Calcitonin Gene-Related Peptide Inhibitors for Migraine and Cluster Headache Prevention and Treatment

Topic Brief

Washington P&T Committee/DUR Board

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Background

- Migraine is a common condition characterized by recurrent severe headaches
  - Other symptoms include nausea, vomiting, and sensory sensitivity
- Cluster headaches are characterized by severe, unilateral pain, often around the eye
  - Other symptoms include eye discomfort, eyelid drooping, pupil constriction, runny nose, and sweating
- Both can impair an individual's ability to function
- Calcitonin gene-related peptide (CGRP) inhibitors block the action of a neuropeptide involved in migraine pathophysiology, resulting in vasodilation of brain blood vessels

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PICOS *(1 of 3)*

- Populations:
  - Adults with episodic or chronic migraines with no previous treatment history, or adults whose migraines have not responded to other therapies
  - Adults with episodic or chronic cluster headaches with no previous treatment history, or adults whose cluster headaches have not responded to other therapies
  - Adults with acute migraine headaches

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PICOS *(2 of 3)*

Interventions:

Generic Name	Brand Name	Route of Administration	FDA Approval Date	Approved Indication(s)
FDA-Approved Therapies				
Atogepant	Qulipta	Oral	September 2021	. Migraine prevention
Eptinezumab	Vyepti	IV	February 2020	. Migraine prevention
Erenumab	Aimovig	SC	May 2018	. Migraine prevention
Fremanezumab	Ajovy	SC	September 2018	. Migraine prevention
Galcanezumab	Emgality	SC	September 2018	. Migraine prevention . Cluster headache prevention
Rimegepant	Nurtec	Oral	February 2020	. Acute migraine treatment . Migraine prevention
Ubrogepant	Ubrelvy	Oral	December 2019	. Acute migraine treatment
Zavegepant	Zavzpret	Intranasal	March 2023	. Acute migraine treatment
Key Pipeline Therapies				
None currently identified				

Abbreviations. FDA: US Food and Drug Administration; IV: intravenous; SC: subcutaneous.

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PICOS *(3 of 3)*

- Comparators:
  - Another listed intervention
  - Pharmacological agents aimed at treating or preventing migraines or cluster headaches (e.g., amitriptyline, ergotamine, onabotulinumtoxinA)
  - Placebo (for newly approved and pipeline therapies only)
- Outcomes:
  - Migraine events (e.g., frequency, intensity, duration)
  - Pain (e.g., intensity, duration, pain scale range)
  - Function (e.g., cognition, work or school days missed)
  - Disability level
  - Quality of life
  - Use of rescue therapies
  - Adverse events
  - Serious adverse events
  - Discontinuations due to adverse events
- Study Designs:
  - Randomized controlled trials (RCTs) (in countries “very high” on the United Nations Human Development Index)

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Key Questions

1. Effectiveness and harms for preventing migraines or cluster headaches
2. Effectiveness and harms for acute treatment of migraines or cluster headaches
3. Differences in effectiveness or harms by patient or disease characteristic
4. Pipeline therapies for migraines or cluster headaches

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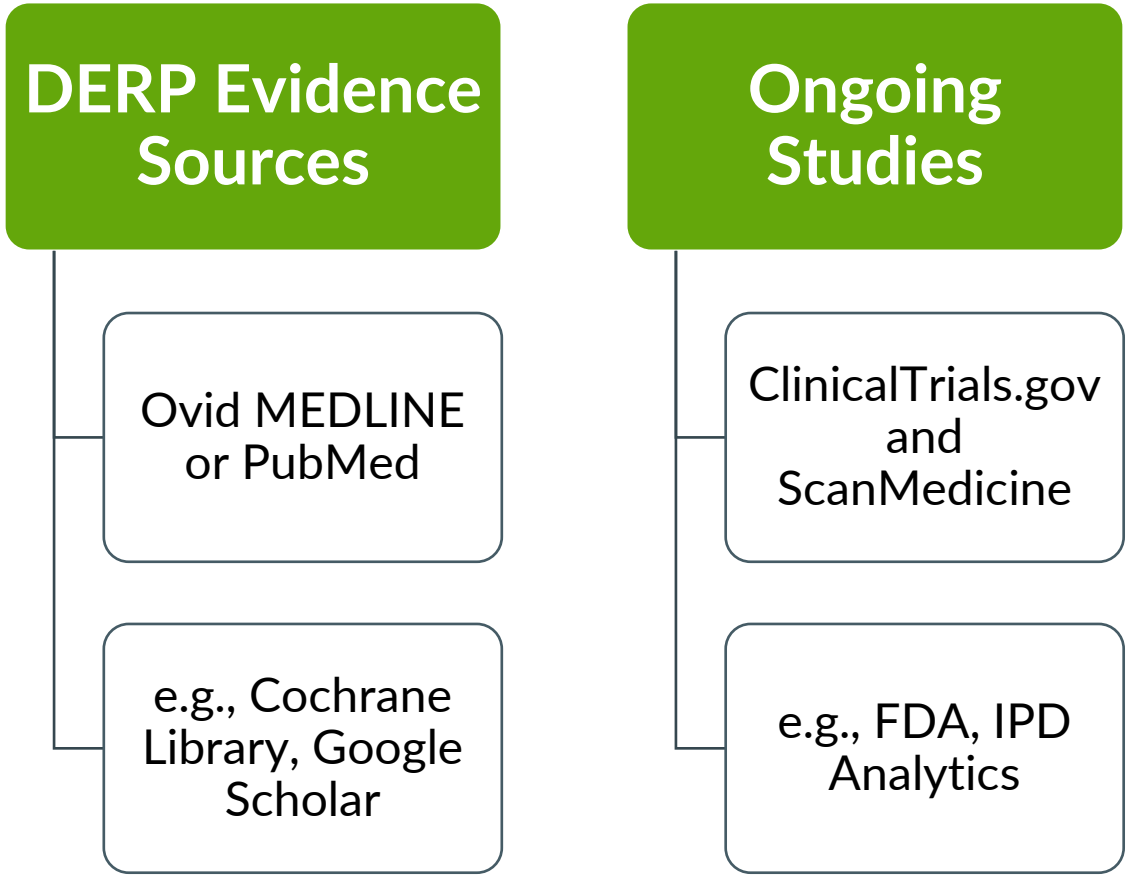
Methods



