Modern Migraine Care in 2026:

Guidance and Gaps for Pediatric Patients

May 2026

Richelle deMayo, MD, CM, MS

Connecticut Children's

Disclosures

- PI for Pfizer/American Headache Society funded research
- Published research with Theranica (maker of Nerivio)
- Previous site investigator for Biohaven funded clinical trial

- In this presentation, I will be discussing off label use of medications that are not FDA approved for patients younger than 18

Today's Learning Objectives

1. Become familiar with the **International Classification of Headache Disorders** (ICHD-3) and use the criteria to distinguish migraine from other primary and secondary headache disorders.

2. Review relevant therapeutic options and analyze clinical scenarios to select appropriate migraine **rescue** strategies.

3. Evaluate current guideline recommendations and recent scientific literature evidence to develop a mechanism-driven **prevention** strategy for a pediatric patient with high frequency migraine.

Why we care about Headache Disorders?

1
COMMON

2
CHRONIC

3
COSTLY

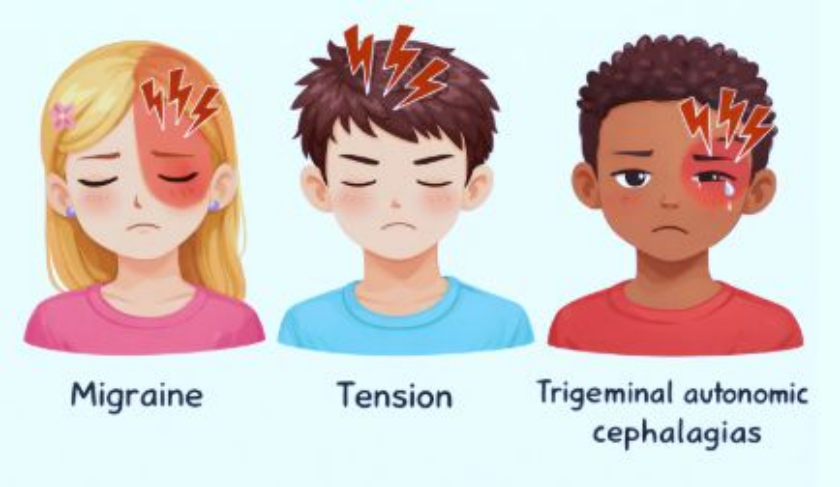
4
CARE SENSITIVE

- Headache is ubiquitous – normal/**physiologic**
- Headache disorders are common – but **pathologic** -- and underdiagnosed
- Most headache is managed by primary care providers

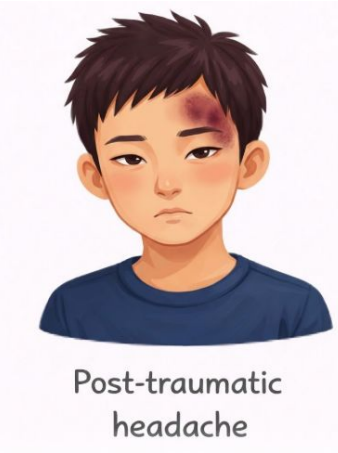
Common Types of Headache

1. Distinguish between 1° and 2° HA
2. Make as precise a diagnosis as you can
3. Evaluate for red flags

PRIMARY



SECONDARY



2SNOOP4

Systemic **Neurologic finding (focal)** **Occurs suddenly** **Progressive**
Secondary risks **Onset <5** **Positional**
Pulsatile tinnitus/papilledema

Precipitated by Valsalva

2S **N** **OO** **P4**

Diagnostic criteria for headache

Migraine without Aura

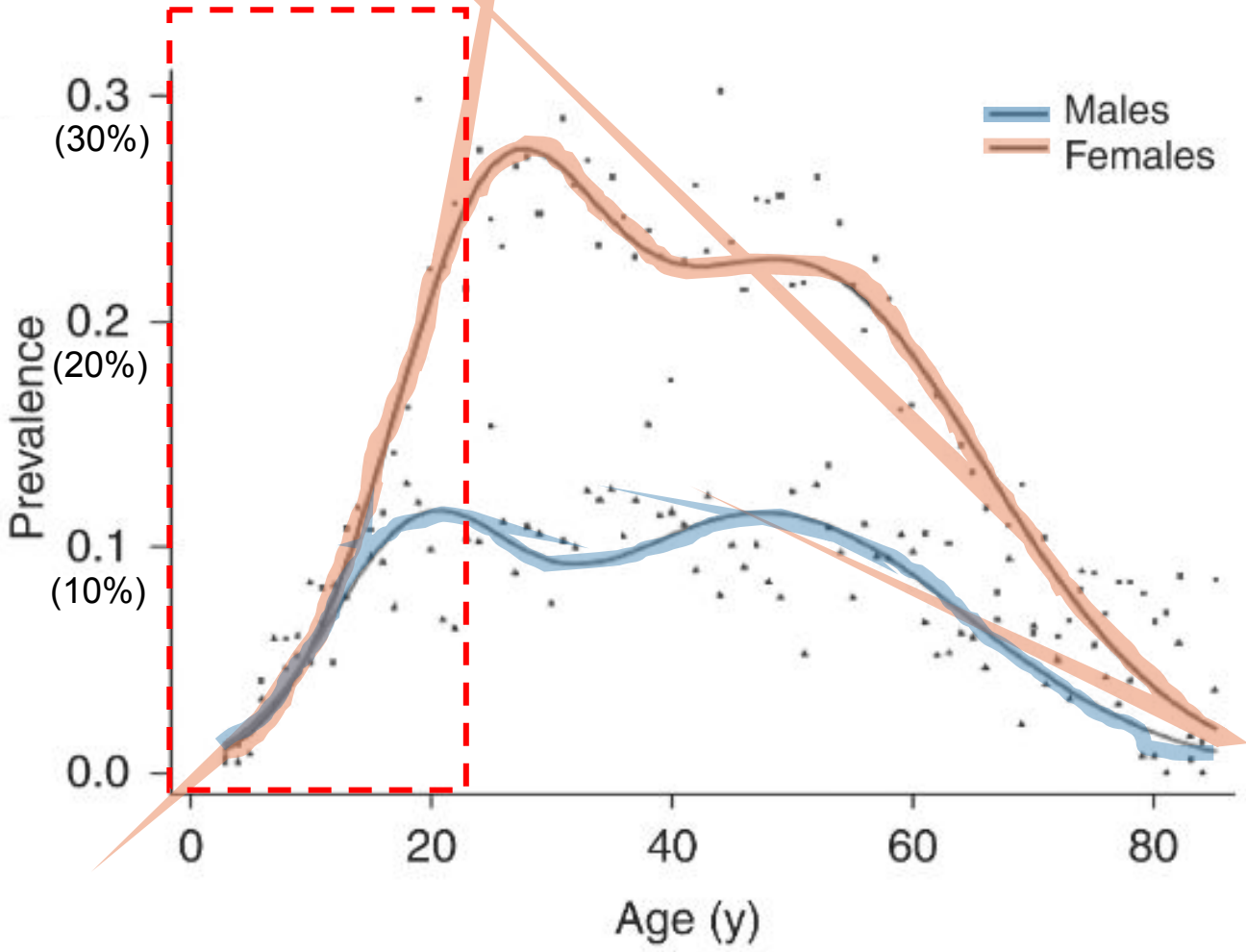
- **5** attacks
- Last **4** hours to **3** days
- **2** of
  - unilateral
  - pulsating
  - moderate – severe
  - activity-avoidant
- **1** of
  - N+/-V
  - Photophobia and Phonophobia

