CHRONIC MIGRAINE

Algorithm for Pharmacists

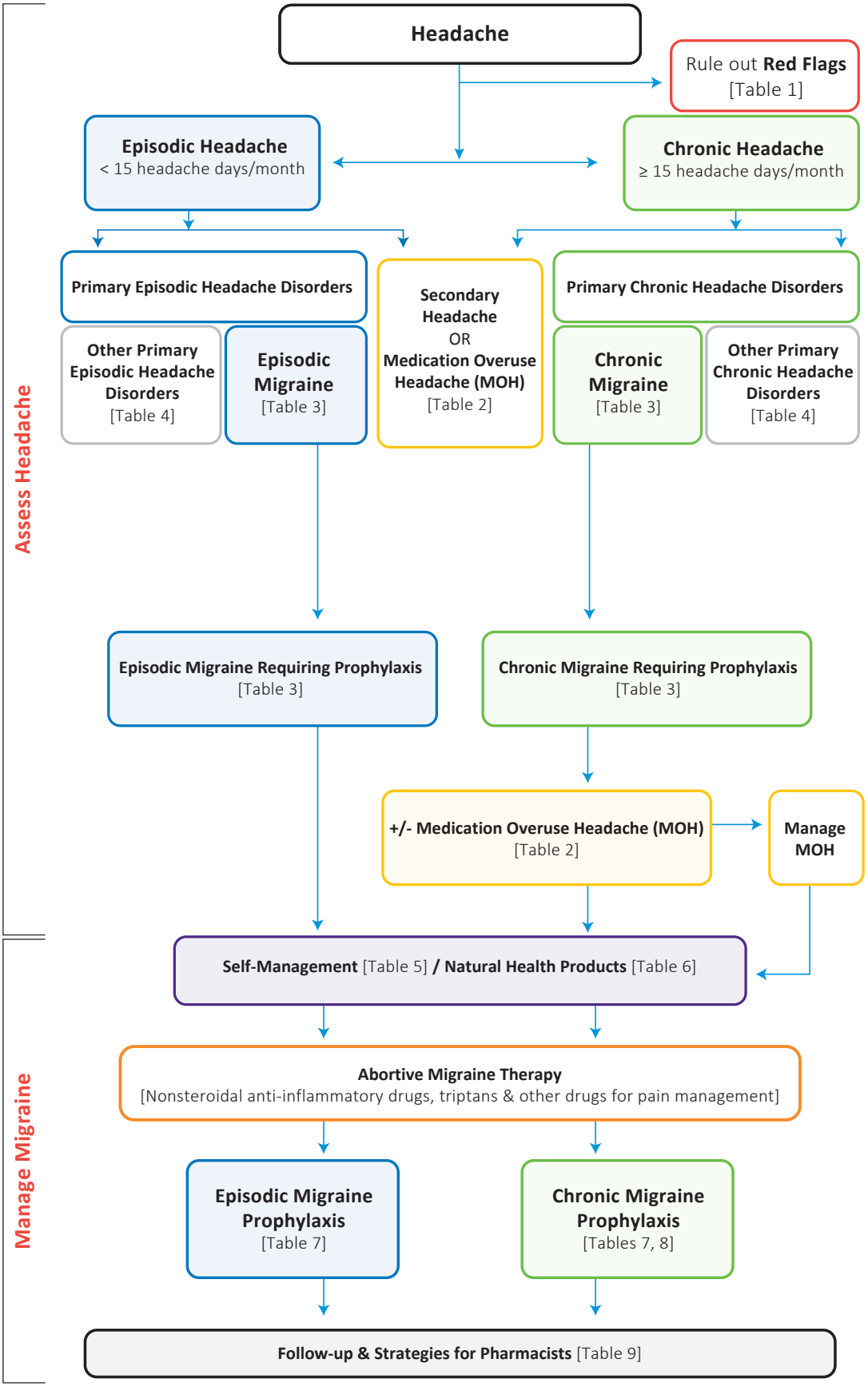

TABLE 1 – Red Flags

Red Flag & Details[1-4]
Systemic signs or symptoms: Fever, weight loss, rash, headache with fever and neck stiffness Secondary risk factors: HIV, cancer, immunosuppression, Lyme disease
Neurologic signs or symptoms: Altered consciousness, visual disturbances, slurred speech, hemiparesis
Onset: "Worst headache of life"; Abrupt, peak intensity reached in seconds to minutes (e.g., thunderclap headache)
Older: New onset headache over 50 years of age and/or signs or symptoms of acute angle-closure glaucoma, temporal arteritis or elderly with new headache and subacute cognitive change
Previous headache history: New (first headache ever), or change in quality, location or frequency of existing headaches
Postural, positional: Changes with exertion, or worsens with Valsalva maneuver
Papilledema: Fleeting disturbances in vision, headache, vomiting, or a combination

TABLE 2 – Secondary Headache and Medication Overuse Headache

Possible Indicators of Secondary Headache[5]

- Unexplained focal signs
- Atypical headaches (not consistent with migraine or tension-type headache)
- Unusual headache precipitants
- Unusual aura symptoms
- Onset after age 50
- Aggravation by neck movement; abnormal neck examination findings (consider cervicogenic headache)
- Jaw symptoms; abnormal jaw examination findings (consider temporomandibular joint disorder)

Medication Overuse Headache (MOH)[1, 5-9]

Consider MOH in patients with chronic daily headache (i.e., ≥ 15 headache days/month) who are using:

- Simple analgesics (e.g., acetaminophen, NSAIDs) on ≥ 15 days/month* for > 3 months; or
- Ergots, triptans, opioids, or combination analgesics with an opioid or barbiturate (e.g., acetaminophen with codeine and caffeine) on ≥ 10 days/month† for > 3 months.

Note: Total use of several different drugs without overuse of any single drug on ≥ 15 days/month* for simple analgesics or ≥ 10 days/month† for ergots, triptans, opioids or combination analgesics is considered overuse.

Table 3 – Diagnostic Criteria for Migraine – Episodic and Chronic[8]

Migraine Diagnostic Criteria

1. Headache attacks lasting 4-72 hours (when untreated or unsuccessfully treated)

AND

2. Headache has ≥ 2 of the following characteristics:
