MIGRAINE SIMPLIFIED

PLAYBOOK

Canadian Headache Society

2025 Conference Edition

Contents

Introduction

Migraine is one of the most common and disabling neurological conditions, affecting an estimated 12% of Canadians, with a significant impact on women aged 15–49 years. Despite its prevalence, migraine remains underdiagnosed and undertreated, often leading to avoidable suffering and long-term complications.

The consequences of unmanaged migraine are substantial. In addition to pain and impairment, patients frequently experience disruptions to work, school, and family life. **Migraine is a leading cause of disability globally**, and in Canada, it significantly contributes to lost productivity and increased healthcare utilization.

Primary care plays a critical role in changing that trajectory. Primary care providers or clinicians, are often the first—and sometimes only—point of contact for patients with recurring headaches. With the right tools and awareness, they can diagnose migraine early, initiate effective treatment, and prevent progression to chronic forms.

Early intervention in primary care not only improves patient outcomes but also helps **reduce the burden on specialty clinics and emergency departments.** By identifying patients at risk, prescribing evidencebased treatments, and educating on lifestyle factors and medication overuse, **primary care providers can prevent the development of chronic migraine** and associated complications, such as medication overuse headache.

Furthermore, family medicine offers a unique opportunity to treat migraine holistically—addressing coexisting conditions such as anxiety, depression, insomnia, and hypertension. This integrated approach supports long-term management and empowers patients to take control of their condition. Incorporating migraine care into routine primary care practice is not only possible—it's essential.

With updated guidelines from the Canadian Headache Society and growing access to new treatments, **primary care providers are well-positioned to lead the way** in reducing the burden of migraine across the country.

Medrea I, et al. Updated Canadian Headache Society Migraine Prevention Guideline with Systematic Review and Meta-analysis. Can J Neurol Sci. Published online November 7, 2024:1-23. doi:10.1017/cjn.2024.285; Becker WJ, et al. Guideline for primary care management of headache in adults. Canadian Family Physician. 2015;61(8):670-679; Tzankova V, Becker WJ, Chan TLH. Diagnosis and acute management of migraine. CMAJ. 2023;195(4):E153-E158. doi:10.1503/cmaj.211969

Acknowledgments

SCIENTIFIC COMMITTEE

Alex Melinyshyn, MD, FRCPC, London, ON, Chair

Paul Cooper, MD, FRCPC, London, ON

Danny Monsour, MD, FRCPC, Burlington, ON

CONTRIBUTORS

Taryn Williams, MD, Cambridge, ON

Allan Horii, MD, Vancouver, BC

Shirin Lal, MD, Ottawa, ON

John Robrock, MD, Thunder Bay, ON

Azadeh Yasinian, MD, Ancaster, ON

SPONSORS

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Referral To A Headache Specialist

Referral Checklist

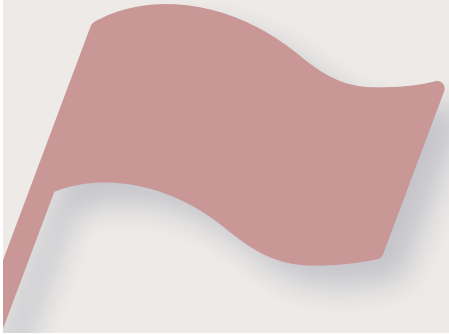
The content provided is for informational purposes for medical professionals only and is not intended to be used or relied upon by them as specific medical advice, diagnosis, or treatment, the determination of which remains the responsibility of the medical professionals for their patients.

WHO SHOULD BE REFERRED TO URGENT CARE?

Primary stabbing headache with recurring symptoms or present with ***red flags (SNOOP$_6$)*** to investigate:

Systemic symptoms ..... Order MRI
Neurological symptoms .... Order MRI
Onset peak <1 min ..... Send to ER ("thunderclap")
Older >50 y ..... Order ESR/CRP for giant cell arteritis, order MRI
Papilloedema ..... Send to urgent neurology clinic, order MRI/MRV
Postural ..... Order MRI
Previous ..... Order MRI
Precipitated by Valsalva .... Send to ER
Pregnancy/post-partum ... If new onset, send to ER, order MRI/MRV
Progression ..... Order MRI

In the absence of red flags, patients should trial at least two oral preventive medications for a minimum of two months before being referred to a headache specialist.



RULE OUT RED FLAGS

Sudden change in headache features, fever, weight loss, significant vision changes, weakness, numbness, and aphasia are red flags.

If red flags are present, consider urgent referral or investigation.

Headache that peaks in intensity in less than a minute is a **NEUROLOGICAL EMERGENCY.**

WHO SHOULD BE REFERRED TO A HEADACHE SPECIALIST FOR MIGRAINE?

- Patients not responding to acute or preventive therapies despite treatment optimization (failure of ≥3 medications/failed >2 triptans and >2 preventive treatments)
- Complex patients, or patients who are contraindicated for acute or preventive therapies
- Patients on preventive therapies experiencing persistent (>8 weeks) worsening in severity or duration
- Referral to a general neurologist may be appropriate if the wait to see a headache specialist in your catchment is too long.

