January 2025

Veoza▼ (fezolinetant): risk of drug-induced liver injury and new recommendations on monitoring of liver function before and during treatment

Dear Healthcare Professional,

Astellas Pharma Ltd. in agreement with the Medicines and Healthcare Products Regulatory Agency (MHRA) would like to inform you of the following:

Summary

- **Serious liver injury has been observed with fezolinetant.**
- **Liver function tests (LFTs) must be performed prior to initiation of fezolinetant. Treatment with fezolinetant must not be initiated if serum alanine aminotransferase (ALT) or serum aspartate aminotransferase (AST) levels are ≥2x ULN or if total bilirubin levels are ≥2x ULN.**
- **During the first three months of treatment, monthly LFTs must be performed, and thereafter based on clinical judgement. LFTs must also be performed when symptoms suggestive of liver injury occur.**
- **Treatment with fezolinetant must be discontinued if:**
  - **Transaminase elevations are ≥3x ULN with: total bilirubin >2x ULN OR if patients develop symptoms of liver injury;**
  - **Transaminase elevations >5x ULN.**
- **LFT monitoring should be maintained until LFTs have normalised.**
- **Patients must be advised to immediately seek medical attention if they experience signs or symptoms that may suggest liver injury such as fatigue, pruritus, jaundice, dark urine, pale faeces, nausea, vomiting, decreased appetite and/or abdominal pain.**

Background on the safety concern

Veoza contains fezolinetant, a neurokinin-3 receptor antagonist. It is indicated for the treatment of moderate to severe vasomotor symptoms (VMS) associated with menopause.

Recently identified safety information on liver injury prompted an EU-wide review of data in association with the potential of fezolinetant to cause drug-induced liver injury (DILI) by the European Medicines Agency. Information from all available

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sources, including adverse drug reaction reports and studies published in the scientific literature, was considered.

Elevations in serum ALT and AST were already observed in clinical trials with fezolinetant and are described in the product information.

Serious cases with elevations of ALT and/or AST (>10x ULN) with concurrent elevations in bilirubin and/or alkaline phosphatase (ALP) were reported post-marketing. In some cases, elevated LFTs were associated with signs or symptoms suggestive of liver injury such as fatigue, pruritus, jaundice, dark urine, decreased appetite or abdominal pain.

Since Veoza is indicated for a condition in otherwise healthy women, the risk of serious liver injury may significantly affect its benefit-risk balance. Consequently, exposure to Veoza should be avoided in women at higher risk for liver disease and early recognition of potential liver injury is essential. Therefore, LFTs should be performed before treatment initiation. Treatment should not be initiated if ALT and/or AST levels are ≥2x ULN or bilirubin levels are ≥2x ULN.

Elevated liver function tests and/or symptoms suggestive of liver injury were generally reversible on discontinuation of therapy. During the first three months of treatment, monthly LFTs must be performed, and thereafter based on clinical judgement. Throughout LFTs must be performed if symptoms suggestive of liver injury occur. Treatment should be discontinued in the following situations:

- Transaminase elevations are ≥3x ULN with: total bilirubin >2x ULN OR patients develop symptoms of liver injury

- Transaminase elevations are >5x ULN.

Monitoring of liver function should be maintained until they have normalised.

Patients should be advised to be vigilant for signs and symptoms of potential liver injury, including fatigue, pruritus, jaundice, dark urine, pale faeces, nausea, vomiting, decreased appetite and/or abdominal pain, and to seek immediate medical attention if such symptoms arise. The summary of product characteristics and package leaflet of Veoza are being updated in accordance with the new risk information and recommendations described above. Drug-induced liver injury is also being included as adverse drug reaction with the frequency “not known” since the frequency cannot be calculated from the data provided.

Call for reporting

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Please report any suspected adverse drug reactions (ADRs) to drugs and vaccines identified by the black triangle▼ to the MHRA through the Yellow Card Scheme.

Please report:

- all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason
- all suspected ADRs associated with new drugs and vaccines identified by the black triangle▼

You can report via:

- the Yellow Card website
- the free Yellow Card app available from the Apple App Store or Google Play Store
- some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) for healthcare professionals

Alternatively, you can report a suspected side effect to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, timing onset, treatment dates, and product brand name.

Company contact point

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Should you have any questions regarding the contents of this letter or the use of VEOZA™, please contact: medinfo.est-m@astellas.com.

Sincerely,

Signed by:
7064363E05A3497...

Dr T Patel
Medical Director Astellas UK
Astellas Pharma Ltd

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