   - Unilateral location
   - Pulsating
   - Moderate to severe pain intensity
   - Interference with, or aggravated by, routine physical activity

AND

3. Accompanied by ≥ 1 of the following:
   - Nausea and/or vomiting
   - Photophobia and phonophobia

+

Episodic Migraine Requiring Prophylaxis < 15 headache days/month[1, 5]	Chronic Migraine Requiring Prophylaxis ≥ 15 headache days/month[8]
• Moderate to severe headache > 3 days/month when abortive medications are not effective, **OR** • Headache > 8 days/month and at risk of medication overuse headache (MOH), **OR** • Recurrent migraine attacks causing considerable disability despite optimal abortive therapy.	Headache on ≥ 15 days per month: • For > 3 months, **AND** • Where ≥ 8 days/month the headaches are migraines.

Table 4 – Other Primary Headache Disorders

Episodic	Features	
Cluster Headache*	Severe or very severe, unilateral headache, lasting 15 minutes to 3 hours with either autonomic features (e.g., tearing, nasal congestion, lid edema, forehead and facial sweating, etc.) on the same side as the headache, or restlessness/agitation	
Episodic Tension-type Headache	Mild to moderate intensity, bilateral headache, lasting 30 minutes to 7-days, non-pulsating (pressing or tightening), not aggravated by routine physical activity; no nausea but photophobia or phonophobia may be present	
Chronic	**Features**	**Duration**
Chronic Tension-type Headache	Mild to moderate intensity, bilateral headache, lasting hours to days, non-pulsating (pressing or tightening), not aggravated by routine physical activity; mild nausea, photophobia or phonophobia may be present	Headache on ≥ 15 days/ month for > 3 months
Hemicrania Continua*	Continuous headache, strictly unilateral pain with autonomic features (e.g., tearing, nasal congestion, lid edema, forehead and facial sweating, etc.) on the same side as the headache and a dramatic indomethacin response	Continuous daily headache for > 3 months
New Daily Persistent Headache	Continuous headache (migraine-like or tension-type like), clearly remembered onset on a remembered day	

Adapted from Bigal ME et al 2007[10], Becker WJ 2017[9], International Headache Society[8].
*Cluster Headache and Hemicrania Continua are part of the Trigeminal Autonomic Cephalalgias (TACs).

