19-12-2024

Alofisel® (darvadstrocel): Withdrawal from the EU market as its clinical benefit is no longer demonstrated to justify its continued use

Dear Healthcare Professional,

Takeda, in agreement with the European Medicines Agency (EMA) and the Italian Medicines Agency, would like to inform you of the following:

Summary

- **Alofisel is being withdrawn from the EU market. The totality of data applicable to the EU marketing authorization, including the results of ADMIRE-CD II study, indicates that the clinical benefit of Alofisel is no longer demonstrated to justify its continued use in the EU and therefore, it would not outweigh the risks associated with its use.**
- **ADMIRE-CD II, a randomised placebo-controlled study investigating a single administration of Alofisel for the treatment of complex perianal fistulas in 568 patients with Crohn's disease, did not meet its primary endpoint of combined remission at 24 weeks or any of its secondary endpoints. This was a post authorization measure agreed with EMA upon initial approval to confirm clinical benefit.**
- **The safety profile for Alofisel in ADMIRE CD-II study was consistent with prior studies, as no new, emerging safety signals were identified.**
  • Alofisel is therefore being withdrawn from the European Union (EU) market.
- **No new patients should be treated in the EU/EEA with Alofisel after the 13 December 2024.**

Background

Alofisel® (darvadstrocel) is an allogeneic mesenchymal stem cell therapy for the treatment of complex perianal fistulas in adults with non-active/mildly active luminal Crohn's disease, when fistulas have shown an inadequate response to at least one conventional or biological therapy. Alofisel should have been be used only after conditioning of the fistulas.

The initial authorisation of Alofisel in the EU was based on results from the Phase 3 ADMIRE-CD placebo-controlled registrational study. Given the small population size (n = 212) and modest benefit observed in the ADMIRE-CD study (a difference of 15.8% between the modified intention-to-treat population and placebo at 24 weeks), Takeda provided the EMA with results from ADMIRE-CD II, a study that was underway at the time, to confirm

Alofisel's efficacy (a difference of 2.4% between the intention-to-treat population and placebo at 24 weeks).

ADMIRE-CD II, a randomised placebo-controlled Phase 3 study of 568 patients with complex Crohn's Perianal Fistulas, did not meet its primary endpoint of combined remission at 24 weeks or any of its secondary endpoints. The safety profile for Alofisel was consistent with prior studies as no new, emerging safety signals were identified in the ADMIRE CD-II study.

Alofisel is being withdrawn from the EU market. This decision is based on the totality of Alofisel data, which indicates that the clinical benefit of Alofisel is no longer demonstrated to justify its continued use, and no longer outweighs the risks associated with Alofisel.

Next Steps and Health Care Professionals Action

Health care professionals should be prepared to answer questions from patients about the withdrawal of Alofisel and alternative treatments.

Reporting Patients Adverse Events and Medication Errors

Please report any adverse events experienced by your patients who received Alofisel. When reporting, please provide as much information as possible including information about batch details, medical history, any concomitant medication, onset and treatment dates.

If you learn of an Adverse Event (AE) or Special Situation Report (SSR), you must submit a report to pharmacovigilancemailbox@takeda.com within one business day (not to exceed three calendar days if received before a weekend or holiday); the same timeframe applies to a Product Quality Complaint (PQC), which should be submitted to PQC@takeda.com.

Your country may have specific processes in place to handle reports of adverse events. To report an adverse event to the local health authority, please contact your local health authority.