Eptinezumab

Approved indication: migraine

Vyepti (Lundbeck)
vials containing 100 mg/mL concentrated solution for dilution

Drugs aimed at the calcitonin gene-related peptide (CGRP) are recent additions to the options for the prevention of migraine attacks.[1] This peptide is involved in vasodilation and high concentrations are associated with migraine. Like the previously approved drugs, erenumab, fremanezumab and galcanezumab, eptinezumab is a monoclonal antibody. It binds to CGRP to stop the peptide binding to its receptors.

While the other drugs are given by subcutaneous injection, eptinezumab is given intravenously. The concentrate must be diluted then infused over 30 minutes and subsequent doses are only required 12 weeks apart. The half-life of eptinezumab is 27 days. It is metabolised like other antibodies, so no dose adjustments are recommended in renal or hepatic impairment and pharmacokinetic drug interactions are unlikely.

PROMISE–1 was a placebo-controlled trial of eptinezumab in episodic migraine. The 888 patients in the trial were having up to 14 days of headaches each month including at least four days of migraine. Infusions were given every 12 weeks with the patients randomised to eptinezumab receiving 30 mg, 100 mg or 300 mg doses. When efficacy was assessed after 12 weeks, treatment had reduced the mean number of migraine days per month by approximately four from a baseline of 8.6 days. The reduction in the placebo group was approximately three days (see Table).[2] After a year the reductions from baseline were 4.5 days with eptinezumab 100 mg and 5.3 days with 300 mg. The reduction in the placebo group was 4.1 days.[3]

The PROMISE–2 trial studied 1072 patients with chronic migraine. In a 28-day period, these patients had an average of 20.5 days of headache with 16.1 days of migraine. The patients were randomised to receive eptinezumab 100 mg, 300 mg or an infusion of placebo. After 12 weeks the mean number of migraine days each month reduced by 7.7 days with eptinezumab 100 mg, 8.2 days with 300 mg and 5.6 days with placebo.[4] After 24 weeks the respective reductions were 8.2, 8.8 and 6.2 days (see Table).[5]

Patients with chronic migraine were also studied in the open-label PREVAIL trial. They were given an infusion of eptinezumab 300 mg every 12 weeks for up to eight doses. There were 118 patients who were treated for 48 weeks and 101 who continued treatment to week 84 of the trial. The majority of the 100 patients who completed the study felt improved and found their migraine less disabling when they were reviewed at 104 weeks.[6]

During the PREVAIL trial 7.8% of the patients stopped eptinezumab because of an adverse reaction. The most common of these problems was extravasation at the infusion site.[6] Infusing an antibody can also cause allergic reactions including anaphylaxis. In the

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Table **Short-term efficacy of eptinezumab for migraine prophylaxis**

Trial regimen	Numbers of patients assessed for efficacy	Assessment	Mean days of migraine per month		Proportion of patients with 75% or greater response
			Baseline	Change with prophylaxis	
PROMISE-1[2] (episodic migraine)					
Eptinezumab					
30 mg	223	12 weeks	8.7	–4.0	24.7%
100 mg	221		8.7	–3.9	22.2%
300 mg	222		8.6	–4.3	29.7%
Placebo	222		8.4	–3.2	16.2%
PROMISE-2[4,5] (chronic migraine)					
Eptinezumab					
100 mg	356	12 weeks (24 weeks)	16.1	–7.7 (–8.2)	26.7% (39.3%)
300 mg	350		16.1	–8.2 (–8.8)	33.1% (43.1%)
Placebo	366		16.2	–5.6 (–6.2)	15% (23.8%)

NEW DRUGS

PREVAIL trial 7% of the patients developed potentially neutralising antibodies to eptinezumab, but their effect is unclear.[6] Symptoms related to the upper respiratory tract, such as nasopharyngitis, were the most frequent adverse events reported in PROMISE-1[2] and PROMISE-2.[4]

The main trials of eptinezumab excluded patients with cardiovascular disease, diabetes and obesity. Data about using the drug in children and pregnant or lactating women are also lacking.

The evidence shows that infusions of eptinezumab have greater efficacy than placebo at preventing migraine. While the main difference over placebo in episodic migraine may only be about one less day of migraine each month,[2] this may be of benefit to some patients. If a patient has migraine that is severe enough to warrant prophylaxis with a CGRP antagonist, it is unclear which of the class is most effective and whether someone who has not responded to one drug will respond to another drug in the class. Unlike the other formulations, eptinezumab cannot be self-administered. One factor that may influence the future use of eptinezumab is the finding that the infusion can bring rapid relief during an acute attack.[7] For now, its indication is limited to the prevention of migraine in adults.

T manufacturer provided information regarding availability

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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 Food and Drug Administration in the USA, the European Medicines Agency and the Therapeutic Goods Administration.