Acknowledging pediatric phenotypes:

- Duration – can be 2 hours or longer
- Bilaterality - common

Migraine Epidemiology

- The average U.S. public school classroom is 25 students
- That means 2 or more kids in the class likely have migraine
- Risk factors: family history, SES disadvantage, co-occurring chronic conditions (epilepsy, celiac, obesity, hypermobility)
- Migraine is a clinical diagnosis. There is no imaging or laboratory test used in practice to diagnose migraine.
- At puberty, we begin see sex prevalence separation

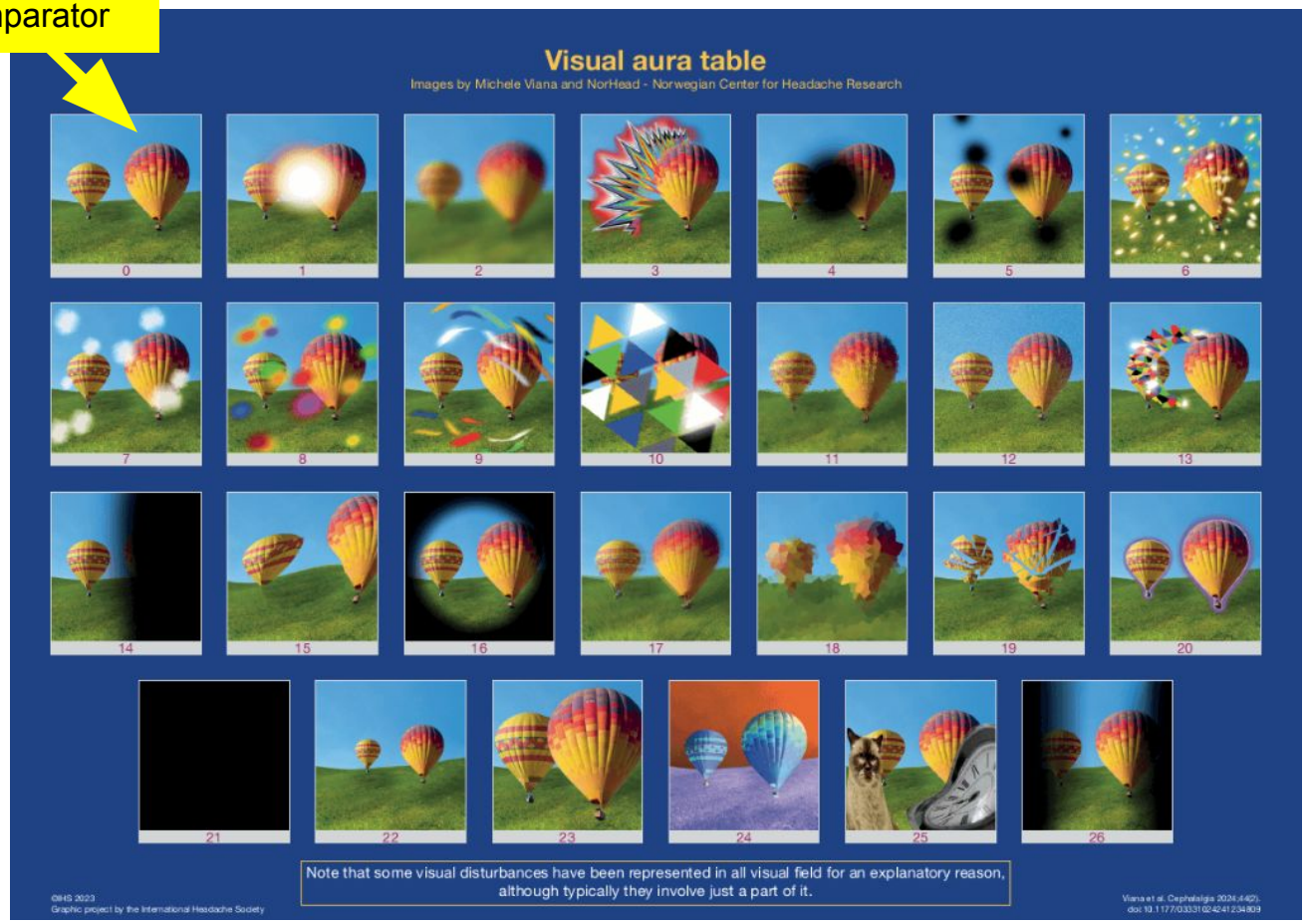


Victor TW, Hu X, Campbell JC, Buse DC, Lipton RB. Migraine prevalence by age and sex in the United States: a life-span study. *Cephalalgia*. 2010;30(9):1065-1072. doi:10.1177/0333102409355601

Asking About Aura

- Aura = *a complex of neurological symptoms that **usually** occurs before the head pain*
- Affects 1/3rd of patients with migraine
- Patients with MWA usually also have MWoA
- The most common form of aura is visual (>90% is visual) > sensory
- It's hard to describe aura in words. Use pictures or videos.
- Mayo Clinic Visual Aura Youtube video https://www.youtube.com/watch?v=qVFIcF9lyk8
- Why aura matters:
  - Diagnostic specificity
  - Reflects "cortical spreading depression" physiology
  - Impacts counseling (vascular risk, estrogen, smoking)
  - Does not change acute rescue efficacy

Image "0" is the normal comparator



https://ihs-headache.org/wp-content/uploads/2024/09/Visual-aura-table-A3-Landscape-rv.pdf

Migraine Pathophysiology Refresher

We no longer regard migraine as a “vascular” disease.
Migraine is a sensory network disorder.

1. Migraine attacks seem to be initiated by abnormal activation of the **trigeminovascular** system via peripheral meningeal nociceptors.
2. Synapses in the **trigeminal nucleus caudalis** (spinal trigeminal nucleus)
3. Ascending nociception to **thalamus**
4. Thalamus relays and amplifies signals to **cortex sensory network** (conscious pain, photophobia, phonophobia, cognitive fog etc.)

   Functional imaging shows **hypothalamic** activation hours or days before headache (premonitory phase)

   Failure of descending pain modulation (LC, PAG).
5. **CGRP** (a key neuropeptide) acts in both periphery and CNS to sustain neurogenic inflammation and central sensitization

