<Date>

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 [affiliate to include country specific information to reflect global or local company name] in agreement with the European Medicines Agency and the <National Competent Authority> 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 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

Healthcare professionals are asked to report any suspected adverse drug reactions in accordance with the national spontaneous reporting system and include batch/Lot number if available.

<include the details (e.g. name, postal address, fax number, website address) on how to access the national spontaneous reporting system>.

Company contact point

<Contact point details for access to further information, including relevant website address(es), telephone numbers and a postal address>

Communication Plan for Veoza DHPC in the EU

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	Veoza (fezolinetant), 45 mg film-coated tablets
Marketing authorisation holder(s)	Astellas Pharma Europe B.V.
Safety concern and purpose of the communication	Risk of drug-induced liver injury and new recommendations on evaluation of hepatic function before and during treatment
DHPC recipients	Gynaecologists, general practitioners/family physicians, specialists in hepatology and gastroenterology, community pharmacists, hospital pharmacists, relevant professional societies (gynaecology, hepatology, gastroenterology), relevant national associations and pharmacists (per local requirements). Target groups will be further defined at national level, in agreement with the respective national competent authority.
Member States where the DHPC will be distributed	All EU/EEA Member states where the medicinal product is marketed

Timetable	Date
DHPC and communication plan (in English) agreed by PRAC	28/11/2024
DHPC and communication plan (in English) agreed by CHMP	12/12/2024
Submission of translated DHPCs to the national competent authorities for review	17/12/2024
Agreement of translations by national competent authorities	06/01/2025
Dissemination of DHPC	13/01/2025