Tzankova V, et al. Diagnosis and acute management of migraine. CMAJ. 2023;195(4):E153-E158; Headache. Choosing Wisely Canada; Lipton RB, et al. A self-administered screener for migraine in primary care. Neurology. 2003;61(3):375-382; Gago-Veiga AB, et al. How and when to refer patients diagnosed with primary headache and craniofacial neuralgia in the emergency department or primary care: Recommendations of the Spanish Society of Neurology's Headache Study Group. Neurol Engl Ed. 2020;35(3):176-184; Red Flags in Headache History. American Headache Society; Micieli A, Kingston W. An Approach to Identifying Headache Patients That Require Neuroimaging. Front Public Health. 2019;7; Utukuri PS, et al. ACR Appropriateness Criteria® Headache: 2022 Update. J Am Coll Radiol. 2023;20(5):S70-S93; Evans RW, et al. Neuroimaging for Migraine: The American Headache Society Systematic Review and Evidence-Based Guideline. Headache J Head Face Pain. 2020;60(2):318-336; Loder E, et al. Choosing Wisely in Headache Medicine: The American Headache Society's List of Five Things Physicians and Patients Should Question. Headache J Head Face Pain. 2013;53(10):1651-1659.

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INFORMATION TO INCLUDE IN YOUR REFERRAL

Including critical information in your referral can help specialists to appropriately triage patients.

PATIENT INFO

- Name,
- Date of Birth,
- Sex,
- Healthcare #,
- Telephone,
- Email for intake survey,
- Current Pharmacy

URGENCY

- ☐ **Emergency** (Direct to the nearest emergency department)
- ☐ **Urgent** (Direct to the nearest urgent neurology clinic)
- ☐ **Non-Urgent** (Next available appointment)

HISTORY

- ☐ Previous medical history (including blood pressure, cardiovascular history)
- ☐ Comorbid conditions
- ☐ Family history (Headache, Neurological disorders; including stroke, Unexplained miscarriages, Other genetic conditions

MEDICATION

- ☐ Previous medication trials
- ☐ Acute medication (OTC or prescription)
- ☐ Current preventive medication. For previous medication trials, add (acute AND preventive)
- ☐ Other medications (OTC or prescription)

HEADACHE

- ☐ Details of headache presentation
- ☐ Level of disability (impact on work, sleep, mood, ADLs)
- ☐ Headache history (age when started/got worse
  - Number of headache days/headache-free days
  - Time of day/year headaches start
  - Duration of headaches/time to reach max intensity
  - Headache triggers
  - What makes the headaches feel worse or better?

RESULTS

- ☐ Relevant blood work and investigations to date
- ☐ Results of PHQ-4 and/or HIT-6, if available

Wongsiriroj S, Grillo E, Levi S, et al. Management of Migraine and the Accessibility of Specialist Care: Findings from an Extended Multinational Survey (My Migraine Center Survey). Neurol Toer. 2020;9(2):551-565. doi:10.1007/s40120-020-00205-4. Headache. Chooeing Wisely canada. Accessed September 28,2024. https://choosingwiselycanada.org/reccmmenclation/headache/. Do TP, Remmers A, Schytz HW, et al. Reel and orange flags for secondary headaches indinical practice. Neurology. 2019;92(3):134-144. doi:10.1212/WNL0000000000006697. Gago-Veiga AB, Garcia-Azorin D, Mas-Sala N, et al. How and when to refer patients diagnosed with primary headache and aaniofacial neuralgia in the emergency department or primary care: Recommendations of the Spanish Society of Neurology's Headache Study Group. Neurol Engl Ed. 2020;35(3):176-184. doi:10.1016/j.nrleng.2017.08.004. Red Rags in Headache History. AmericanHeadache Society. Accessed August 14, 2024. htlps://americanheadachesociety.orglnews/red-flags-headache-history/

Referral To A Headache Specialist

Best Practices

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DO

- Look for **"red flags"** to rule out other causes of headache (secondary headache) using $SNOOP_6$ Criteria.
  If red flags are present, consider urgent referral or investigation.
- Ask patients to **keep a headache diary** with the Canadian Migraine Tracker app to establish baseline patterns.
- **Treat with acute medications early.** Offer a **second dose in 2–4 hours** if needed.
- Patients with **>4 headache days per month** should be offered **preventive medication** for a minimum of 2 months.
- Patients should **trial ≥2 oral preventive medications**, preferably from different classes, prior to referral to a neurologist/headache specialist.

STOP

- Do not prescribe opioids to treat migraine.
- Stable headaches meeting criteria for migraine with normal neurologic examination **do not require routine neuroimaging.**

CONSIDER

- Consider imaging and additional investigations in patients with red flags.
- Most preventives will have 50% chance of a 50% improvement, not a cure.
- Most patients presenting with recurring headaches have migraine.
- Refer to neurology while awaiting headache specialist if the wait time is long.