TABLE 5 – Self Management Strategies for Migraine[1, 5, 7, 9, 11]

Use a headache diary to monitor headache frequency, intensity, triggers and medication use.

Triggers	Strategies
• Delayed, missed or inadequate meals • Dehydration • Caffeine excess or withdrawal • Alcohol	 Eat ≥ 3 x per day Eat breakfast Avoid > 4 hours without eating during the day  Drink water  Limit coffee to ≤ 1 cup (or equivalent) per day  Limit alcohol
• Lack of regular exercise • Intense exercise • Obesity	 Maintain a healthy BMI  Exercise 3 – 5 x per week
• Irregular or lack of sleep • Stressful lifestyle	 Sleep ≥ 7-8 hours per night Maintain good sleep habits  Use stress managment skills, relaxation therapy, pacing, biofeedback therapy, cognitive behavioural therapy

Table 6 – Natural Health Products for Migraine Prophylaxis* [1, 7, 12-15]

Drug	Dose
Butterbur (*Petasites hybridus* extract†)	75-150 mg/day, once daily or divided BID
Coenzyme Q10	100 mg TID
Riboflavin (vitamin B_2)	400 mg/day, once daily or divided BID
Magnesium citrate‡	300 mg elemental magnesium BID
Vitamin D	2000 IU once daily

* Based on evidence for episodic migraine prophylaxis.
† Use products labelled as free of hepatotoxic pyrrolizidine alkaloids.
‡ Controversial for continuous use in pregnancy. Used for acute treatment of toxemia and headaches.

Table 7 – Maintenance Doses - Episodic and Chronic Migraine Prophylaxis Prescription Therapies[1, 6, 7, 9, 12, 13, 16-19]

Episodic Migraine	Maintenance Dose
Beta-Blockers	
Atenolol	100-150 mg/day
Metoprolol	100-200 mg/day (divided BID; SR once daily)
Nadolol	80-160 mg/day
Propranolol*	40-120 mg BID (or 80-160 mg LA tablet once daily)
Timolol	10 mg BID or 20 mg once daily
Calcium Channel Blockers	
Flunarizine	10 mg HS
Verapamil	240 mg/day (divided TID; SR divided BID)
Angiotensin Receptor Blockers	
Candesartan†	16 mg/day
Antiepileptics	
Divalproex sodium†	750-1,500 mg/day (divided BID)
Gabapentin†	1,200-1,500 mg/day (divided TID), up to 1,800 mg/day
Topiramate†	100-200 mg/day (divided BID)
Antidepressants	
Amitriptyline‡	20-40 mg HS; up to 100-150 mg/day
Nortriptyline	20-40 mg HS; up to 150 mg/day
Venlafaxine	150 mg/day; up to 225 mg/day
Calcitonin Gene Receptor Peptide (CGRP) Blocker	
Erenumab†	70-140 mg SC monthly
Chronic Migraine Prophylaxis	
OnabotulinumtoxinA†	155-195 Allergan Units IM every 12 weeks
Erenumab†	70-140 mg SC monthly
Topiramate†	100-200 mg/day (divided BID)

Note: Drugs in **bold face** have established efficacy and/or are indicated.
* Propranolol is the preferred agent during pregnancy or lactation.
† Not for use in pregnancy. Divalproex sodium: neural tube defects if used in pregnancy. Gabapentin: may cause fetal harm. Topiramate: oral clefts if used in 1st trimester.
‡ Amitriptyline may be considered for use during pregnancy or lactation if propranolol is contraindicated or ineffective.
LA = long acting; SR = sustained release.

