

<p><b><u>PLEASE READ</u></b></p> <p><b>IMPORTANT MEDICINE SAFETY INFORMATION</b></p>	<p>APPROVED BY THE</p>	<p><b>HPRA</b> An tÚdarás Rialála Táirgí Sláinte Health Products Regulatory Authority</p> 
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13 January 2025

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

Dear Healthcare Professional,

Astellas Pharma Co., Ltd. in agreement with the European Medicines Agency and the Health Products Regulatory Authority (HPRA) 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  $\geq 2x$  upper limit of normal (ULN) or if total bilirubin levels are  $\geq 2x$  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  $\geq 3x$  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**

Veozav 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 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  $\geq 2x$  ULN or bilirubin levels are  $\geq 2x$  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 treatment LFTs must be performed if symptoms suggestive of liver injury occur. Treatment should be discontinued in the following situations:

- Transaminase elevations are  $\geq 3x$  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. Healthcare professionals are asked to report any suspected adverse drug reactions via HPR Pharmacovigilance, website: [www.hpra.ie](http://www.hpra.ie).

**PLEASE READ**

**IMPORTANT MEDICINE  
SAFETY INFORMATION**

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***Company contact point***

Please report any suspected adverse reactions to:

**Astellas Drug Safety**

Tel: +353 1 467 1555

Email: [irishdrugsafety@astellas.com](mailto:irishdrugsafety@astellas.com)

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

Sincerely,

DocuSigned by:  
  
12205E1D17AD4B8...

**Olga Wedemeier**  
**Senior Medical Director BeNeLux and Ireland**  
**Astellas Pharma Europe**

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