Northern (NHS) Treatment Advisory Group

Treatment Appraisal: Decision Summary

Date	20th November 2018
Appraisal & Details	The Northern (NHS) Treatment Advisory Group considered an appraisal of **Erenumab and galcanezumab for prophylaxis of migraine.** A new class of monoclonal antibodies specific for CGRP (a neuropeptide involved in pain signalling) has been developed for the prophylaxis of migraine. One of these (erenumab) has been launched while a second (galcanezumab) has been given a positive opinion by the CHMP of the EMA. Two more (fremanezumab and eptinezumab) are expected to launch in the next 1-3 years.
Recommendation	**The Northern (NHS) Treatment Advisory Group <u>does not</u> recommend the use of Erenumab and galcanezumab for prophylaxis of migraine.** The group was concerned about the cost-effectiveness, clinical trials to date included a low proportion of patients with previous use of preventive medicines, lack of clinical trial evidence comparing with other treatment options for migraine, and the current lack of long term safety data. Patients with recent use of botulinum toxin were also excluded entirely from published trials to date. The group noted that NICE is due to issue a technology appraisal for eremumab expected in the 3rd quarter of 2018.
Clinical evidence summary	Erenumab is licensed for prophylaxis in people with ≥4 migraine days per month. The bulk of the clinical data are from phase III trials in patients with episodic migraine treated for 12-24 weeks. Pooled data from these trials found that erenumab was associated with a larger reduction in mean migraine days than placebo (2 vs. 3 days per month, treatment difference -1.2 days, 95% CI -1.5 to 0.8, p<0.001). These trials had extensive limitations, e.g. more than half of participants had never tried any other prophylactic medicines, so the efficacy of erenumab in patients with previous treatment failure is unclear. This gap in the evidence has been partially addressed by the LIBERTY trial, which found a benefit of erenumab 140 mg over placebo in patients with episodic migraine and prior failure of 2-4 preventive drugs (treatment response in 30% vs. 14%, odds ratio 2.7,p=0.002). The trial was limited to 12 weeks duration, and does not provide any information on patients with previous failure of Botox therapy. In patients with chronic migraine, a phase II RCT found that erenumab 70 mg & 140 mg was associated with a reduction in monthly migraine days versus placebo (-6.6 vs. -4.2 days, treatment difference -2.5 days, 95% CI -3.5 to -1.4). The reduction in monthly migraine days was identical for both doses. Galcanezumab is also licensed for prophylaxis of migraine in people with ≥4 migraine days per month, but there are no published data for people with chronic migraine (≥15 headache days per month). Two 6 month trials in people with episodic migraine found that galcanezumab reduced the mean number of migraine days by roughly 5 days, compared to roughly 3 days for placebo. The treatment effect was similar irrespective of galcanezumab dose. Limitations were similar to those highlighted for erenumab.

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Safety	Most adverse events with erenumab were of mild-moderate severity, and there were few differences between placebo and active treatment groups. Some evidence suggests that erenumab may lead to increases in systolic and diastolic blood pressure, but the overall cardiovascular safety profile is not clear. The EMA has requested additional studies. Adverse event rates were similar between galcanezumab and placebo, with the main difference being injection site reactions. There was no difference in serious adverse events.
Patient Perspective	The likely target population for CGRP-specific antibodies is patients with significant disease burden despite standard care with the currently-available options. Current management of these patients will vary depending on their migraine subtype: • Episodic migraine: oral preventive medicines, with or without acute treatments • Chronic migraine: Botox every 12 weeks, with or without oral preventives and acute treatments. Due to the design of the clinical trials it is not clear to what degree these existing treatments would be displaced if anti-CGRP antibodies were to be introduced. Erenumab may be more acceptable to patients than Botox, since it can be self-administered as a single injection each 4 weeks. By contrast Botox requires attendance at clinic every 3 months, and each treatment consists of multiple injections.
Cost analysis summary	Erenumab costs £386.50 per 70 mg dose (NHS List Price), equating to £5,025-£10,049 per patient per year depending on dose and exclusive of VAT. Results from one economic study suggest that this could result in an ICER of £54,000-£109,000 per QALY in the UK. It is not yet known whether any commercial arrangements will be offered. The price for galcanezumab is not yet available.
Financial impact **PbR: CCG Commisioned Excluded Drug**	The financial impact of this recommendation is expected to be nil.