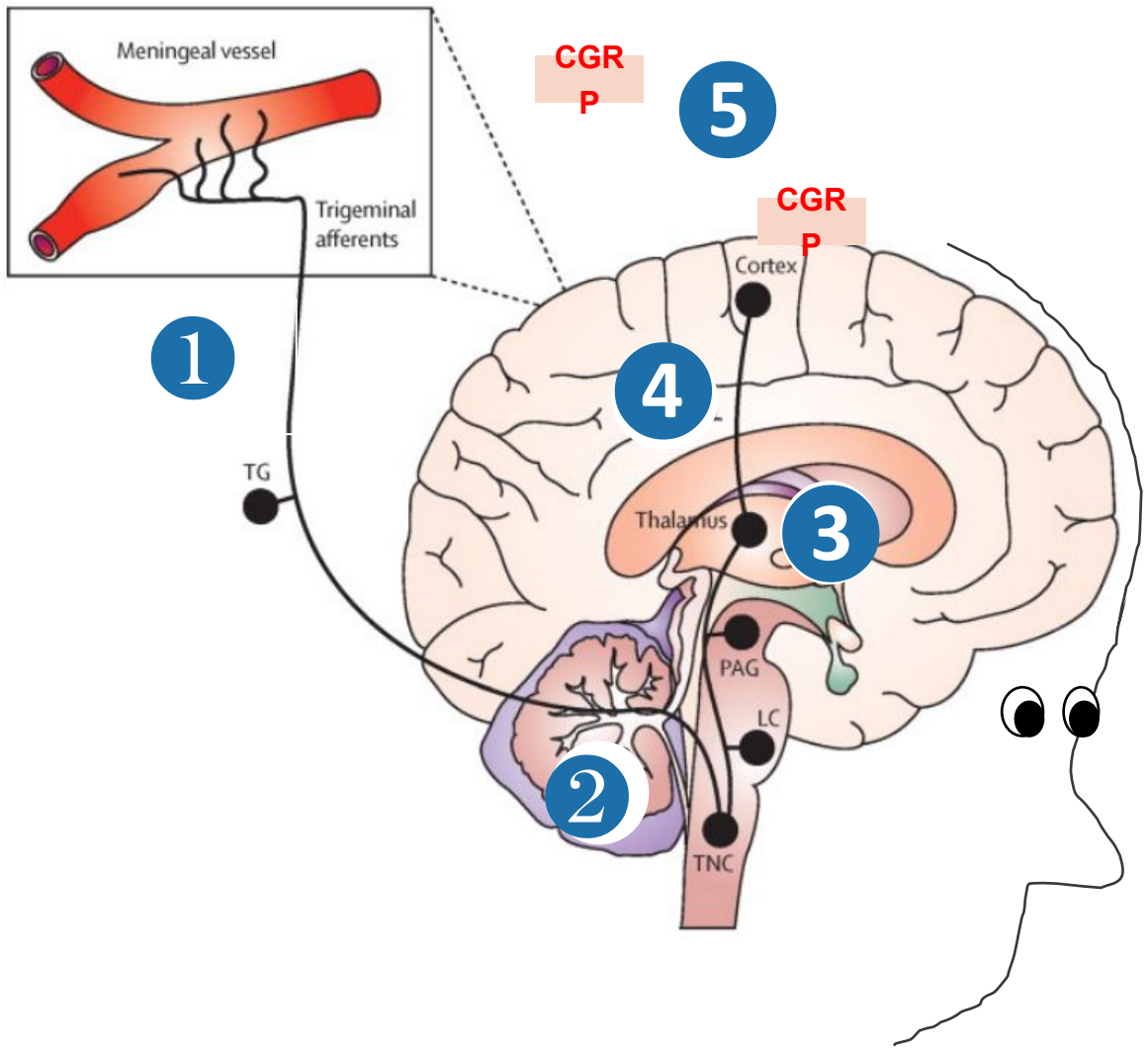


Figure adapted from Ferrari MD, Klever RR, Terwindt GM, Ayata C, van den Maagdenberg AM. Migraine pathophysiology: lessons from mouse models and human genetics. *Lancet Neurol*. 2015;14(1):65-80. doi:10.1016/S1474-4422(14)70220-0

Case #1 Example

- 9 y/o  with ADHD, anxiety
- Severe HA for past year ~1d/weekly;
- Often misses school on those days despite ibuprofen
- Taking Sertraline 75mg daily for anxiety
- HA phenotype:
  - Pulsing
  - Bifrontal and bitemporal
  - Rated 7 out of 10
  - Lasts “the whole day”
  - Sensitivity to light/sound
  - Denies aura

- Well appearing
- Normal PE
- No papilledema
- No TMD
- Normal tonsils

✔ **5 attacks**
✔ **4 h – 3 d**
2 of:
unilateral
✔ **moderate to severe**
✔ **pulsating**
avoidance of routine physical activity
1 of:
✔ **photo and phono phobia**
nausea and/or vomiting
✔ **Not better accounted for**

Diagnosis: This is migraine (episodic, without aura)

Migraine Rescue Treatment - Guidance in 2026

Endorsed by AAN, AHS, AAP: Oskoui M, Pringsheim T, Holler-Managan Y, et al. Practice guideline update summary: Acute treatment of migraine in children and adolescents: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Headache Society. *Headache*. 2019;59(8):1158-1173. doi:10.1111/head.13628

OTC Options
Acetaminophen
Ibuprofen
Naproxen

"Clinicians should prescribe ibuprofen (10mg/kg) as an initial option to reduce pain in children and adolescents with migraine"

- *Don't forget the basics, but patients often have tried these by the time they reach you*
- *Limit to 15 days per month*

Rx Options
Triptan
7 licensed in US
4 for pedi

"For adolescents with migraine, clinicians should prescribe…"
Rizatriptan ODT (5 or 10 mg) – 6y+
Almotriptan (6.25 or 12.5 mg) – 12y+
Zolmitriptan (5 mg) – 12y+
Sumatriptan/naproxen (10/60 or 85/500 mg) – 12y+

- *Tx when pain is mild*
- *Combine with NSAID*
- *Treating during aura does not avert migraine*
- *Nasal sprays: work fast, taste awful, one nostril*
- *Gepants are newer rescue option (not FDA approved <18)*

Non-med RxOptions
Neuromodulation

Nerivio, Savi Dual, Gammacore,

- *Not (yet) part of guideline*
- *Well-tolerated, less well covered by insurance*

Hassan A, Elmazny A, Elgenidi A, et al. Management of migraine in children and adolescents: A systematic review of guidelines and practice recommendations. *Cephalalgia*. 2026;46(2):3331024251413283. doi:10.1177/03331024251413283

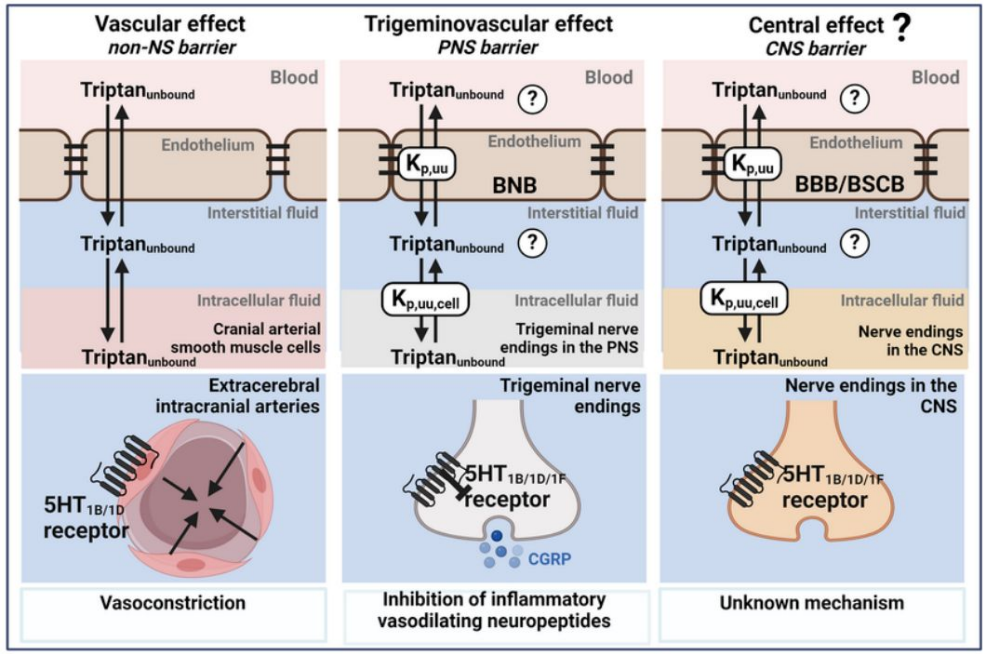
What should we do for our patient?

