


	Generic/ TRADE	PREGNANCY CATEGORY	INDICATIONS and CONTRAINDICATIONS (CI)	SIDE EFFECTS	DRUG (DI) INTERACTIONS	COMMENTS	DOSING usual; MAX/24hr	\$ per 6 doses
TRIPANS	Naratriptan AMERGE (1,2.5mg D shaped tab)	C	1st line for severe attacks ♦ ≤40% of all attacks & 25% of all patients do not respond ¹ ; high recurrence rate (~40% @24hr ^{MITREX})	For all: Chest discomfort or tightness (or tightness of neck/throat) facial flushing, tingling & paresthesia, nausea Riza / Zolmi ⇒ dizziness, fatigue, somnolence (8-10%) Suma / Nara ⇒ sulfa allergy?	•Serotonin syndrome (e.g. agitation, excitement, hypomania, myoclonus, tremor, hyperreflexia, ataxia, motor weakness, fever/chills, diarrhea) with concurrent MAOIs, SSRIs, TCAs or lithium. MAOIs = stop at least 2 weeks prior to triptans (except Nara); caution with other agents	•Selective 5HT-1 receptor agonists • Effective any time during an attack but the sooner the better ; for SC IMITREX taking during aura phase may be too early • If failure with one, can try another • Frequent use of triptans can result in rebound & chronic daily headache (MAX weekly/monthly dose? Some clinicians suggest 12-18 doses per month; no supporting data ²) •Less nausea vs DHE but ↑ recurrence rate	1 mg or 2.5mg; may repeat in 4h MAX=5mg/24h	104
	Rizatriptan MAXALT (5,10mg capsule shaped tab; 5,10mg wafer)	C	CI •cardiac or cerebrovascular disease (or risk factors for same) (risk of MI ~1/5,000,000 migraine attacks treated ³)	Differences generally not clinically significant; trends: •Nara = less adverse effects? •Zolmi = more adverse effects? • Suma = 50mg dose appears as effective as 100mg & as well tolerated as 25mg³	•Do NOT use within 24hr of DHE , other ergot preps or other triptans (risk of additive vasoconstriction/coronary vasospasm) •↑ levels of Zolmi (use ≤5mg/24h) with cimetidine,ciprofloxacin & fluvoxamine	SC IMITREX⁴ •best bioavailability/fastest onset ^{-15min} versus oral onset 30-120min Nasal IMITREX, MAXALT Wafer, &/OR ZOMIG RAPIMELT⁴ may be preferred if •fast relief required ^{-15min} •nausea &/or vomiting present	5mg or 10mg; may repeat in 2h MAX 20mg/24h <small>With Propranolol: 5mg; 15mg/24hr</small>	103
	Sumatriptan IMITREX (25,50,100mg DF tab; 5,20mg Nasal spray; 6mg/0.5ml SC inj)	C	•uncontrolled hypertension •?diabetes •hemiplegic or basilar migraine Caution: decrease dose/avoid •Renal dysfunction with nara/suma •Hepatic dysfn with all triptans •aspartame ZOMIG Rapimelt, MAXALT wafer ⇒ caution in PKU pts EDS Criteria:Treat migraine headache (Age >18 or <65)	♦ baseline cardiac evaluation/ECG recommended for ♂ >40yr & ♀ >50yr		AMERGE⁴ - slowest onset but •better tolerability, less drug interactions •longest duration •lowest recurrence rate	50-100mg PO; may repeat in 2h (MAX 200mg/24h) 5mg or 20mg in one nostril; may rpt in 2h (MAX 40mg/24h) 6mg SC; may rpt x1in 1h; (MAX 12mg/24h)	104 104 289
	Zolmitriptan ZOMIG (2.5mg tab; 2.5mg ZOMIG Rapimelt tab)	C	♦Almotriptan AXERT 6.25-12.5mg tab may repeat x1 in 2hr; similar to po sumatriptan; \$100/6 doses. ♦Frovatriptan FROVA 2.5mg; may repeat after 2hr. MAX 3tabs/24hrs; long t½. ? less effective but less recurrence: Approved by FDA, but not yet available in Canada:				1.25mg or 2.5mg; may repeat after 2hr MAX 10mg/24h <small>With Propranolol ↓ zolmi dose</small>	103
ERGOTS	Dihydroergotamine DHE MIGRANAL /generic (1mg/ml inj) (4mg/ml nasal spray) NOTE: pump 4Xs into the air to prime nasal spray for 1 st use.	X	1st line agent for severe & ultra-severe attacks (for status migrainosus, pre-dose antiemetic, e.g. metoclopramide, x2-3 days) CI •cardiac or cerebrovascular disease(or risk factors);uncontrolled hypertension, ?diabetes, pregnancy •hemiplegic or basilar migraine Caution: renal/hepatic dysfunction	Metoclopramide MAXERAN, REGLAN alone sometimes effective Chest discomfort, tingling & paresthesia, nausea, drowsiness, dizziness, diarrhea, muscle cramp Nasal spray = rhinitis, taste disturbance but ↓ nausea ♦ baseline cardiac evaluation/ECG recommended for ♂ >40yr & ♀ >50yr	•Do NOT use within 12hr of triptans or 24hrs for naratriptan⁵ (risk of additive vasoconstriction/coronary vasospasm) •↑ toxicity (eg. severe ischemia) of ergot preps: with clarithromycin, erythromycin, itraconazole, propranolol, & protease inhibitors	•Non-selective 5HT agonist • More nausea than triptans but less chest pain •May precede with 10mg metoclopramide, or prochlorperazine ^{5-10mg} esp. if severe attack requiring repeat doses or if nausea present • IV = rapid onset but more adverse effects so reserve for severe attack ⁵ • SC = slower response rate vs IMITREX but longer acting & lower recurrence rate at 24hr ⁶ • Nasal spray =response rate similar to oral triptans, or nasal IMITREX⁵	0.5-1mg q1h SC, IM or IV;repeat q1h to MAX 3x/24h <small>(IV 1mg/50ml over ≥15min)</small> 1 spray into <u>each</u> nostril stat;repeat in 15 minutes prn MAX 4 spray/attack; 8 sprays/24h	32 \$ 39 per 1 pkg (3 bottles X4 doses per bottle)
