Abbreviated prescribing information of Veoza

Abbreviated prescribing information of Veoza® Tablets

Version: 001

Composition:

Fezolinetant

Indications:

Veoza is indicated for the treatment of moderate to severe vasomotor symptoms (VMS) associated with menopause.

Dosage:

Posology

The recommended dose is 45 mg once daily.

Benefit of long-term treatment should be periodically assessed since the duration of VMS can vary by individual.

Missed dose

If a dose of Veoza is missed or not taken at the usual time, the missed dose should be taken as soon as possible, unless there is less than 12 hours before the next scheduled dose. Individuals should return to the regular schedule the following day.

Elderly

Fezolinetant has not been studied for safety and efficacy in women initiating Veoza treatment over 65 years of age. No dose recommendation can be made for this population.

Hepatic impairment

No dose modification is recommended for individuals with Child-Pugh Class A (mild) chronic hepatic impairment.

Veoza is not recommended for use in individuals with Child-Pugh Class B (moderate) or C (severe) chronic hepatic impairment. Fezolinetant has not been studied in individuals with Child-Pugh Class C (severe) chronic hepatic impairment.

Renal impairment

No dose modification is recommended for individuals with mild (eGFR 60 to less than 90 ml/min/1.73 m^2) or moderate (eGFR 30 to less than 60 ml/min/1.73 m^2) renal impairment.

Veoza is not recommended for use in individuals with severe (eGFR less than 30 ml/min/1.73 m^2) renal impairment. Fezolinetant has not been studied in individuals with end-stage renal disease (eGFR less than 15 ml/min/1.73 m^2) and is not recommended for use in this population.

Paediatric population

There is no relevant use of Veoza in the paediatric population for the indication of moderate to severe VMS associated with menopause.

Administration:

Veoza should be administered orally once daily at about the same time each day with or without food and taken with liquids. Tablets are to be swallowed whole and not broken, crushed, or chewed due to the absence of clinical data under these conditions.

Contraindications:

− Hypersensitivity to the active substance or to any of the excipients listed in full prescribing information.

− Concomitant use of moderate or strong CYP1A2 inhibitors.

− Known or suspected pregnancy.

Special warnings and precautions for use:

Medical examination/consultation

Prior to the initiation or reinstitution of Veoza, a careful diagnosis should be made, and complete medical history (including family history) must be taken. During treatment, periodic check-ups must be carried out according to standard clinical practice.

Liver disease

Veoza is not recommended for use in individuals with Child-Pugh Class B (moderate) or C (severe) chronic hepatic impairment. Women with active liver disease or Child-Pugh Class B (moderate) or C (severe) chronic hepatic impairment have not been included in the clinical efficacy and safety studies with fezolinetant and this information cannot be reliably extrapolated. The pharmacokinetics of fezolinetant has been studied in women with Child-Pugh Class A (mild) and B (moderate) chronic hepatic impairment.

Drug-induced liver injury (DILI)

Elevations in serum alanine aminotransferase (ALT) levels and serum aspartate aminotransferase (AST) at least 3 times the upper limit of normal (ULN) were observed in women treated with fezolinetant, including serious cases with increased total bilirubin and symptoms suggesting liver injury. Elevated liver function tests (LFTs) and symptoms suggestive of liver injury were generally reversible on discontinuation of therapy. LFTs must be performed prior to treatment initiation with fezolinetant. Treatment should not be started if ALT or AST is ≥ 2 x ULN or if total bilirubin is elevated (e.g., ≥ 2 x ULN). LFTs must be performed monthly during the first three months of treatment, then based on clinical judgement. LFTs must also be performed when symptoms suggestive of liver injury occur.

Treatment should be discontinued in the following situations:

− Transaminase elevations are ≥ 3 x ULN with: total bilirubin > 2 x ULN OR symptoms of liver injury.

− Transaminase elevations > 5 x ULN.

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

Patients should be informed about the signs and symptoms of liver injury and should be advised to contact their doctor immediately once these occur.

Known or previous breast cancer or oestrogen-dependent malignancies

Women undergoing oncologic treatment (e.g., chemotherapy, radiation therapy, anti-hormone therapy) for breast cancer or other oestrogen-dependent malignancies have not been included in the clinical studies. Therefore, Veoza is not recommended for use in this population as the safety and efficacy are unknown.

Women with previous breast cancer or other oestrogen-dependent malignancies and no longer on any oncologic treatment have not been included in the clinical studies. A decision to treat these women with Veoza should be based on a benefit-risk consideration for the individual.

Concomitant use of hormone replacement therapy with oestrogens (local vaginal preparations excluded)

Concomitant use of fezolinetant and hormone replacement therapy with oestrogens has not been studied, and therefore concomitant use is not recommended.

Seizures or other convulsive disorders

Fezolinetant has not been studied in women with a history of seizures or other convulsive disorders.

There were no cases of seizures or convulsive disorders during clinical studies. A decision to treat these women with Veoza should be based on a benefit-risk consideration for the individual.

Undesirable effects:

Summary of the safety profile

The most frequent adverse reactions with fezolinetant 45 mg were diarrhoea (3.2%) and insomnia (3.0%).

There were no serious adverse reactions reported at an incidence greater than 1% across the total study population. On fezolinetant 45 mg, four serious adverse reactions were reported. The most serious adverse reaction was an event of endometrial adenocarcinoma (0.1%).

The most frequent adverse reactions leading to dose discontinuation with fezolinetant 45 mg were alanine aminotransferase (ALT) increased (0.3%) and insomnia (0.2%).

Tabulated list of adverse reactions

The safety of fezolinetant has been studied in 2203 women with VMS associated with menopause receiving fezolinetant once daily in phase 3 clinical studies.

Adverse reactions observed during clinical studies and from spontaneous reporting are listed below by frequency category in each system organ class. Frequency categories are defined as follows: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000); and not known (cannot be estimated from the available data).

Table 1. Adverse reactions for fezolinetant 45 mg

MedDRA system organ class (SOC)	Frequency category	Adverse reaction
Psychiatric disorders	Common	Insomnia
Gastrointestinal disorders	Common	Diarrhoea, Abdominal pain
Hepatobiliary disorders	Common	Alanine aminotransferase (ALT) increased, Aspartate aminotransferase (AST) increased*
	Not known	Drug-induced liver injury (DILI)*

*see Description of selected adverse reactions

Description of selected adverse reactions

ALT increased/AST increased/DILI

In clinical trials, elevations in ALT levels > 3 x ULN occurred in 2.1% of women receiving fezolinetant compared to 0.8% of women receiving placebo. Elevations in AST levels > 3 x ULN occurred in 1.0% of women receiving fezolinetant compared to 0.4% of women receiving placebo.

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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions.

Full prescribing information is available upon request.