- **Prescribe a triptan =**migraine-specific pain relievers.
- **After confirming:**
  - No peripheral, cardio or neurovascular disease
  - No uncontrolled hypertension
  - Technically also contraindicated in WPW, hemiplegic migraine and migraine with brainstem aura (largely historical artifact)
- **Risk of serotonin toxicity?** 5-$HT_{1B/1D/1F}$ receptor agonists

  Orlova Y, Rizzoli P, Loder E. Association of Coprescription of Triptan Antimigraine Drugs and Selective Serotonin Reuptake Inhibitor or Selective Norepinephrine Reuptake Inhibitor Antidepressants With Serotonin Syndrome. *JAMA Neurol*. 2018;75(5):566-572. doi:10.1001/jamaneurol.2017.5144

  Evans RW, Tepper SJ, Shapiro RE, Sun-Edelstein C, Tietjen GE. The FDA alert on serotonin syndrome with use of triptans combined with selective serotonin reuptake inhibitors or selective serotonin-norepinephrine reuptake inhibitors: American Headache Society position paper. *Headache*. 2010;50(6):1089-1099. doi:10.1111/j.1526-4610.2010.01691.x
- **Counsel**
  - **Co-administer with NSAID** for the *first* dose of the day
  - Take when sx are mild (less likely to work if HA is already severe but still better than placebo)
  - Avoid using >10 days per month
  - Triptan effects

How triptans work



Svane N, Bällgren F, Ginosyan A, Kristensen M, Brodin B, Loryan I. Regional distribution of unbound eletriptan and sumatriptan in the CNS and PNS in rats: implications for a potential central action. *J Headache Pain*. 2024;25(1):187. Published 2024 Oct 30. doi:10.1186/s10194-024-01894-0

Choosing Among Triptans

Comparison Table: Triptans

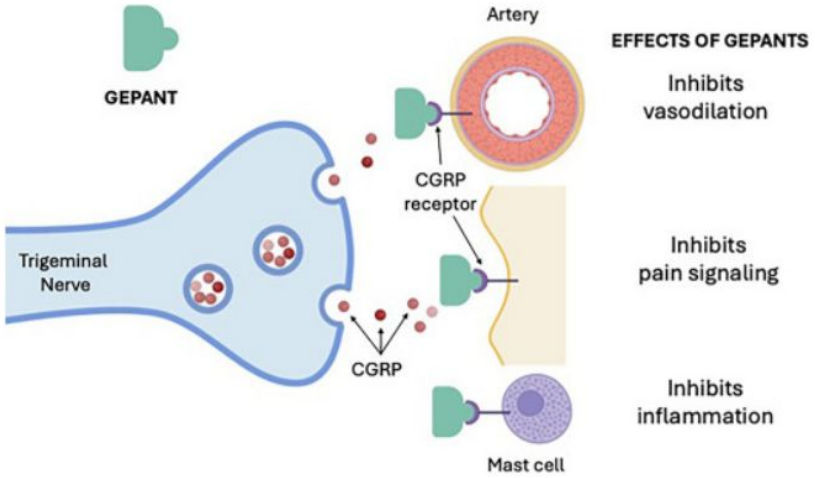
Drug	Almotriptan *	Eletriptan	Frovatriptan	Naratriptan	Rizatriptan *	Sumatriptan[1] *	Zolmitriptan *
Adult Dosage for Hepatic Impairment	6.25 mg starting dose (max 12.5 mg/day)	Severe[5]: not recommended	Severe[5]: caution recommended	Severe: contraindicated Mild-moderate: 1 mg starting dose (max 2.5 mg/day)	No dosage adjustment needed	Mild-moderate (oral): max single dose 50 mg Severe (oral, intranasal, and SC): contraindicated	Moderate-severe (oral): 1.25 mg (max 5 mg/day) Moderate-severe (intranasal): not recommended
Adult Dosage-Adjustment for Drug Interactions	With a strong CYP3A4 inhibitor[6]: 6.25 mg starting dose (max 12.5 mg/day); avoid strong CYP3A4 inhibitors in patients with renal or hepatic impairment	With a strong CYP3A4 inhibitor: avoid use within 72 hrs of treatment	No dosage adjustment needed	No dosage adjustment needed	With propranolol: only the 5 mg dose is recommended (max 15 mg/day)	No dosage adjustment needed	With cimetidine: 2.5 mg (max 5 mg/day)
Usual Pediatric Dosage	12-17 yrs: 6.25 or 12.5 mg PO; can be repeated after 2 hrs	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	6-17 yrs: 5 mg (<40 kg) or 10 mg (≥40 kg)	Not FDA-approved for pediatric use	Oral: not FDA-approved for pediatric use Nasal: (≥12 yrs): 2.5 or 5 mg intranasally; can be repeated after 2 hrs
Max Pediatric Dose	25 mg/day	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	The efficacy and safety of redosing within 24 hrs have not been established	Not FDA-approved for pediatric use	10 mg/day
Pediatric Dosage for Renal Impairment	Severe (CrCl 10-30 mL/min): 6.25 mg starting dose (max 12.5 mg/day)	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	No dosage adjustment needed	Not FDA-approved for pediatric use	No dosage adjustment needed
Pediatric Dosage for Hepatic Impairment	6.25 mg starting dose (max 12.5 mg/day)	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	No dosage adjustment needed	Not FDA-approved for pediatric use	Moderate-severe: not recommended
Pediatric Dosage Adjustment for Drug Interactions	With a strong CYP3A4 inhibitor: 6.25 mg starting dose (max 12.5 mg/day); avoid strong CYP3A4 inhibitors in patients with renal or hepatic impairment	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	Not FDA-approved for pediatric use	With propranolol: avoid concurrent use (<40 kg); only a single 5 mg dose is recommended (≥40 kg)	Not FDA-approved for pediatric use	With cimetidine: 2.5 mg (max 5 mg/day)
Class Adverse Effects	Tingling, flushing, dizziness, drowsiness, fatigue, and heaviness or tightness in the chest (can occur with any triptan, but most frequently with SC sumatriptan); angina, myocardial infarction, cardiac arrhythmia, stroke, seizure, and death have occurred very rarely with triptans[7]; peripheral vascular ischemia, gastrointestinal vascular ischemia and infarction, and Raynaud phenomenon have also occurred						
Other Adverse Effects	Most common (≥1%): nausea, dry mouth, paresthesia	Most common (≥5%): asthenia, nausea, dizziness, somnolence	Most common (≥2%): dizziness, headache, paresthesia, dry mouth, dyspepsia, fatigue, hot or cold sensation, chest pain, skeletal pain, flushing	Most common (≥2%): paresthesia, nausea, dizziness, drowsiness, throat or neck pain/pressure	Most common (≥5%): asthenia/fatigue, somnolence, pain or pressure sensation, dizziness	Most common (≥2%): paresthesia, warm/cold sensation, chest/neck/throat/jaw pain, tightness, or pressure, vertigo, fatigue SC: burning at injection site, adverse effects more likely with SC formulation Intranasal: abnormal taste, nasal discomfort, rhinorrhea, rhinitis	Most common (≥5%): neck/throat/jaw pain, tightness, or pressure, dizziness, paresthesia, asthenia, somnolence, warm/cold sensation, nausea, heaviness sensation, dry mouth Intranasal: abnormal taste
Class Drug Interactions	A triptan should generally not be used within 24 hours of another triptan or an ergot because vasoconstriction could be additive; cases of serotonin syndrome reported with SSRIs and SNRIs, but risk is likely low[8]						
Other Drug Interactions	CYP3A4 inhibitors[6] can increase serum concentrations; dose adjustment is recommended	Propranolol can increase serum concentrations CYP3A4 inhibitors[6] can increase serum concentrations; contraindicated for use within 72 hours of treatment with a strong CYP3A4 inhibitor	Propranolol can increase serum concentrations	None	MAO inhibitors can increase serum concentrations; contraindicated for use within 2 weeks after an MAO-A inhibitor Propranolol can increase serum concentrations; dosage adjustment is recommended	MAO inhibitors can increase serum concentrations; contraindicated for use within 2 weeks after an MAO-A inhibitor	MAO inhibitors can increase serum concentrations; contraindicated for use within 2 weeks after an MAO-A inhibitor Propranolol and cimetidine can increase serum concentrations; dosage adjustment recommended with cimetidine