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While Waiting For A Consult

Step By Step

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WHILE YOUR PATIENT IS WAITING FOR A HEADACHE SPECIALIST CONSULT, YOU SHOULD:

1 RULE OUT RED FLAGS (SNOOP$_6$)

Systemic symptoms ..... Order MRI
Neurological symptoms .... Order MRI
Onset peak <1 min ..... Send to ER ("thunderclap")
Older >50 y ..... Order ESR/CRP for giant cell arteritis, order MRI
Papilloedema ..... Send to urgent neurology clinic, order MRI/MRV
Postural ..... Order MRI
Previous ..... Order MRI
Precipitated by Valsalva .... Send to ER
Pregnancy/post-partum .... If new onset, send to ER, order MRI/MRV
Progression ..... Order MRI

Headache that peaks in intensity in less than a minute is a **NEUROLOGICAL EMERGENCY.**

CONSIDER IMAGING/ADDITIONAL INVESTIGATIONS:

- Neuroimaging should be ordered in patients with an **abnormal neurologic examination OR red flags.**
- **ROUTINE NEUROIMAGING** is **NOT** needed in patients with **normal** neurologic examination and **stable** headaches meeting criteria for migraine.
- **New headache in patients age >50:** screen for giant cell arteritis (pain in temples/scalp/jaw, visual problems) using erythrocyte sedimentation rate and C-reactive protein levels.
- **MRI is preferred over CT:** MRI detects subtle lesions and shows brain parenchyma with fewer artifacts.
- **Add contrast** when considering intracranial mass, infection, vascular causes, or inflammation.
- **CT** is preferred when hemorrhage or fracture is suspected—especially useful in **urgent or emergency settings** when there is concern for acute abnormalities or if MRI is unavailable.

2 CONFIRM MIGRAINE: PIN SCREENING

P **Photophobia**
Does light bother you much more when you have a headache?

I **Impairment**
In the past 3 months, did your headache limit your ability to work, study, or do what you needed to do for at least 1 day?

N **Nausea**
Do you feel nauseated or sick to your stomach during your headaches?

After excluding red flags, if the patient answers "yes" to ≥2 PIN questions, they are likely to have migraine.
Sensitivity: 0.81 | Specificity: 0.75 | Positive Predictive Value: 0.93

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3 USE ACUTE MEDICATION TO RELIEVE MIGRAINE SYMPTOMS

Treat migraine attacks early (within 15–30 minutes of onset) with nonsteroidal anti-inflammatory drugs, triptans, or gepants for a better chance of success. Acute medications can be used individually or combined. For severe attacks, consider parenteral medications, combinations, or antiemetics.

Do not prescribe opioids to treat migraine.

Class	Medication	Dose	Dosing	Max Daily Dose	Warnings
NSAIDS	Naproxen	500 mg	Repeat in 2–4 h as needed	1000 mg	**AVOID IN:** peptic ulcer disease, IBD, oral anticoagulation, bariatric surgery.Do not combine with other NSAIDs.
	Diclofenac powder	50 mg	Safety/efficacy of a second dose has not been evaluated	50 mg	
Triptans Two common triptans are listed here. Others include almotriptan, eletriptan, frovatriptan, naratriptan, or zolmitriptan.	Rizatriptan	10 mg	Repeat in 2–4 h as needed	20 mg	**AVOID IN:** pregnancy, uncontrolled hypertension, coronary artery disease, stroke, transient ischemic attack, myocardial infarction, angina, or peripheral vascular disease.
	Sumatriptan	100 mg	Repeat in 2–4 h as needed	200 mg	
Gepants	Ubrogepant	100 mg*	Repeat in 2–4 h as needed	200 mg	**MEDCHECK:** CYP3A4 interactions *Reduce to 50 mg in severe renal/ hepatic impairment
	Rimegepant	75 mg	Do not repeat within 24h	75 mg	

4 AVOID MEDICATION OVERUSE HEADACHE BY LIMITING ACUTE MEDICATION USE TO NO MORE THAN 15 DAYS PER MONTH (TOTAL)

- <15 days: simple analgesics (e.g. acetaminophen, ibuprofen)
- <10 days: compound analgesics / triptans
- Repeated doses within a single 24–hour period = 1 day of medication use

Total acute medication use = <15 days /month

Gepants are not associated with medication overuse headache

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5 START MIGRAINE PREVENTIVE MEDICATION IF HEADACHES ARE OCCURRING ≥4 DAYS/MONTH

- Many patients who might benefit from preventive therapy do not receive it.
- Adequate therapeutic trials should last 2–3 months; don't give up too early!
- Ensure that patients reach an adequate target dose to ensure efficacy.
- Several preventive medications in different classes may need to be trialed before finding the one that works best.
- Simple questionnaires can also be used (HIT6, MIDAS, available in the Canadian Migraine Tracker app) to track scores required by private insurance coverage.

Episodic migraine (<15 days/m)	Candesartan	8-16 mg PO OD
	Amitriptyline	30-75 mg PO QHS
	Propranolol	20-30 mg PO BID
Chronic migraine (≥15 days/m)	Topiramate	100 mg PO QHS or divided BID

CHS POSITION STATEMENT:
In the absence of red flags, patients should trial at least two oral preventive medications for a minimum of 2 months before referral to a headache specialist.

Before prescribing, **scan the QR code for titration instructions** that can be copied into your EMR prescriptions, extra advice, and side effect profiles.

6 ASK YOUR PATIENT TO RECORD A HEADACHE DIARY

The Canadian Migraine Tracker app is used to keep a record of the frequency of attacks and efficacy of medication, and is the most helpful tool for headache specialists.