Table 8 – Chronic Migraine Prophylaxis Prescription Therapies* [1, 6, 7, 12, 13, 16-19]

Drug / Dose	Points To Consider
OnabotulinumtoxinA injection of 50, 100 & 200 Allergan units† 155-195 Allergan units† IM to multiple sites in the head and neck as per injection protocol, can be repeated every 12 weeks if necessary	• Indicated, and evidence for use, in chronic migraine prophylaxis. • Evidence for efficacy in associated medication overuse headache. • *Adverse effects*: pain at injection sites, neck pain, muscle weakness, brow ptosis, lid ptosis (rare), dysphagia (rare). • Avoid in pre-existing dysphagia, breathing difficulties or muscle weakness, myasthenia gravis (or other neuromuscular transmission disorder), and pregnancy. • Administer by a trained injector: **www.mychronicmigraine.ca**
Erenumab 70 mg/mL injection 70 mg/month, up to 140 mg/month, by SC injection	• Evidence for efficacy in chronic migraine prophylaxis. Indicated for prevention of migraine in adults who have at least 4 migraine days per month. • *Adverse effects:* injection site reactions, nausea, upper respiratory tract infection, constipation, muscle spasms. • Avoid in pregnancy. • May be self-administered.
Topiramate **25, 100 & 200 mg tablets and 15 & 25 mg sprinkle capsules** Start with 25 mg/day; increase slowly up to 100 mg/day, divided BID (up to 200 mg/day divided BID can be used, but with greater risk of adverse effects)	• Evidence for efficacy in chronic migraine and associated medication overuse headache. Indicated in adults for the prophylaxis of migraine headache. • *Adverse effects:* CNS effects (e.g., dizziness, tremor, sedation, cognitive impairment, word finding difficulty), GI effects (e.g., nausea, anorexia), weight loss, paresthesia, renal calculi, oral clefts (if used during the 1st trimester of pregnancy). • Drug interactions (e.g., carbamazepine, phenytoin, CNS depressants, CYP2C19 inhibitors, oral contraceptives, divalproex). • Avoid in kidney stones, renal failure, angle-closure glaucoma, and pregnancy. Caution use in depression and in patients with cognitive concerns.

CNS = central nervous system; GI = gastrointestinal.

* Drugs used in episodic migraine prophylaxis (e.g., beta-blockers, antidepressants, etc.) may be considered in chronic migraine prophylaxis without specific evidence, and may be considered if co-morbidities such as hypertension or anxiety exist.

† The term "Allergan unit" is a specific measurement of toxin activity that is unique to Allergan's formulation of onabotulinumtoxinA.

Table 9 – Follow-up & Strategies for Pharmacists

Clinical Practice	Potential Questions to Ask
1. Identify triggers and recommend self-management strategies, where possible.	Are self management strategies, such as lifestyle/diet changes, being implemented to help manage headaches?
2. Identify potential or actual medication overuse headache (MOH).	Is the patient at risk for MOH? Have the consequences of MOH been discussed?
3. Ensure abortive therapy is appropriate.	Are abortive therapies effective? Are simple analgesics used on $\geq$ 15 days per month? Are ergots, triptans, opioids or combination analgesics with an opioid or barbiturate used on $\geq$ 10 days/month?
4. Identify patients in need of prophylaxis.	How many days a month does the patient have headaches? Of those days, how many are migraines? Are headaches bothersome and significantly affecting their quality of life?
5. Set the patient up with a diary and recommend a regimen of natural health products prior to next physician visit. [Headache diaries available online e.g., **www.migrainecanada.org**].	Would the patient consider tracking headaches and triggers in a headache diary for the next doctor's appointment, to help expedite the treatment process?
6. Review migraine prophylaxis options with patient, considering comorbidities. 7. Assess appropriateness and adherence to prophylaxis regimens, and follow-up.	Is the current chronic prophylaxis therapy working? Is the treatment tolerable?

*Consider creating a therapeutic focus for medication reviews, such as pain management.

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