The Medical letter on drugs and therapeutics (English ed.), 2023-06, Vol.65 (1678), p.e97-e99

- 4 are FDA licensed for pediatrics * (Sumatriptan only as combo w/ Naproxen)
- **Choose preferred route**
- **Assess need for long-acting** (used for menstrual migraine) Frovatriptan or Naratriptan
- **No water required**: Rizatriptan or Zolmitriptan ODTs
- **? Less likely to cause triptan effects:** Almotriptan

Gepants: Newer Oral Agents for Rescue & Prevention

- **No gepant is yet FDA licensed for pediatric patients**
- Gepants act as CGRP receptor antagonists
- Lower efficacy for pain freedom and pain relief at 2 hours compared with triptans but better tolerated
- Most common side effect: drowsiness, nausea
- Indicated for vascular contraindications to triptans; triptan non-response or intolerance
- No association with medication overuse HA
- Most have CYP3A4 drug interactions



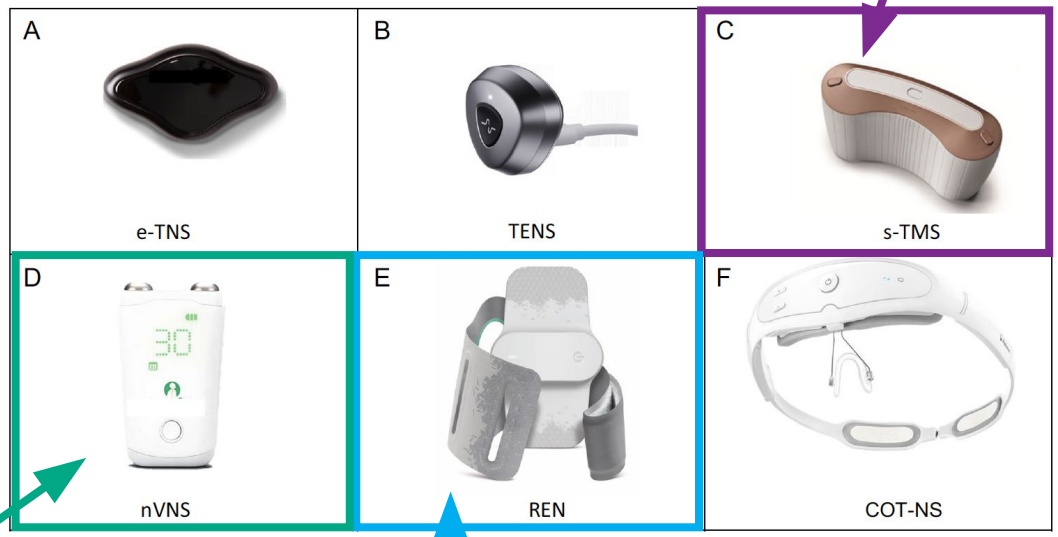
Gepant	Brand Name	Formulation	FDA-Approved Indication	Dosing	Key Drug Interactions
Ubrogepant	Ubrelvy	Oral tablet	**Acute** treatment of migraine with or without aura in adults	50 mg or 100 mg as needed; may repeat after 2 hours if needed; maximum 200 mg/24 hours	Avoid with strong CYP3A4 inhibitors; avoid another dose within 48 hours with moderate CYP3A4 inhibitors; avoid with strong/moderate CYP3A4 inducers
Rimegepant	Nurtec ODT	Orally disintegrating tablet	**Acute** treatment of migraine with or without aura in adults; **preventive** treatment of episodic migraine in adults	**Acute:** 75 mg as needed; maximum 75 mg/24 hours **Preventive:** 75 mg every other day	Avoid with strong CYP3A4 inhibitors; avoid another dose within 48 hours with moderate CYP3A4 inhibitors; avoid with strong/moderate CYP3A4 inducers; CYP2C9 does not play meaningful role
Zavegepant	Zavzpret	Intranasal spray	**Acute** treatment of migraine with or without aura in adults	10 mg (one spray in one nostril) as needed; maximum 10 mg/24 hours	Minimal CYP3A4 metabolism; fewer drug interactions than oral gepants
Atogepant	Qulipta	Oral tablet	**Preventive** treatment of episodic migraine in adults	10 mg 30 mg 60 mg once daily	Avoid with strong CYP3A4 inhibitors; dose adjustment with moderate CYP3A4 inhibitors; avoid with strong CYP3A4 inducers

Irimia P, Espinoza Vinces CA, Abedrabbo FS. Gepants. In: Filippi M, Messina R, eds. *Insights into Migraine Treatments*. Academic Press; 2026:157-174. doi:10.1016/B978-0-443-23649-5.00006-2.

Other possibilities – Device based therapy

- **Neuromodulation** = alteration of neural pathways, through targeted delivery of electrical, magnetic, or chemical stimulation, to restore function or to relieve symptoms of a neurological basis
- Several devices are FDA-cleared in the U.S. for pediatric use
- Indications: Migraine and Trigeminal Autonomic Cephalalgias
- All pediatric cleared devices have preventive AND rescue indications

Single pulse transcranial magnetic stimulator
"SAVI Dual"
Modulates cortical excitability
12y+
Migraine



Transcervical non-invasive vagal nerve stimulator
"gammaCore"
Autonomic balancing, neurogenic inflammation
12y+
Migraine, Cluster, Hemicrania

Remote electrical neuromodulator
"Nerivio"
Conditioned pain modulation
18y+
Migraine

Cocores AN, Smirnoff L, Greco G, Herrera R, Monteith TS. Update on Neuromodulation for Migraine and Other Primary Headache Disorders: Recent Advances and New Indications. *Curr Pain Headache Rep*. 2025;29(1):47. Published 2025 Feb 15. doi:10.1007/s11916-024-01314-7

Case #2

- 15 y/o  HR 75 BP 110/70 Ht: 1.63m Wt: 62kg
- Severe HA 4d/weekly x past year
- HA phenotype:
  - Throbbing
  - Bilateral periorbital
  - Rated 8 out of 10
  - Lasts 3 hours
  - Sensitivity to light/sound
  - Sees fortification spectra growing x 20 min then HA

Diagnosis: This is migraine (chronic, with aura)

- ✔ **5 attacks**
- ✔ **4 h – 3 d**

  2 of:

  unilateral
- ✔ **moderate to severe**
- ✔ **pulsating**

  avoidance of routine physical activity

  1 of:
- ✔ **photo and phono phobia**

  nausea and/or vomiting
- ✔ **Not better accounted for**

- ✔ **Chronic: HA 15d/month (≥8 migraine)**
- ✔ **Aura: ≥1 fully reversible sx**

  ≥3 of:

  Unilateral — In succession

  Positive — **Lasts 5 – 60”**

  Gradual — Within 60” of HA

What should we do for our patient?

