NEW DRUGS

New drugs

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Fremanezumab

Approved indication: migraine

Ajovy (Teva)
pre-filled syringe containing 225 mg/1.5 mL

Patients with frequent migraine attacks can benefit from prophylactic drugs. Some patients will still be troubled by migraine despite prophylaxis. As the mechanisms of action of prophylactic drugs are not specific for migraine, there has been research into targeted drugs for prophylaxis. One target is the calcitonin gene-related peptide (CGRP). This peptide is involved in nociception and inflammatory processes. Like the previously approved galcanezumab, fremanezumab is a monoclonal antibody against CGRP.

The antibody has to be given by subcutaneous injection. It can be injected as 225 mg monthly or 675 mg (as three injections) every three months. When multiple injections are required, they should be given at different sites. After injection it takes about a week for the concentration of fremanezumab to reach its maximum. A steady state is achieved after approximately six months. The half-life is estimated to be 31 days.

Fremanezumab has been compared to placebo in patients with episodic and chronic migraine. The phase III trials evaluated both dose regimens over 12 weeks (see Table).[1,2] Patients with cardiovascular diseases were excluded.

The trial for preventing episodic migraine randomised 875 patients who had approximately nine days of migraine in 28 days. Treatment with fremanezumab reduced the number of migraine days per month by 3.7 days with monthly injection and by 3.4 days with quarterly injection. The reduction in the placebo group was 2.2 days. The proportions of patients who had a 50% reduction in migraine days were 47.7% with monthly doses, 44.4% with a quarterly dose and 27.9% with placebo.[1]

The trial in chronic migraine enrolled 1130 patients who reported headaches on at least 15 days per month. On average, the participants had approximately 16 days of migraine every 28 days. At the end of the trial, monthly injections had reduced the number of headache days by 4.6 days and the number of migraine days by 5.0 days. With quarterly injection the reductions were 4.3 days for headache and 4.9 days for migraine. Both regimens were significantly better than the reductions of 2.5 days and 3.2 days seen in the placebo group. A reduction of at least 50% in the number of headache days was seen in 41% of the monthly group, 38% of the quarterly group and 18% of the placebo group.[2]

During the trials, adverse reactions to fremanezumab were more frequent than with placebo. In the patients with chronic migraine 47% developed injection-site reactions compared with 40% of the placebo group. These reactions consisted of pain, induration and erythema.[2] Some patients will develop antibodies to fremanezumab, but so far there have been few cases of neutralising antibodies or hypersensitivity reactions. Fremanezumab will cross the placenta, but caused no toxicity in animal studies.

Table **Efficacy of fremanezumab for migraine prophylaxis**

Trial regimen (number of patients)	Number of days of migraine per month		Proportion of patients with at least a 50% reduction in days of migraine[1] or headache[2] per month
	Baseline	Change at 12 weeks	
Episodic migraine[1]			
Fremanezumab monthly (290)	8.9	–3.7	47.7%
Fremanezumab quarterly (291)	9.3	–3.4	44.4%
Placebo (294)	9.1	–2.2	27.9%
Chronic migraine[2]			
Fremanezumab monthly (379)	16.0	–5.0	41%
Fremanezumab quarterly (376)	16.2	–4.9	38%
Placebo (375)	16.4	–3.2	18%

Some of the views expressed in the following notes on newly approved products should be regarded as preliminary, as there may be limited published data at the time of publication, and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. Before new drugs are prescribed, the Committee believes it is important that more detailed information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

The short-term trials show that fremanezumab is better than placebo, but the difference is small. A review of CGRP monoclonal antibodies by the US Institute for Clinical and Economic Review considered that the benefit was similar to other options for preventing migraine. It suggested that drugs such as fremanezumab may have a role if there has been an inadequate response to these other options.[3] A subsequent phase III trial has studied fremanezumab in 838 patients with migraine that had failed to respond to at least two, and up to four, prophylactic drugs. They were having an average of about 14 days of migraine a month. After 12 weeks, this had reduced by 4.1 days with monthly injections and 3.7 days with quarterly injection. Placebo resulted in a reduction of only 0.6 days. There was a reduction of at least half in the mean number of migraine days per month in 34% of the patients injecting fremanezumab compared with 9% of the placebo group.[4]

Despite the targeted approach, fremanezumab will benefit only a minority of patients with migraine. In the trial of patients who had not responded to other drugs, only 1% were free from migraine during treatment with monthly fremanezumab.[4] In patients with migraine who do respond, there is a need to see if this response is maintained in the longer term. Patients who used the quarterly regimen only received a single dose of fremanezumab in the 12–week trials.[1,2] The effectiveness of fremanezumab should be evaluated after 8–12 weeks to assess whether or not it should be continued.

T manufacturer provided the AusPAR and the product information

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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.