Astellas Response to 12-Month Follow Up of Fezolinetant for Moderate to Severe Vasomotor Symptoms Associated with Menopause Evidence Report – January 2024

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Since the publication of the ICER final evidence report on January 23, 2023, several publications have added evidence of fezolinetant's clinical benefits as an effective treatment for moderate to severe vasomotor symptoms (VMS) associated with menopause.

- The manuscript with data from SKYLIGHT 1 supports the clinical use of fezolinetant as a non-hormonal treatment for moderate to severe VMS associated with menopause. The population studied was diverse and representative of the potential target population for fezolinetant. Compared with placebo, fezolinetant demonstrated a statistically significant reduction in the frequency and the severity of vasomotor symptoms at week 4 and week 12. Improvements in frequency and severity of vasomotor symptoms were observed after 1 week and maintained over 52 weeks. During the first 12 weeks, treatment-emergent adverse events (TEAEs) occurred in 65 (37%) of 174 women in the fezolinetant 30 mg group, 75 (43%) of 173 in the fezolinetant 45 mg group, and 78 (45%) of 175 in the placebo group. The incidence of liver enzyme elevations was low (placebo n=1; fezolinetant 30 mg n=2; fezolinetant 45 mg n=0) and these events were generally asymptomatic, transient, and resolved while on treatment or after treatment discontinuation.[1]
- The manuscript with results from SKYLIGHT 2 found fezolinetant was efficacious and well tolerated for treating moderate to severe VMS associated with menopause. Fezolinetant statistically significantly reduced VMS frequency/severity at W4 and W12 vs placebo. Improvement in VMS frequency and severity was observed by W1 and maintained through W52. Serious TEAEs were infrequent, reported by 2%, 1%, and 0% of those receiving fezolinetant 30 mg, fezolinetant 45 mg, and placebo, respectively.[2]
- The manuscript with results from SKYLIGHT 4 confirms the 52-week safety and tolerability of fezolinetant. TEAEs occurred in 64.1% of the placebo group, 67.9% and 63.9% of the fezolinetant 30 mg and 45 mg groups. TEAEs leading to discontinuation were similar across groups.[3]

Several pooled analyses were presented at 2023 scientific meetings:

- Safety data from SKYLIGHT 1, 2, and 4 affirm the safety and tolerability of fezolinetant over 52 weeks. The most frequent TEAEs (>5% in either group) were upper respiratory tract infections (8.2% placebo, 7.7% fezolinetant 45mg); headache (7.7% placebo, 8.2% fezolinetant 45mg); and COVID (4.1% placebo, 6.1% fezolinetant 45mg).[4]
- SKYLIGHT 1 / 2 demonstrated
    - the efficacy of fezolinetant in participants considered unsuitable for or unwilling to take HT, consistent with the overall participant population. The most frequent TEAE was headache (5.5% placebo; 4.2% fezolinetant 30 mg; 5.6% fezolinetant 45 mg).[5]

- fezolinetant reduced both the frequency and severity of moderate-to-severe daytime and night-time VMS compared with placebo.[6]
- fezolinetant was efficacious across intrinsic (age range, race, BMI) and extrinsic (smoking status, residency) factors, demonstrating its potential utility in a diverse patient population.[7]

A published network meta-analysis concluded that fezolinetant demonstrated comparable efficacy to 27 HT regimens (no statistically significant difference in frequency of VMS) and was statistically significantly more effective than other non-HTs in reducing the frequency of moderate to severe VMS.[8]

References

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