2019 Guidelines for prevention:

Noted a lack of evidence from RCTs & high response to placebo

- Amitriptyline with CBT (Level B)
- Propranolol (Level B)
- Topiramate (Level B)

- Screen for (and treat) Mood/Anxiety Issues

2026 Real World Practice

- CGRP Antagonist (Fremanezumab) FDA-approved for 6y+ (SPACE trial) though payer step therapy often required
- Onabotulinumtoxin A is safe but lacks trials establishing superiority over placebo

American Headache Society and European Headache Federation consider anti-CGRP therapies first line prevention.

Not all insurers agree.

Paradigm shift from “fail older drugs first” to mechanism-driven therapy

Charles AC, Digre KB, Goadsby PJ, Robbins MS, Hershey A; American Headache Society. Calcitonin gene-related peptide-targeting therapies are a first-line option for the prevention of migraine: An American Headache Society position statement update. *Headache*. 2024;64(4):333-341. doi:10.1111/head.14692

CGRP Monoclonal Antibodies

Properties of CGRP Antagonist mAbs

	Fremanezumab-vfrm	Erenumab-aooe	Galcanezumab-gnlm	Eptinezumab-jjmr
Dosage Form	SC, prefilled syringe	SC, prefilled autoinjector	SC, prefilled pen/syringe	IV
Target	CGRP ligand	CGRP receptor	CGRP ligand	CGRP ligand
Dosing	225 mg mo or 675 mg q3m prefilled syringe	70-140 mg mo autoinjector	Loading dose: 240 mg; 120 mg mo	100-300 mg q3m IV infusion
Adverse Effects	HS reactions, injection-site pain, URTI	HS reactions, injection-site pain, URTI, constipation	HS reactions, injection-site pain, URTI	Hypersensitivity reactions, URTI
Half-Life	31 days	28 days	25-30 days	26-31 days

CGRP: calcitonin gene-related peptide; HS: hypersensitivity; mAb: monoclonal antibody; mo: monthly; q3m: every 3 months; SQ: subcutaneous; URTI: upper respiratory tract infection. Source: References 359-392.

<45 kg: 120 mg
≥45 kg: 225 mg

- 4 on market; 1 is pediatric labeled
- "reasonable clinical trial" is ~3-6m. Many respond in first month
- Most target ligand; Erenumab targets receptor
- Monitor BP, constipation
- Most common s/e: injection site rxns

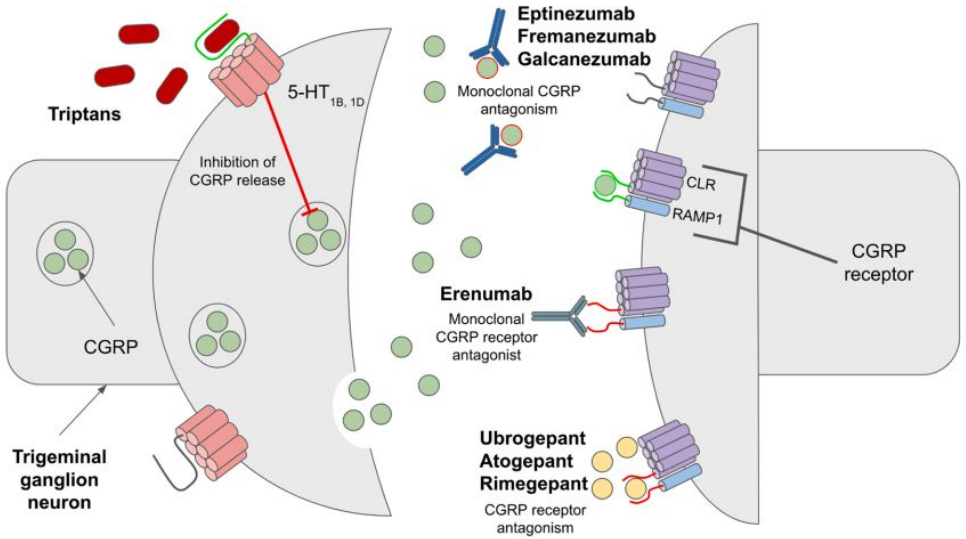
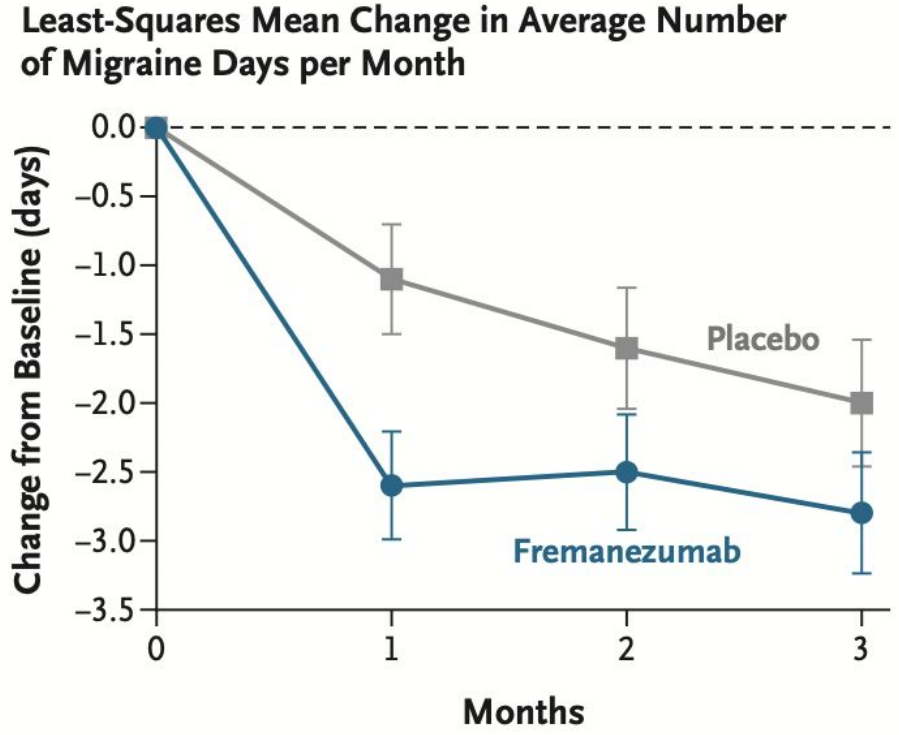
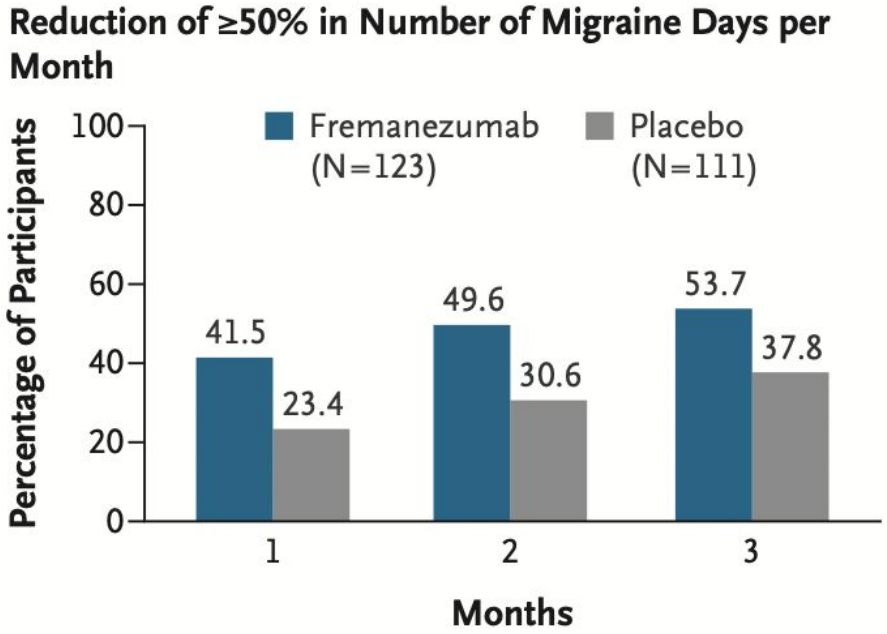