We included only studies conducted in countries categorized as *very high* on the United Nations Human Development Index

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Findings

Published RCTs

Findings: Published RCTs

18 ELIGIBLE RCTS

- 16 new since 2023 report
- 2 older studies

HEAD-TO-HEAD STUDIES

- Galcanezumab vs. rimegepant
- Ubrogepant, alone or with erenumab or galcanezumab

PLACEBO- OR SOC[a]-CONTROLLED STUDIES

18 studies on 7 drugs

(0 studies for fremanezumab)

CONDITIONS

- Migraine prevention
- Acute migraine
- Medication overuse headache
- Vestibular migraine

LOCATIONS

- US: 8
- International + US: 4
- Japan: 1
- Europe: 2
- Pan-Asian 1

COMMON OUTCOMES

- Prevention: change from baseline in mean monthly migraine days
- Acute: effect within 2 hours postdose

Note. [a] *SOC: standard of care.*

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Characteristics of Head-to-Head Published RCTs

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Author (year)	Setting	Interventions and Sample Sizes	Demographics	Study Duration
Schwedt (2024)	US	• Galcanezumab 120 mg (initial loading dose of 240 mg) and placebo for rimegepant • Rimegepant 75 mg ODT and placebo for galcanezumab N = 580	Adults (18 to 75 yrs) with migraines (4 to 14 migraine days per month)	3 months
Jakete (2021)	US	• Ubrogepant 100 mg alone • Ubrogepant 100 mg + erenumab 140 mg • Ubrogepant 100 mg + galcanezumab 240 mg N = 518	Adults (18 to 50 yrs) with ≥ 1-year history of migraines	45 days

Abbreviations. RCT: randomized controlled trial; mg: milligram; ODT: orally disintegrating tablet; N: number; yrs: years.

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Findings: Placebo- or SOC-Controlled Published RCTs by Drug

Drug	Number of RCTs	Study Size Range	Total N	Study Duration (weeks)
Atogepant	3	315 to 778	1,867	12 to 52
Eptinezumab	1	193	193	12
Erenumab	6	40 to 621	2,338	8 to 52
Galcanezumab	2	40 to 520	560	12
Rimegepant	2	1,162 to 1,431	2,593	6
Ubrogepant	1	518	518	8
Zavegepant	1	1,405	1,405	6
Total	16	**40 to 1,431**	**193 to 2,593**	1.5 to 52

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Abbreviations. SOC: standard of care; RCT: randomized controlled trial; N: number.

Findings

Ongoing Studies

Findings: Ongoing RCTs

ELIGIBLE RCTS

24 ongoing RCTs

HEAD-TO-HEAD STUDY

1 RCT: Erenumab, fremanezumab, and galcanezumab

PLACEBO- OR SOC[a]-CONTROLLED STUDIES

23 RCTs for 7 drugs

(0 RCTs for galcanezumab)

CONDITIONS

- Migraine prevention
- Acute migraine
- Medication overuse headache
- Menstrual migraine
- Cluster headache prevention

COMPLETION DATES

August 2022 to September 2027

COMMON OUTCOMES

- Prevention: change from baseline in mean monthly migraine days
- Acute: effect within 2 hours postdose

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Note. [a] *SOC: standard of care.*

Characteristics of Head-to-Head Ongoing RCTs

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Study ID	Completion Date	Interventions	Demographics Sample Size	Study Duration
jRCT1041230151	NR	• Erenumab • Fremanezumab • Galcanezumab (doses not specified)	Adults with high-frequency episodic migraine or chronic migraine, including MOH N = 60 (estimated)	"immediate effects" at 1 week

Abbreviations. RCT: randomized controlled trial; ID: identification; MOH: medication overuse headache; NR: not reported: N: number.

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Findings: Placebo- or SOC-Controlled Ongoing RCTs by Drug

Drug	Number of RCTs	Study Size Range	Total N	Completion Date(s)
Atogepant	4	430 to 1,300	2,798	2025 to 2027
Eptinezumab	4	102 to 981	1,923	2023 to 2025
Erenumab	1	512	512	2023
Fremanezumab	2	72 to 353	425	2022 to 2026
Rimegepant	8	80 to 897	4,806	2024 to 2026
Ubrogepant	2	450 to 645	1,095	2026 to 2027
Zavegepant	2	1,280 to 1,400	2,680	2025 to 2027
Total	23	**80 to 1,400**	**425 to 4,806**	2022 to 2027

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Abbreviations. SOC: standard of care; RCT: randomized controlled trial; N: number.

Questions?


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