Canadian Migraine Tracker

Loder E, et al. Choosing Wisely in Headache Medicine: The American Headache Society's List of Five Things Physicians and Patients Should Question. Headache J Head Face Pain. 2013;53(10):1651-1659; Hird MA, Sandoe CH. Medication Overuse Headache: an Updated Review and Clinical Recommendations on Management. Curr Neurol Neurosci Rep. 2023;23(7):389-398; Becker WJ, et al. Guideline for primary care management of headache in adults. Can Fam Physician. 2015;61(8):670-679. Medrea I, et al. Updated Canadian Headache Society Migraine Prevention Guideline with Systematic Review and Meta-analysis. Can J Neurol Sci J Can Sci Neurol. Published online November 7, 2024:1-23. Charles AC, et al. The AHS. Calcitonin gene-related peptide-targeting therapies are a first-line option for the prevention of migraine: An American Headache Society position statement update. Headache J Head Face Pain. 2024;64(4):333-341. Canadian Headache Society Prophylactic Guidelines Development Group, Lawler V, Lay C. Primary Care Guide to Migraine Therapies. Published online February 2024, Product Monographs.

Treatment
Acute Therapies

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GOALS OF ACUTE THERAPY

- ☐ Rapid and consistent relief from migraine attack (headache and any associated symptoms) without recurrence
- ☐ Return to usual functioning
- ☐ Reduced need for repeat dosing, rescue medications and emergency room visits
- ☐ Minimal or no adverse events

CHS POSITION STATEMENT:

Migraine patients require acute therapy; suboptimal therapy leads to increased disability.

Attack Severity & Disability	Medication and Adult Dosing	Best Practices
"I can GO." 	If therapy is needed: Diclofenac K+ for oral solution, dissolved in a small amount of water Diclofenac Na+ 50 mg Indomethacin 25-50 mg Mefenamic acid 500 mg Nabumetone 500 mg Naproxen 440-550 mg Rimegepant‡ orally disintegrating tablet 75 mg Ubrogepant‡ 50, 100 mg tab	Treating **EARLY** at the first sign of a migraine attack is critical for best results. Some **GREEN** attacks don't need treatment if they resolve on their own with no recurrence. If **GREEN** usually progresses to **YELLOW**, consider triptan during the **GREEN** phase.
"I have to SLOW DOWN." 	Almotriptan*† 12.5 mg tab Eletriptan 40 mg tab Frovatriptan 2.5 mg tab Naratriptan* 2.5 mg tab Rizatriptan* 10 mg tab or rapidly disintegrating preparation Sumatriptan* 100 mg tab, 6 mg subcutaneous injection, or20 mg nasal spray Sumatriptan 85 mg + naproxen 500 mg combined in 1 tab Zolmitriptan 5 mg nasal spray (2.5 mg oral may be under-dosed) Rimegepant‡ orally disintegrating tablet 75 mg Ubrogepant‡ 50, 100 mg tab	Both triptans and gepants can be effective. Choose a non-oral route if severe nausea or vomiting (eg, zolmitriptan nasal spray or sumatriptan subcutaneous injection) and consider the addition of an oral antiemetic
"I have to STOP." 	Triptan or gepant + NSAID combination (for an early morning attack, consider non-oral triptan) OR Sumatriptan 85 mg + naproxen 500 mg combined in 1 tab	Limit triptan use to an average of 2 days per week to avoid medication overuse / induced headache. If therapy is ineffective or suboptimal, switch to a different medication.

- If acute medications are needed 1 day per week or more, a preventive medication should be offered.
- If prevention is already in place, the dose can be increased or a different agent can be layered in.
- Acute medication could also be changed.
- Opioids are never recommended; Opioids contribute to worsening headache and ineffectiveness of migraine therapy.

*Exceptional Access Program may cover
‡Ubrogepant and rimegepant are migraine-specific oral CGRP receptor antagonists (gepant)
†Health Canada approved for ≥12 years old

Used with permission from the authors: Valerie Lawler NP, Christine Lay MD, Centre for Headache, Women's College Hospital.

The American Headache Society Consensus Statement: Update on Integrating New Migraine Treatments into Clinical Practice. Headache. 2021;61:1021-1039. Canadian Headache Society Acute Migraine Treatment Guideline Development Group. Canadian Headache Society Acute Drug Therapy for Migraine Headache. Can J Neurol Sci. 2013;40:5(Suppl 3): S1-79. Lagman-Bartolome, A.M, Lay, C. The Traffic Light of Headache: Simplifying Acute Migraine Management for Physicians and Patients Using the Canadian Headache Society Guidelines. Headache 2019;59:250-252.

Treatment
Preventive Therapies

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RECOMMENDED FOR USE IN EPISODIC MIGRAINE (USE)

Drug	Strength	Quality of Evidence	Dosage	2012
Amitriptyline	Strong	High	10–100 mg QHS	X
Erenumab	Strong	High	70–140 mg SC Q1M	
Metoprolol	Strong	High	50–100 mg BID	X
Propranolol	Strong	High	40–120 mg BID	X
Atogepant	Strong	Moderate	30–60 mg QD	
Candesartan	Strong	Moderate	8–16 mg QD	
Eptinezumab	Strong	Moderate	100–300 mg IV Q3M	
Fremanezumab	Strong	Moderate	225 mg SC Q1M	
Galcanezumab	Strong	Moderate	120 mg SC Q1M	
Nadolol	Strong	Moderate	40–160 mg QD	X
Coenzyme Q10	Strong	Low	100 mg TID	X
Magnesium citrate	Strong	Low	300 mg BID	X
Riboflavin	Strong	Low	400 mg QD	X
Divalproex sodium	Weak	High	750–1500 mg QD	X
Flunarizine	Weak	High	5–10 mg QHS	X
Pizotifen	Weak	High	1–2 mg BID	X
Memantine	Weak	Moderate	10 mg QD	
Rimegepant	Weak	Moderate	75 mg QOD	
Topiramate	Weak	Moderate	25–100 mg QHS	
Levetiracetam	Weak	Low	500–1000 mg OD	
Lisinopril	Weak	Low	10–20 mg QD	X
Venlafaxine	Weak	Low	37.5–150 mg QD	X
Verapamil	Weak	Low	80 mg BID	X
Enalapril	Weak	Very Low	2.5- 5 mg OD	
Melatonin	Weak	Very Low	3–10 mg QHS	