Fig. 2. Target mechanisms of CGRP antagonists.

DeMaagd GA, Norville K, Philip A. The pharmacologic management of migraine. *JournalCE (PowerPak)*. Published January 1, 2022.
Mehkri Y, Hanna C, Sriram S, Lucke-Wold B, Johnson RD, Busl K. Calcitonin gene-related peptide and neurologic injury: An emerging target for headache management. *Clin Neurol Neurosurg*. 2022;220:107355. doi:10.1016/j.clineuro.2022.107355

Fremanezumab is the only FDA labeled CGRP mAb for pediatric patients





- Fremanezumab (Ajovy) is FDA approved for patients 6y and older
- Fremanezumab SPACE trial (123 drug/111 control)
- Reduction in migraine days as early as Wk 4 & Fewer days of acute medication use
- Comparable safety profile to adults (injection site reactions)

Hershey AD, Szperka CL, Barbanti P, et al. Fremanezumab in Children and Adolescents with Episodic Migraine. *N Engl J Med*. 2026;394(3):243-252. doi:10.1056/NEJMoa2504546

Pediatric Evidence Pipeline

TABLE 1 Ongoing clinical trials for migraine treatment in children and adolescents and year of expected completion.

Medication	NCT number	Study Type	Target enrollment[a]	Age (years)	Diagnosis	Estimated study completion date
Preventive						
Atogepant	NCT05711394	Phase 3	450	6–17	EM	2028
	NCT06810505	Phase 3	420	12–17	CM	2031
	NCT05707949	Phase 3 open label	650	6–17	EM + CM	2032
Rimegepant	NCT05156398	Phase 3	640	6–17	EM	2032
	NCT06616194	Phase 3+ OLE	200	12–17	CM, not continuous	2027
Erenumab	NCT03836040	Phase 3+ OLE (says, "dose level blinded extension phase)	457 (closed)	6–17	EM	2026
	NCT03832998	Phase 3+ OLE (says, "dose level blinded extension phase")	284 (closed)	6–17	CM	2026
Galcanezumab	NCT03432286	Phase 3+ OLE	325	6–17	EM	2026
	NCT04616326	Phase 3+ OLE	300	12–17	CM	2026
Eptinezumab	NCT05897320	Phase 3	315	6–17	EM	2027
	NCT04965675	Phase 3	285	12–17	CM, not continuous	2026
	NCT05164172	OLE of Phase 3	600	6–17	EM+CM	2028
CBT ± open label amitriptyline	NCT05889624	Comparative effectiveness	400	10–17	EM+CM	2027
Topiramate extended release form	NCT04748601	Phase 4	132	6–17	EM, CM (not continuous)	2026
Cannabidiol-enriched cannabis extract	NCT05337033	Phase 2	20	14–17	CM, without response to ≥2 preventives	2025

Pediatric evidence expected this year (2026):

- Erenumab, Galcanzumab, Eptinezumab
- Ubrogepant

Medication	NCT number	Study Type	Target enrollment[a]	Age (years)	Diagnosis	Estimated study completion date
Acute						
Rimegepant	NCT04649242	Phase 3	2100	6–17	1–8 moderate or severe attacks/month	2029
	NCT04743141	OLE, including some enrolled directly and some after Phase 3	600	6–17	1–8 moderate or severe attacks/month	2030
Ubrogepant	NCT05125302	Phase 3	1059	6–17	1–14 migraine attacks/month with moderate to severe headache	2026
	NCT05127954	OLE	1200	6–17	Participants from phase 3 and pK studies.	2028
Zavegepant	NCT06995729	Phase 1	16	6–11	Migraine, not continuous	2027
Lasmitidan	NCT04396236	Phase 3	1633	6–17	2–8 moderate-to-severe migraine attacks/month	2026
	NCT04396574	OLE	1000	6–17	Completed a previousvstudy of ladmiditan	2028

Future Directions?

