



---

## Frequent migraines are a headache: Can biologics help?

### CLINICAL QUESTION

**What is the efficacy of Calcitonin Gene Related Peptide (CGRP) inhibitors in migraine prophylaxis?**

---

### BOTTOM LINE

**For patients with episodic and chronic migraines, treating 5-8 patients with a CGRP-inhibitor will lead to one patient experiencing at least a 50% reduction in monthly migraine days compared to placebo. From baseline, a decrease of 1-2 monthly migraine days may be seen. Cost may limit use.**

### EVIDENCE

- Results statistically significant unless otherwise stated. Studies in episodic and chronic migraines.
  - Erenumab (Aimovig®) 70-140mg subcutaneously monthly versus placebo:
    - 1 systematic review [5 randomized controlled trials (RCTs), 2928 patients, 9-18 monthly migraine days, 84% female, mean 41 years old, duration 12 weeks].<sup>1</sup>
      - Achieving at least 50% reduction in monthly migraine days:
        - 70mg dose: 42% versus 27% (placebo) [number needed to treat (NNT)=7].
        - 140mg dose: 40% versus 21% (placebo) (NNT=5).

- Reduction of monthly migraines: 1.5-2.0 days.
- Galcanezumab (Emgality®) 120-240mg subcutaneously monthly versus placebo:
  - 1 systematic review (3 RCTs, 2886 patients, 9-19 monthly migraine days, 85% female, mean ~41 years old, duration 12-24 weeks).<sup>2</sup>
    - Achieving at least a 50% reduction in monthly migraine days:
      - 41% versus 26% (placebo) (NNT=7).
    - Reduction of monthly migraines: 1.9 days.
- Fremanezumab (Ajovy®) 675mg subcutaneously every 3 months versus placebo:
  - 5 RCT (3379 patients, ~16 monthly migraine days, mean 41 years old).<sup>3</sup>
    - Achieving at least 50% reduction in monthly migraine days:
      - 41% versus 19% (placebo) (NNT=5).
    - Reduction of monthly migraines: 2.2 days.
- Other systematic reviews found similar.<sup>4-6</sup>
- Adverse events: No difference except for injection site pain (11% versus 8.1% placebo).<sup>1,2,4,7</sup>
- Limitations: Short duration studies (12-24 weeks) for a chronic condition. Sustained efficacy and long-term safety unknown. Trials often excluded patients who failed more than 2-3 medication groups. Majority RCTs industry sponsored.

## CONTEXT

- Other medications with evidence of benefit:
  - Achieving >50% reduction in monthly migraine days: Propranolol (NNT=4)<sup>8</sup>, tricyclic antidepressants (NNT=5).<sup>9</sup>
  - Headache frequency reduction over placebo: Candesartan (~1.5 days), topiramate (~1 day).<sup>8,10</sup>
- Cost for CGRP-inhibitors in Canada is ~\$7000/year.<sup>11</sup>
- Guidelines<sup>12,13</sup> recommend a trial of at least 2 oral agents prior to CGRP-inhibitors.

## REFERENCES

1. Zhu C, Guan J, Xiao H, *et al.* *Medicine (Baltimore)*. 2019 Dec; 98(52):e18483.
2. Förderreuther S, Zhang Q, Stauffer VL, *et al.* *J Headache Pain*. 2018 Dec 29; 19(1):121.
3. Gao B, Sun N, Yang Y, *et al.* *Front Neurol* . 2020 May 19; 11:435.
4. Deng H, Li G, Nie H, *et al.* *BMC Neurol*. 2020 Feb 15; 20(1):57.
5. Wang X, Chen Y, Song J, *et al.* *Front Pharmacol*. 2021 Mar 25; 12:649143.
6. Lattanzi S, Brigo F, Trinko E, *et al.* *Drugs*. 2019 Mar 1; 79, 417–431.
7. Reuter U, Goadsby PJ, Lanteri-Minet M, *et al.* *Lancet*. 2018 Nov 24; 392(10161):2280-2287.
8. Kapusta M, Allan GM. Tools for Practice #52. Available at: [https://gomainpro.ca/wp-content/uploads/tools-for-practice/1433184708\\_updatedtftp52antihypertensivesmigraineprophylaxis.pdf](https://gomainpro.ca/wp-content/uploads/tools-for-practice/1433184708_updatedtftp52antihypertensivesmigraineprophylaxis.pdf). Last accessed: July 21, 2021.
9. Allan GM, Levy M. Tools for Practice #51. Available at: <https://gomainpro.ca/wp-content/uploads/tools-for->

## AUTHORS

**Sandra Trkulja**,  
BScPharm, PharmD,  
**Trudy Huyghebaert**,  
PharmD, **Joey Ton**,  
PharmD, **Clark Svrcek**, MD CCFP

*Authors do not have any conflicts of interest to declare.*

- [practice/1433184684\\_updatedtftp51antidepressantsheadaches.pdf](#). Last accessed: July 21, 2021.
10. Linde M, Mulleners WM, Chronicle EP, *et al.* Cochrane Database Syst Rev . 2013 Jun 24; 2013(6):CD010610.
  11. Rxfiles. Migraine: Agents for Prophylaxis. Available at: <https://www.rxfiles.ca/RxFiles/uploads/documents/members/CHT-MIGRAINE.pdf>. Last accessed: June 4, 2021
  12. Sacco S, Bendtsen L, Ashina M, *et al.* J Headache Pain. 2019 Jan 16;20(1):6.
  13. American Headache Society. Headache. 2019 Jan; 59(1):1-18.