NOT RECOMMENDED FOR USE IN EPISODIC MIGRAINE (DO NOT USE)

Drug	Strength	Quality of Evidence	2012
Onabotulinum toxin A	Strong	High	X
Ginger	Strong	High	X
Feverfew	Strong	Moderate	X
Gabapentin	Weak	Very Low	
Statin, alone or add on	Weak	Very Low	

WHO SHOULD RECEIVE PREVENTIVE TREATMENT?

- ☐ 4 headache days/month not responding to acute medication.
- ☐ 8 headache days/month, even when acute medications are effective (risk of medication overuse headache).
- ☐ Maybe ≤3 days/month if the impact is severe despite good acute treatment, trigger avoidance, lifestyle modification, etc.

WHAT CONSTITUTES AN ADEQUATE PREVENTIVE TRIAL?

- ☐ At least two months at target dose for older oral preventive medications.
- ☐ For older oral preventive medications, start at low dose and build up slowly Q2W to target response and tolerability.
- ☐ For CGRP-targeted monoclonal antibodies, a trial of 3 months for most, 6 months suggested in treatment-resistant chronic migraine.
- ☐ For onabotulinum toxin A, a minimum of 2 quarterly injections.
- ☐ Aiming for 50% reduction in headache frequency or severity.

Q = every; D = day; M = month; W = week; BID = twice daily; TID = three times daily; QHS = quaque hora somni/hs = at bedtime; QOD: every other day; IV = intravenous; SC = subcutaneous injection2012 = change from previous guidelines. No previous recommendations were available for chronic migraine.

Medrea I, et al. Canadian Headache Society Updated Guideline on Migraine Prevention. Can J Neurol Sci. 2024;1;455. Pringsheim, T et al, Canadian Headache Society Guideline for Migraine Prophylaxis, Can J Neurol Sci. 2012;39:Suppl. 2 - S1-S2. Charles A. C. et al. 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: 333-341. Amoozegar F et al. The Burden of Illness of Migraine in Canada: New Insights on Humanistic and Economic Cost. Can J Neurol Sci. 2022;49: 249–262. Sacco S. et al. European Headache Federation guideline on the use of monoclonal antibodies targeting the calcitonin gene related peptide pathway for migraine prevention – 2022 update. J Headache Pain. 2022; 23(1):67.

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RECOMMENDED FOR USE IN CHRONIC MIGRAINE (USE)

Drug	Strength	Quality of Evidence	Dosage
Onabotulinum toxin A	Strong	High	155–195 U injected Q12W
Atogepant	Strong	High	30–60 mg QD
Eptinezumab	Strong	High	100–300 mg IV Q3M
Erenumab	Strong	High	70–140 mg SC Q1M
Fremanezumab	Strong	High	225 mg SC Q1M
Galcanezumab	Strong	High	120 mg SC Q1M
Propranolol	Strong	Moderate	20–80 mg BID
Topiramate	Weak	Very Low	25–100 mg QHS

Q = every; D = day; M = month; W = week; BID = twice daily; TID = three times daily; QHS = quaque hora somni/hs = at bedtime; QOD: every other day; IV = intravenous; SC = subcutaneous injection2012 = change from previous guidelines. No previous recommendations were available for chronic migraine.

ACCESS TO MEDICATION

Payers are currently requiring that patients with migraine—including Chronic Migraine (CM) and High-Frequency Episodic Migraine (HFEM)—fail at least two older oral preventive medications before initiating CGRP-targeted agents or onabotulinumtoxinA.

We oppose this requirement due to the significant indirect societal costs associated with both CM and HFEM, which have not been dequately considered in payer deliberations.

We recommend that CGRP antagonists and onabotulinumtoxinA be made available as first-line options, alongside other first-line treatments for patients with CM and HFEM who experience moderate disability. Treatment decisions should be based on the clinical judgment of the treating practitioner and patient preference.

The recommendations of the Canadian Headache Society Migraine Prevention Guideline are grounded in the best available research evidence and clinical experience, and are aligned with international guidelines and consensus statements. We strongly urge payers to align their approval processes with these published guidelines.

Medrea I, et al. Canadian Headache Society Updated Guideline on Migraine Prevention. Can J Neurol Sci. 2024;1;455. Pringsheim, T et al, Canadian Headache Society Guideline for Migraine Prophylaxis, Can J Neurol Sci. 2012;39:Suppl. 2 - S1-S2. Charles A. C. et al. 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: 333-341. Amoozegar F et al. The Burden of Illness of Migraine in Canada: New Insights on Humanistic and Economic Cost. Can J Neurol Sci. 2022;49: 249–262. Sacco S. et al. European Headache Federation guideline on the use of monoclonal antibodies targeting the calcitonin gene related peptide pathway for migraine prevention – 2022 update. J Headache Pain. 2022; 23(1):67.