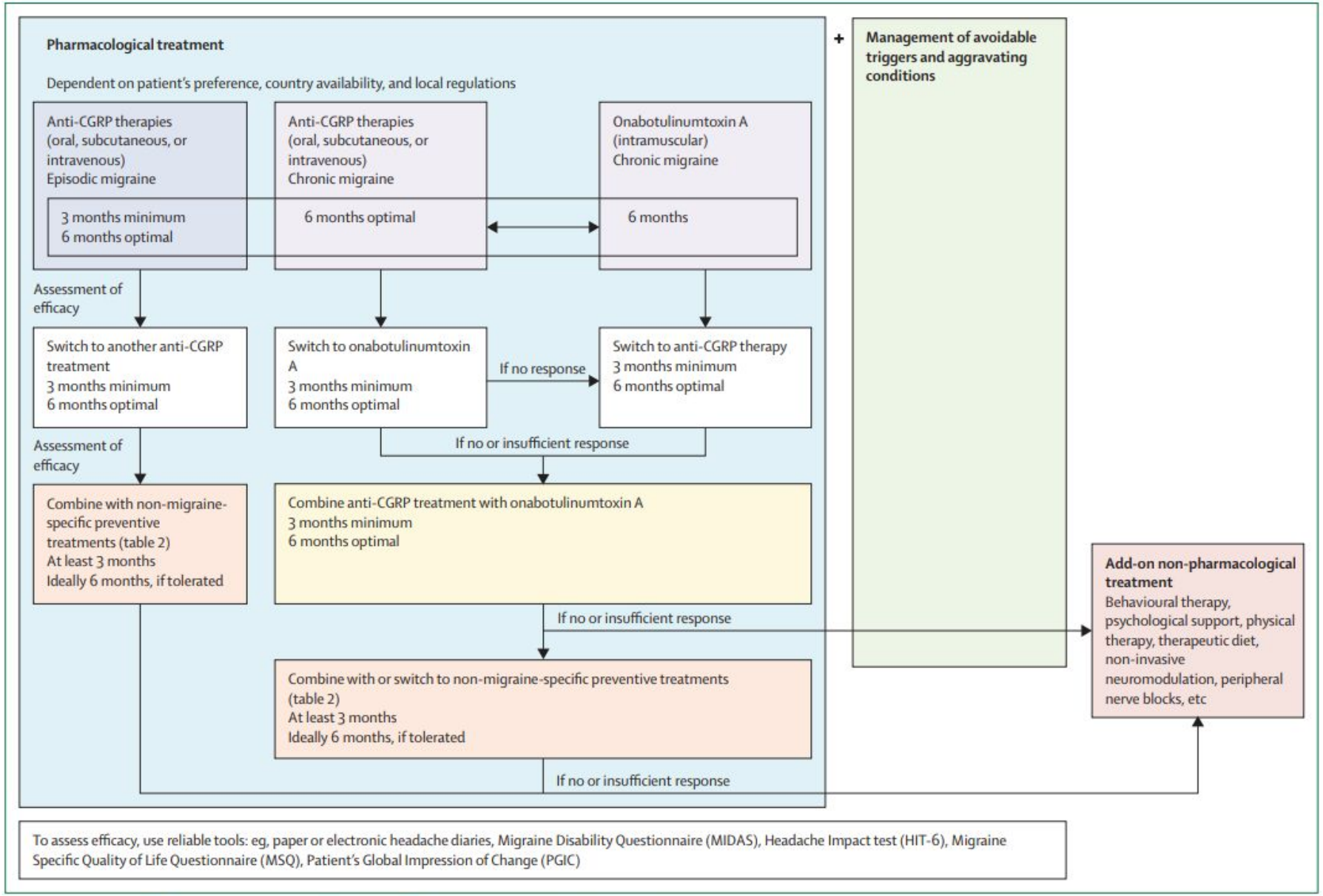


Figure 2: **Proposed optimised approach to migraine prevention for episodic and chronic migraine**
Based on the evidence from the Italian Headache Society and International Headache Society (SISC-IHS) guidelines.[23] A stepwise approach is presented, with a series of time points every 3–6 months to assess efficacy and suggest alternatives or combination therapies, if necessary. The approach is integrated with the management of triggers and aggravating factors and non-pharmacological treatments. Monitoring of the response with reliable tools is important to quantify the effect of interventions on disease severity and its effect on patients' wellbeing. CGRP=calcitonin gene-related peptide.

Martinelli D, De Icco R, Al-Khazali HM, et al. Advances in migraine prevention. *Lancet Neurol*. 2026;25(3):279-293. doi:10.1016/S1474-4422(25)00477-6

Beyond Symptoms: Biomarkers & Precision Therapy

- Candidate biomarkers:
  - CGRP - elevated interictally in some pediatric cohorts; may correlate with response to CGRP-targeted therapy
  - PACAP – therapeutic antagonists in development
  - Substance P – inconsistent data
  - Vasoactive Intestinal Peptide – possible role in trigeminovascular activation
- Brain-Gut Axis
  - Emerging evidence linking dysbiosis to migraine susceptibility
  - SCFAs, inflammatory signaling, vagal pathways
  - Pediatric data limited and heterogeneous

Fan PC, Kuo PH, Lee MT, Chang SH, Chiou LC. Plasma Calcitonin Gene-Related Peptide: A Potential Biomarker for Diagnosis and Therapeutic Responses in Pediatric Migraine. *Front Neurol*. 2019;10:10. Published 2019 Jan 24. doi:10.3389/fneur.2019.00010

Orak SA, Polat M, Pak M, et al. Can serum neuropeptide levels help diagnose pediatric migraine? A prospective case-control study. *Headache*. 2025;65(10):1821-1830. doi:10.1111/head.14981

Akbar A, Deshpande G, Tripathi S. The Use of Anti-CGRP Medications for Management of Intractable Chronic Daily Headaches in the Pediatric Population: Case Series and Literature Review. *J Child Neurol*. Published online September 15, 2025. doi:10.1177/08830738251374537

Optimal Pediatric Migraine Care is More than Pharmacology and Technology

Young Adults with Headache (18–25y)

- Median 7 monthly headache days
- 31.5% lacked an identifiable headache provider
- 45.4% reported their pain had been dismissed
- Transition services, transition skills, and stigma independently predicted care continuity

	Has Headache Provider	Lacks Headache Provider	Δ	Ratio
SERVICES RECEIVED				
Was helped to find an adult provider	42%	7%	34%	5.70
Received clear explanations of diagnosis & treatment	57%	15%	43%	3.92
Was offered preventive strategies	55%	17%	37%	3.19
Was offered rescue strategies	65%	27%	38%	2.41
Was oriented to practice operations	71%	43%	29%	1.67
SKILLS ACHIEVED				
Communicated with care team	63%	28%	35%	2.25
Filled or refilled Rx	73%	44%	29%	1.66
Viewed health information via portal or app	88%	56%	32%	1.56
Scheduled appointment	88%	61%	27%	1.45
Completed pre-visit forms	79%	67%	12%	1.18
STIGMA PERCEIVED				
Others view as easily treatable	47%	37%	10%	1.28
Others lack understanding of pain	53%	34%	19%	1.54
Others lack understanding of burden	28%	15%	13%	1.85
Prompts hiding or concealing pain	18%	14%	4%	1.31

Patients with Migraine… in their own words

Stigma-Specific Themes in Young Adult Headache Care Transition

Theme	Representative quotes
Invalidation compromising therapeutic relationships	*The worst part about transition is "finding doctors willing to actually help you and not make you the villain."* *"Try to be assertive as you will often be ignored if you are quiet and indirect."* *"Sometimes there's a sense of hesitation from the healthcare providers and I have to fight a little bit harder to prove them wrong."* *"It's critical to make the initial impression as true to reality as possible. Find a doctor who validates your experience.* *"As you age, there are things that you cannot tell the physician out of shame."*
Stigma leading to delayed care-seeking and provider switching	*"I've never gone to a professional because I'm afraid they won't take it seriously. My sister had similar headaches and they didn't do anything about it and she's still suffering "* *"Don't be afraid to speak up when you feel like your provider's not listening to you and being sympathetic to your needs. It's okay to switch care providers until you find a good match."* *"After my experiences when I was younger, I have an instinctive aversion to healthcare visits, even though I know it is important to have yearly checkups."* *The hardest part has been the uncertainty in finding the right provider who understands my history with headaches."* *"Keep switching until they believe you and don't just blame your pain on work or life."*
Lack of confidence in care due to diagnostic delegitimization	*"My migraines that severely impact my life just get brushed off as stressed-based, or I'm told to sleep more... even though I'm already very proactive in matters I can control."* *"Advocate for yourself. They told me that I may just be being dramatic."* *"They told me it was just anxiety, but I felt they were telling me that because I am a woman."* *"As a child I was regularly told I was making it up for attention, then as an adult I was accused of drug-seeking behaviour even though I was open to any method of solution."* *"I have had a primary care doctor say that my headaches (now diagnosed as chronic migraines) could just be solved by reducing stress."*

Thank You!

rdemayo@connecticutchildrens.org

Connecticut Children's