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# FEZOLINETANT MEDICATION - A new medication for menopausal hot flushes

Fezolinetant or Veoza, was approved by the TGA in 2024 for the treatment of moderately severe menopausal flushes. It is the first approved drug in a new class called "NK3 antagonists".

## MECHANISM OF ACTION – HOW DOES IT WORK?

The hypothalamus in the brain controls many automatic functions such as heart rate and blood pressure. Within this area of the brain lies the thermoregulatory centre which controls body temperature. For example, it regulates sweating or shivering. This control is mediated through highly specialised nerve cells called "kisspeptin/neurokinin B [NKB]/dynorphin (KNDy) neurons", which are inhibited by oestrogen and stimulated by the neuropeptide NKB.

Through the menopausal transition, declining oestrogen disrupts the balance with NKB. Unopposed, NKB signalling increases KNDy nerve activity leading to hot flushes and night sweats. Fezolinetant is a nonhormonal drug that blocks the neuropeptide NKB from 'switching on' the neurons in the thermoregulatory centre that cause the hot flushes. It is not a sex hormone. It does not alter serum levels of any hormones, including LH, FSH, or oestradiol.

## CLINICAL INFORMATION

Dosage: 45mg tablet taken once a day. It is not affected by food.

Indication: moderate-severe hot flushing vasomotor symptoms associated with menopause.

Long-term study data: Nothing is available beyond 12 months.

Short-term side effects: very well tolerated. Side effect profile in the SKYLIGHT studies was the same as the placebo. There is no sedation/ drowsiness.

How well did it work? (Efficacy): The average reduction of frequency of flushes at 12 weeks of treatment was 6.9 (placebo: 4.4; pooled results from SKYLIGHT Studies 1 and 2). In many women, the drug reduced symptoms rather than completely eradicated them.

An Asian study of the 30mg dose showed it was no better than a placebo/fake pill. See Astellas' menopause drug suffers rare setback as failed Asian trial blots previously pristine record | Fierce Biotech.

## CONTRAINDICATIONS

There is no data available using the product in women over 65 years of age or for young/paediatric populations.

Fezolinetant should not be used in people with severe liver or renal impairment (the drug is excreted mostly through the kidneys).

Beware if you are taking a moderate-strong dose of CYP1A2 inhibitors, used for a wide range of conditions from mental health/OCD, arthritis, heart arrhythmias and some contraceptives. These include:

Fluvoxamine, ethinyl oestradiol contraceptives, mexiletine (these all increase blood levels of fezolinetant); ciprofloxacin, rofecoxib, quinidine. **Fluvoxamine** seems to be the most important interaction.

## SPECIAL PRECAUTIONS

Liver: 2-5% of patients taking fezolinetant will develop raised liver enzymes (ALT). Two percent of patients will have ALT levels (a liver enzyme) more than 3 times the normal level.

Monitoring: baseline liver function tests are recommended before starting, then 3, 6 and 9 months according to the Company's US guidelines:
https://www.astellas.com/us/system/files/veozah_uspi.pdf

There is no data about giving the drug to:

- Patients with breast cancer (including those on hormone therapies).
- People using GnRH antagonists (Zoladex or Synarel).
- Pregnant or breastfeeding women.

The company does not recommend taking fezolinetant with menopausal hormonal therapy (MHT). Local vaginal oestrogens are permitted.

## OTHER POINTS

Cost: $60-80 per month

## SUMMARY

Fezolinetant is the first drug in a new class of medicines. Effective non-oestrogen treatments are needed for women who cannot or do not want to take MHT. The new drug seems to have a low side effect profile. However, it is concerning that 3 monthly liver function tests are required, that there is only 12 months of data (many women have flushes for years) and that an Asian study failed to show any benefit over the placebo.

## DISCLAIMER

This information should not be considered as medical advice. You should discuss if this medicine is suitable for you with your healthcare provider.

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