Transitioning Back to Primary Care
Best Practices

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DO

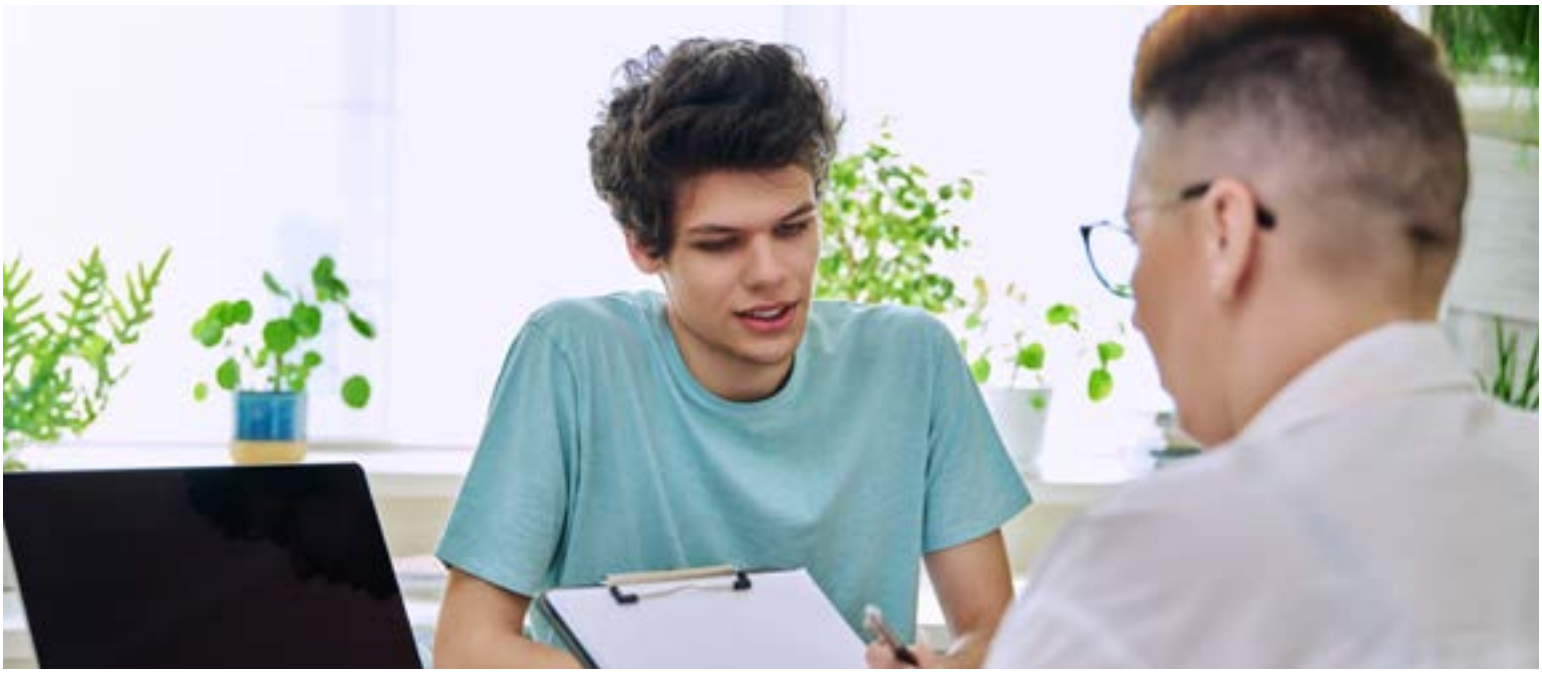
- Do take advantage of the services offered by patient support programs.
- In the case of a new or different migraine presentation, reevaluate for red flags.

STOP

- In the case of new cardiovascular conditions, pause CGRP antagonist use for 6–8 months;
- If symptoms are stable and secondary prevention has been optimized, check back with the specialist for the green light to restart.
- In case of planned/ pregnancy/breastfeeding, stop CGRP antagonist use before attempting to conceive. Duration is specific to each medication.

CONSIDER

- Migraine severity is likely to fluctuate, especially if triggers are present (e.g., stress, hormones).
- If migraine frequency/ severity increase persists beyond two months, consult with the referring specialist for strategies.



Becker WJ, et al. Guideline for primary care management of headache in adults. Can Fam Physician. 2015;61(8):670-679. Medrea I, et al. Updated Canadian Headache Society Migraine Prevention Guideline with Systematic Review and Meta-analysis. Can J Neurol Sci J Can Sci Neurol. Published online November 7, 2024:1-23.Aditya S, Rattan A. Advances in CGRP Monoclonal Antibodies as Migraine Therapy: A Narrative Review. Saudi J Med Med Sci. 2023;11(1):11-18. Nisar A, Ahmed Z, Yuan H. Novel Therapeutic Targets for Migraine. Biomedicines. 2023;11(2):569. Charles AC, et al. Calcitonin gene-related peptide-targeting therapies are a first-line option for the prevention of migraine: An American Headache Society position statement update. Headache J Head Face Pain. 2024;64(4):333-341.Product monographs.

Transitioning Back to Primary Care
Common Questions

WHAT TO KNOW ABOUT LONG-TERM USE OF CGRP ANTAGONISTS

Calcitonin gene-related peptide (CGRP) antagonists

- Include anti-CGRP monoclonal antibodies (mAbs) and oral CGRP antagonists (gepants, specifically atogepant) that preventively target migraine pathophysiology.
- They are effective, safe, and well-tolerated treatment options for adults.
- CGRP antagonists can be prescribed by any prescribing provider.

