Lanadelumab

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Approved indication: hereditary angioedema

Takhzyro (Takeda)
pre-filled syringes containing 150 mg/mL solution for injection

Hereditary angioedema is a rare autosomal dominant disorder caused by the deficiency or dysfunction of C1 esterase inhibitor. This results in increased plasma kallikrein activity and excess production of the vasodilator bradykinin, which leads to unpredictable recurrences of severe swelling in subcutaneous or submucosal tissues that are potentially fatal. One approach to preventing angioedema is therefore to control the activity of kallikrein.[1] Lanadelumab is a fully human monoclonal antibody that inhibits active plasma kallikrein proteolytic activity and thereby reduces bradykinin production.

Lanadelumab is given by subcutaneous injection every two weeks. The half-life is 14–15 days, so it takes about 70 days to reach a steady state. No dose adjustment is recommended in mild-to-moderate renal impairment, but the effects of severe impairment and hepatic impairment are unknown.

The phase III, multicentre Hereditary Angioedema Long-term Prophylaxis (HELP) trial randomised 125 patients to receive lanadelumab 150 mg (n = 28) or 300 mg (n = 29) every four weeks, 300 mg every two weeks (n = 27), or a placebo (n = 41). During a four-week run-in period, these patients had a mean of 3.2–4 attacks of angioedema. After 26 weeks, lanadelumab reduced the attack rate to 0.26–0.53 attacks/month compared with 1.97 attacks/month in the placebo group. Among the patients receiving injections of lanadelumab every two weeks, 44.4% remained attack free.[2] The benefits were seen from the first dose and were sustained throughout the trial.[3] Improvements in health-related quality of life following lanadelumab treatment were also noted.[4]

The most common adverse events during the HELP trial were injection-site reactions, which affected 52.4% of the patients receiving lanadelumab compared with 34.1% of the placebo group. Headache and dizziness were also more frequent than in the placebo group. Antidrug antibodies, but few neutralising antibodies, were detected in some patients. No deaths or severe treatment-emergent adverse events were reported.[2]

Based on the trial results, the recommended starting dose of lanadelumab is 300 mg. This may be reduced to 300 mg every four weeks if the attacks are well controlled. As children were not included in the HELP trial, lanadelumab is indicated for the prevention of recurrent episodes of hereditary angioedema in patients 12 years of age and older.

The safety and efficacy of lanadelumab are unknown in pregnant or lactating women, and information is limited in patients older than 65 years of age.

Regarding longer term efficacy and safety, an open-label extension of the HELP trial found that 300 mg lanadelumab given every two weeks reduced the mean attack rate from 3.1 attacks/month in the four weeks leading up to the trial to 0.4 attacks/month in the first four weeks of the trial. After a mean of 29.6 months, 75.5% of 204 patients achieved a reduction in the attack rate of at least 90%, and 37.3% remained attack free. The injection-site reactions were similar to those in the initial HELP trial, with no deaths or severe treatment-emergent adverse events.[5]

Lanadelumab is well tolerated and prolongs the attack-free period in patients with hereditary angioedema. With a sustained decline in attacks, the frequency of doses may be reduced. Clinicians should, however, continue to monitor for breakthrough attacks.

T manufacturer provided the AusPAR and the product information

REFERENCES

1. Banerji A, Busse P, Shennak M, Lumry WR, Davis-Lorton M, Wedner HJ, et al. Inhibiting plasma kallikrein for hereditary angioedema prophylaxis. N Engl J Med 2017;376:717–28. https://doi.org/10.1056/NEJMoa1605767
2. Banerji A, Riedl MA, Bernstein JA, Cicardi M, Longhurst HJ, Zuraw BL, et al. Effect of lanadelumab compared with placebo on prevention of hereditary angioedema attacks: a randomized clinical trial. JAMA. 2018;320:2108-21. https://doi.org/10.1001/jama.2018.16773
3. Riedl MA, Maurer M, Bernstein JA, Banerji A, Longhurst HJ, Li HH, et al. Lanadelumab demonstrates rapid and sustained prevention of hereditary angioedema attacks. Allergy 2020;75:2879–87. https://doi.org/10.1111/all.14416
4. Lumry WR, Weller K, Magerl M, Banerji A, Longhurst HJ, Riedl MA, et al. Impact of lanadelumab on health-related quality of life in patients with hereditary angioedema in the HELP study. Allergy 2021;76:1188–98. https://doi.org/10.1111/all.14680
5. Banerji A, Bernstein JA, Johnston DT, Lumry WR, Magerl M, Maurer M, et al. Long-term prevention of hereditary angioedema attacks with lanadelumab: the HELP OLE study. Allergy 2021 [Epub 2021 Jul 21]. https://doi.org/10.1111/all.15011

The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the European Medicines Agency and the Therapeutic Goods Administration.