the Agency's opinion. The CHMP opinion will now be forwarded to the European Commission, which will issue a final legally binding decision applicable in all EU Member States.

Information for patients

- A recent study has shown that Adakveo does not reduce the number of painful crises requiring a healthcare visit or treatment at home in patients with sickle cell disease.
- Because of the latest study results, Adakveo is being taken off the market in the EU and no new patients will be treated with the medicine.
- If you are receiving Adakveo treatment, make an appointment with your doctor at the next possible opportunity to discuss alternative treatments.
- If you have any questions, you should speak to your doctor, nurse or pharmacist.

Information for healthcare professionals

- The sickle cell medicine Adakveo (crizanlizumab) is being taken off the market in the EU because a recent study did not confirm its clinical benefit.
- The STAND study did not show a difference between Adakveo (2.49, 95% CI [1.90, 3.26]) and placebo (2.30, 95% CI [1.75, 3.01]) in annualised rates of vaso-occlusive crises leading to a healthcare visit over the first year. Similar results were seen when looking at crises requiring a healthcare visit or treatment at home: the rates were 4.7, 95% CI: (3.60, 6.14) with Adakveo versus 3.9, 95% CI: (3.00, 5.01) with placebo.
- Healthcare professionals should not start any new patients on Adakveo.

- For patients currently on treatment with Adakveo, healthcare professionals should explain to patients that the medicine is being taken off the market and the reasons why and discuss alternatives with them.

For more information, please see the European Medicines Agency's press release.

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance with Adakveo. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form and sending it to: Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 **or** online to http://www.medicinesauthority.gov.mt/adrportal or to the marketing authorisation holder or their local representatives.

Post-Licensing Directorate

Medicines Authority

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

Feedback Form

The Medicines Authority thanks you for the time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health.

The Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. This may be returned by folding this form (address side up), stapling the ends and then posting (no stamp required).

Feedback:

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