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Anti-CGRP monoclonal antibodies for the prevention of chronic or refractory migraine in adults: efficacy and safety

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Introduction
Chronic and refractory migraine is a major cause of disability, significantly impairing quality of life and imposing a substantial socioeconomic burden. Given the limitations of conventional preventive therapies, anti-calcitonin gene-related peptide (CGRP) monoclonal antibodies have emerged as a promising therapeutic alternative.

Objective
This study aimed to evaluate the efficacy and safety of these agents in adults with chronic or refractory migraine.

Methods
This systematic review followed PRISMA guidelines and was registered in PROSPERO (CRD420261406575). PubMed and Cochrane were searched for studies published between 2017 and 2026. Inclusion criteria comprised English-language randomized controlled trials enrolling adults (≥18 years) with chronic or refractory migraine and evaluating anti-calcitonin gene-related peptide (anti-CGRP) monoclonal antibodies. Eligible studies were required to report at least one efficacy or safety outcome, including monthly migraine days, responder rates, functional outcomes, acute medication use, or treatment-related adverse events. Two reviewers independently screened titles, abstracts, and full texts, with disagreements resolved by a third reviewer. Data on population characteristics, efficacy outcomes, and adverse events were extracted and analyzed. Risk of bias was assessed using the Cochrane RoB 2 tool, and all included studies were judged to have a low overall risk of bias.

Results
The search identified 367 records, of which 20 duplicates were removed. After screening, 11 randomized controlled trials involving more than 8,000 participants were included. The studies evaluated eptinezumab, fremanezumab, galcanezumab, and erenumab in episodic and chronic migraine. Compared with placebo, anti-CGRP therapies reduced monthly migraine days by 1.6–3.7 additional days and increased ≥50% responder rates from 9–44% to 27–64% and ≥75% responder rates from 2–24% to 7–43%. In patients with 2–4 prior preventive treatment failures, reductions in monthly migraine days ranged from 1.6–3.7 days, with ≥50% responder rates of 30–49% versus 9–14% with placebo. Acute medication use decreased by up to 3.4 days/month, HIT-6 scores improved by up to 8.5 points, and MIDAS scores by up to 17.8 points. Sustained efficacy was demonstrated for up to 24 weeks, with monthly migraine day reductions of 8.2–8.8 days versus 6.2 days with placebo during weeks 13–24. Adverse events were mostly mild to moderate, occurring in 41–61% of treated patients, while serious adverse events were uncommon (≤2%) and showed no consistent cardiovascular, hepatic, or treatment-related safety signals.

Conclusion
Anti-CGRP monoclonal antibodies demonstrated consistent efficacy and favorable tolerability in chronic or refractory migraine. They reduced monthly migraine days, increased responder rates, and improved disability outcomes, including in patients with prior treatment failures, supporting their use as an effective preventive therapy.

Keywords:
Migraine
Anti-CGRP monoclonal antibodies
Chronic migraine
Refractory migraine
Efficacy

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