Abbreviated Drug Review

Trade name (generic)[1]

Vyleesi (bremelanotide) for subcutaneous (SC) use

Indications

- Treatment of premenopausal women with acquired, generalized hypoactive sexual desire disorder (HSDD). This is characterized by low sexual desire that causes marked distress or interpersonal difficulty and NOT due to: (1) a co-existing medical or psychiatric condition, (2) problems with the relationship, or (3) effects of a medication or drug substance.
- This indication is an excluded and unfunded condition based on Oregon Health Plan (OHP) prioritized list (line 521).

Dosage

- Inject 1.75 mg SC to the abdomen or thigh, as needed, at least 45 minutes before anticipated sexual activity. Optimal window for administration is not defined.
- Maximum of 1 dose/24 hours and 8 doses/month.
- Supplied as a single-dose, 1.75 mg/0.3 mL auto injector.

Background

- Mechanism of action for HSDD in women is unknown.
- Functions as a melanocortin receptor (MCR) agonist resulting in activation of multiple MCR subtypes.
- MC1R subtype is expressed on melanocytes (see warnings and precautions-focal hyperpigmentation).

Efficacy

FDA approval was obtained with two identical, phase 3, randomized, double-blind, placebo-controlled trials [Study 1 (NCT02333071) and Study 2 (NCT02338960)] of premenopausal women with at least 6 months of acquired, generalized HSDD. The studies were conducted over 24 weeks, followed by a 52-week uncontrolled, open-label extension. Study participants were primarily Caucasian (86%) or Black (12%) with a mean age of 39 years. Average duration in a monogamous relationship was 12 years with mean duration of HSDD of 4 years. The co-primary endpoints for these trials were (1) change from baseline to end of study (EOS) in the Desire domain from the Female Sexual Function Index (FSFI) (5 point scale for each of 2 questions with sum multiplied by 0.6) and (2) change from baseline to EOS in score for feeling bothered by low sexual desire in the Female Sexual Distress Scale (FSDS)(4 point scale). Both endpoints were evaluated using an unadjusted Wilcoxon rank-sum test in a modified intent-to-treat analysis.

	Endpoint (1): FSFI improvement in Desire domain				**Endpoint (2): FSDS improvement**			
	Study 1		Study 2		Study 1		Study 2	
	Bremelanotide (N=313)	Placebo (N=315)	Bremelanotide (N=282)	Placebo (N=288)	Bremelanotide (N=313)	Placebo (N=314)	Bremelanotide (N=282)	Placebo (N=285)
Mean Baseline (SD)	2.1 (0.9)	2.0 (0.8)	2.0 (0.8)	2.1 (0.8)	2.9 (1.0)	2.8 (0.9)	2.9 (0.9)	2.9 (0.9)
Mean change from baseline (SD)	0.5 (1.1)	0.2 (1.0)	0.6 (1.0)	0.2 (0.9)	-0.7 (1.2)	-0.4 (1.1)	-0.7 (1.1)	-0.4 (1.1)
P-value	0.0002		<0.0001		<0.0001		0.0053	

SD-standard deviation

Safety

Common adverse reactions: nausea (40%), flushing (20.3%), injection site reactions (13.2%), headache (11.3%), vomiting (4.8%), cough (3.3%), fatigue (3.2%), hot flush (2.7%), paresthesia (2.6%), dizziness (2.2%), nasal congestion (2.1%)

Contraindications: Uncontrolled hypertension or known cardiovascular disease

Warnings and Precautions: Transient increased blood pressure and reduced heart rate; focal hyperpigmentation, with or without resolution after discontinuation, which may involve face, gingiva, and breasts and is more common in dark skin; nausea sometimes requiring anti-emetic therapy

Special populations: Avoid use in postmenopausal women, men, pregnancy, pediatrics, and geriatrics. Use caution with severe renal (GFR < 30 ml/min/1.73m^2) and hepatic (Child-Pugh C; score 10-15) impairment as these patients have increased incidence and severity of adverse reactions, particularly nausea and vomiting.

Evidence Gaps/Limitations

- Initial publication on safety and efficacy was retracted after multiple journals retracted studies by the lead author due to questions about methods, results, and statistical interpretation.[2]
- No studies found to support evidence for use in the treatment OHP-covered conditions or co-morbidities.

Recommendation

Restrict use for OHP-covered conditions.

References

1. Vyleesi (bremelanotide) for subcutaneous injection [Prescribing Information]. Waltham, MA, USA. AMAG Pharmaceuticals, Inc. 2019.
2. Safarinejad MR. RETRACTED: Evaluation of the safety and efficacy of bremelanotide, a melanocortin receptor agonist, in female subjects with arousal disorder: a double-blind placebo-controlled, fixed dose, randomized study. *J Sex Med.* 2008;5(4):887-897.

Author: S. Fletcher, PharmD, MPH, BCPS

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