Anti-CGRP monoclonal antibodies (eptinezumab, erenumab, fremanezumab, galcanezumab)

- Generally well-tolerated, with favourable safety profiles and no drug-drug interactions, and are not cleared by the kidney or liver via proteolytic degradation.
- Common side effects include injection site reactions, constipation, and fatigue.

Oral CGRP antagonist (atogepant)

- Atogepant is indicated for preventive therapy, whereas other gepants are indicated for acute treatment (rimegepant and ubrogepant).
- Unlike triptans, gepants do not cause blood vessel constriction, which may be favourable for those with certain cardiovascular risk factors.
- Side effects include nausea, fatigue, constipation, or weight loss.

RELATIVE CONTRAINDICATIONS

- <18 years old or geriatric patients (studies ongoing in pediatrics)
- Pregnancy (due to long half life, recommend stopping for ~5–6 half-lives prior to conception)
- Avoid with breastfeeding
- Caution with vascular disease due to CGRP's role in vascular regulation
- Inflammatory bowel disease (Crohn's, ulcerative colitis)
- Hypersensitivity to drug or it's components

Generic Name	Trade Name	Route of Administration	Dosing/Interval	Half Life
Atogepant	Qulipta®	Oral tablet	Episodic: 10, 30, or 60 mg OD Chronic: 60 mg OD	11 hours
Eptinezumab	Vyepti®	Intravenous infusion	100 mg Q12W 300 mg Q12W	29 days
Erenumab	Aimovig®	Subcutaneous injection via autoinjector	70 mg Q1M 140 mg Q1M	28 days
Fremanezumab	Ajovy®	Subcutaneous injection via prefilled syringe or autoinjector	225 mg Q1M 675 mg Q3M	30 days
Galcanezumab	Emgality®	Subcutaneous injection via prefilled syringe or pen	Loading dose 240 mg, then Q1M 120 mg	27 days

Becker WJ, et al. Guideline for primary care management of headache in adults. Can Fam Physician. 2015;61(8):670-679. Medrea I, et al. Updated Canadian Headache Society Migraine Prevention Guideline with Systematic Review and Meta-analysis. Can J Neurol Sci J Can Sci Neurol. Published online November 7, 2024:1-23.Aditya S, Rattan A. Advances in CGRP Monoclonal Antibodies as Migraine Therapy: A Narrative Review. Saudi J Med Med Sci. 2023;11(1):11-18. Nisar A, Ahmed Z, Yuan H. Novel Therapeutic Targets for Migraine. Biomedicines. 2023;11(2):569. Charles AC, et al. Calcitonin gene-related peptide-targeting therapies are a first-line option for the prevention of migraine: An American Headache Society position statement update. Headache J Head Face Pain. 2024;64(4):333-341.Product monographs.

Transitioning Back to Primary Care
Common Questions

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How long will my patient need this medication?

Migraine is a chronic disease and may require lifelong therapy. Research suggests that discontinuing a CGRP antagonist may lead to an increase in migraine frequency, and there are no known safety concerns with use that require stopping these medications. However, a pause or reduction in effective treatment may be considered annually in those with stable or low frequency migraine (<4 days per month). For reduction, decrease dose slowly over several weeks or extend the time between injections and watch for any return of symptoms or withdrawal effects. Medication should be resumed if the frequency of migraine attacks increases.

My patient still has migraine, so why is the specialist discharging them?

Improvement with CGRP antagonists may be subtle over the first 3 months, but become more apparent over 6 months. Some patients living with migraine will receive only partial improvement and will continue to experience recurrent attacks. Research may provide new treatments in the future. While reducing migraine frequency is a key goal of treatment, it's not the only benefit. Other significant improvements include reducing the severity, duration, and disability associated with migraine attacks, as well as improving a patient's quality of life.

What do I do if the patient's headaches start getting worse?

Migraine will fluctuate in severity. Experiencing 4–6 weeks of increased severity is common and no changes need to be made, especially if triggers are involved. If patients experience temporary worsening of migraine, continue CGRP antagonist use to prevent further exacerbation. Enact any back-up plans provided by the specialist.
Review the Canadian Guidelines for options

Stabilize any stressors. If a patient experiences consistent increases in migraine severity >8 weeks, consult with the referring specialist. Reevaluate patients experiencing new or different migraine for red flags. Some migraine require immediate referral to emergency care.

Becker WJ, et al. Guideline for primary care management of headache in adults. Can Fam Physician. 2015;61(8):670-679. Medrea I, et al. Updated Canadian Headache Society Migraine 19 Prevention Guideline with Systematic Review and Meta-analysis. Can J Neurol Sci J Can Sci Neurol. Published online November 7, 2024:1-23. CGRP Monoclonal Antibodies: access, and coverage - Migraine Canada . November 9, 2019. Product monographs. Gantenbein AR, Agosti R, Gobbi C, Flügel D, Schankin CJ, Viceic D, Zecca C, Pohl H. Impact on monthly migraine days of discontinuing anti-CGRP antibodies after one year of treatment – a real-life cohort study. Cephalalgia. 2021 Oct;41(11–12):1181–1186.

Transitioning Back to Primary Care
Common Questions

How do I monitor this patient?

Review the headache diary: A headache diary (paper based or an app) is a key component of successful migraine management. We recommend the Canadian Migraine Tracker app. Patients should be counselled to assess attack frequency and severity, acute medication use and results, triggers, and specific symptoms. Headache diaries can help to offer the right information to guide therapeutic options. Simple questionnaires can also be used (HIT-6, MIDAS, also available in the Canadian Migraine Tracker app).

ROUTINE BLOOD TESTS OR IMAGING ARE NOT REQUIRED TO MONITOR CGRP MABS

Atogepant is metabolized by the liver (CYP3A4) Reassess if live issues are identified

MONITOR PATIENTS FOR:

Raynaud's phenomenon: CGRP antagonist use may increase Raynaud's phenomenon. If Raynaud's is noted, pause to reassess.

Skin reactions: When using CGRP mAbs, injection site reactions will usually occur during the trial period. If they occur later and are mild, they can be treated with antihistamines or topical steroids. If the reaction is significant, reevaluate CGRP mAb use.

Constipation: Patients can be counselled on signs and management of constipation.

Blood pressure: CGRP blockade may lead to increases in blood pressure. Incidence of hypertension is infrequent, but it has been observed in adverse events databases and cohort studies.

If blood pressure is mildly elevated and the patient responds well to the CGRP antagonist, consider the risk/benefits of adding an antihypertensive medication (candesartan, enalapril, propranolol) with efficacy in migraine prevention.

When should I reconsult the specialist?

If the patient experiences: persistent (>8 weeks) worsening in severity or duration. Temporary flare-ups can be expected, especially in the presence of stressors. Remember that a migraine patient can always experience a new, secondary headache, in which case they should be evaluated for red flags.

Becker WJ, et al. Guideline for primary care management of headache in adults. Can Fam Physician. 2015;61(8):670-679. Medrea I, et al. Updated Canadian Headache Society Migraine Prevention Guideline with Systematic Review and Meta-analysis. Can J Neurol Sci J Can Sci Neurol. Published online November 7, 2024:1-23. CGRP Monoclonal Antibodies: access, and coverage - Migraine Canada . November 9, 2019. Product monographs.

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Common Questions

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STOPPING CGRP ANTAGONISTS

What do I do if a patient needs to start a mAb for another condition?

Check with the specialist prescribing the other medication, however, concurrent mAb use is not usually of concern.

What do I do if a patient needs to have surgery?

There is not usually a need to stop CGRP antagonist use prior to surgery.

Under what circumstances should a patient discontinue CGRP antagonist use?

If a patient experiences a vascular event, pause CGRP antagonist use for 6–8 months. If symptoms are stable and secondary prevention has been optimized, check with the specialist for the green light.

What if a patient wants to consider pregnancy?

CGRP mAbs should be stopped 6 months prior to planned pregnancy due to the long half life and role in placental implantation and pregnancy. Atogepant can be stopped a week before planned conception. The possibility of pregnancy should be discussed at every visit. The CHS website offers more information on hormonal aspects of migraine management.

What can I expect if a patient stops taking their prescribed preventive medication?

The effects of discontinuation vary, with some maintaining benefits longer than others.

Patients may experience:

- ☐ Increased number of monthly migraine days after discontinuation.
- ☐ Return to baseline migraine frequency within 3–4 months of discontinuation.
- ☐ Increased use of acute medications as migraine frequency increases.
- ☐ Chronic migraine, converted to episodic frequency with treatment, may relapse after stopping.
- ☐ Some patients may do well with managing lifestyle factors after a drug holiday.

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COVERAGE

CGRP antagonists cost $500–600 CAD per month and require special authorization or prior approval. The prescriber manages the process with the assistance of patient support programs (PSPs). Most private plans will cover CGRP antagonists if:

- ☐ Patients have tried and failed or intolerant of ≥2 oral medications for migraine prevention
- ☐ Patients have ≥8 migraine days per month
- ☐ Scales are used (HIT-6 or MIDAS) to track scores

Government drug plans offer varying levels of coverage; consider reviewing Exceptional Access Programs. PSPs offered by pharmaceutical companies work with patients and care providers to offer personalized reimbursement navigation and investigation and paperwork assistance.

Renewals are required after six months, and annually thereafter. Patients must demonstrate a minimum reduction of 50% in the average number of migraine days per month, calculated over the past 3 months, compared to baseline. PSPs are usually able to manage changes in insurance companies.

Generic Name	Trade Name	PSP Name	Phone	Fax	Email
Atogepant	Qulipta®	AbbVie Care	833-570-0818	833-570-0188	qulipta@abbviecare.ca
Eptinezumab	Vyepti®	Vyepti TODAY	833-8-VYEPTI (893784)	833-9-VYEPTI (893784)	support@vyeptitoday.ca
Erenumab	Aimovig®	Aimovig GO	855-745-5467	855-888-9188	go.program@novartis.com
Fremanezumab	Ajovy®	Teva Support Solutions	833-302-0121	833-302-0122	TSS@ajovycanada.ca
Galcanezumab	Emgality®	Harmony by Organon	855-433-8130	844-684-6152	support@pspharmonybyorganon.ca

The Canadian Headache Society, **Migraine Canada**, and **Migraine Quebec** have resources available to you. Visit www.headachesociety.ca or scan the QR code with your smartphone's camera to learn more.

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