	Ergotamine/ caffeine (1/100 tab ⁵ , supp) CAFERGOT	X	2nd line due to ↓ efficacy & ↑ toxicity	Chest discomfort/ pain, tingling & paresthesia, nausea, vomiting, dizziness, drowsiness, diarrhea, muscle cramps		•Non-selective 5HT agonist • Most nausea of all abortive preps ; recent meta-analysis ?'s efficacy as mainly appeared to ↑ N&V ⁷ • Overuse associated with ergotism (vasoconstriction with numbness, tingling, paresthesia, gangrene of the extremities, headaches, convulsion, and abdominal & chest pain) and chronic daily headache	2 tab SL stat, then 1 tab Q30-60min, MAX 6tab/24h;10/wk 1 cap PO stat (MAX 4cap) then repeat Q30min; MAX 6cap/24h;10/wk	11 13
	Ergotamine/ caffeine/diphenhydramine ERGODRYL 1/100/25 cap	X	CI •cardiac or cerebrovascular disease(or risk factors),uncontrolled hypertension, ?diabetes, pregnancy •hemiplegic or basilar migraine Caution: renal/hepatic dysfunction	CAFERGOT-PB Supp & ERGOMAR SL – DC'd by manufacturer				
NONSPECIFIC ANALGESICS	NSAIDs ie high dose ASA, ibuprofen, naproxen Na+ or naproxenK ⁺ ANAPROX ^{xv}	C/D B/D	Treatment of mild-moderate attack CI •hypersensitivity to ASA/NSAID (ie bronchospasm, nasal polyps) Caution: if cardiovascular or renal disease; GI ulcer risk.	•GI irritation/upset/bleed, dizziness, fatigue, rash •Renal impairment esp. if CrCl <30ml/min	•↑ bleeding with warfarin & antiplatelet agents •Displaces DVA & older sulfonyleureas so ↑ toxicity •May blunt effect of some antihypertensives •others	• Overuse (ie >3x/wk) leads to rebound headache & to medication-induced chronic daily headache ; for short-term & intermittent use •Enteric ASA too slow. Buffered ASA OK •Fast acting (e.g. ANAPROX) may be useful	ASA 650-1300mg po q4h X2 (MAX 4g/24h) Ibuprofen 400-800mg po q4-6h X2 (MAX 3.2g/24h) ANAPROX 275-550mg po q4-6h X2 (MAX 1.65g/24h)	\$ 1 \$ 1 OTC _{200mg} \$ 15
	Combo analgesics (292s, TYLENOL #3 , FIORINAL X, others)	C	Treatment of mild-moderate attack if: •not relieved with simple analgesics •vasoconstrictors are contraindicated acetaminophen TYLENOL ▽ B : doses of ~1gram sometimes effective if taken early	Drowsiness, dysphoria, nausea, constipation (esp. with codeine)	•Products with ASA similar to above •Additive effects with other CNS depressants	• Overuse associated with rebound & medication induced headache (esp. caffeine combos); for short-term & intermittent use • Dependency potential •may mask pain without affecting underlying pathophysiology	1-2 tabs/caps stat: may repeat 3-4h prn MAX 6-8 tabs/caps per 24h	T3=\$ 7 292=\$ 8 Fc/≈ \$ 15
	Butorphanol X 10mg/ml nasal spray (previous STADOL)	C	Reserve for rescue treatment or when DHE/triptans ineffective or contraindicated	Drowsiness, dysphoria, nausea & vomiting, nasal irritation (Dose ~ 1mg/spray)	•↑ CNS depression: CNS depressants, MAOIs, alcohol	• Dependency potential •Mixed agonist-antagonist so can precipitate withdrawal in persons addicted to opiates	1 spray in 1 nostril; may repeat in 3-5hr MAX 16 sprays/24h	\$ 55 (15 doses)

†CORONARY VASOSPASM POTENTIAL: still greatest concern; recent metaanalysis showed no clinically important differences between agents therefore one unlikely to be "safer" than others⁸; ⇒patient selection & counseling important!
ADJUNCT AGENTS: ♦metoclopramide 10mg SC/IV (IV: 10mg /50ml over ≥15min); 5-10mg PO ♦chlorpromazine 5-25mg IV (10-25mg PO) q4-6h (IV: pretreat with ≥ 500ml NS) ♦domperidone 10-40mg PO (or 60mg PR) tid-qid ♦prochlorperazine **STEMETIL** 5-10mg IV (25mg PR) q8h

	Generic/ TRADE	PREGNANCY CATEGORY	INDICATIONS AND CONTRAINDICATIONS CI	SIDE EFFECTS	DRUG (DI) INTERACTIONS	COMMENTS	DOSING range / typical	\$  /month
TCAs	Amitriptyline ELAVIL /generic (10, 25, 50, 75 ^x mg tab)	C	1st line esp. if associated depression, chronic pain, or tension-type headache	Anticholinergic effects: dry mouth, constipation, etc.; dizziness, drowsiness , postural hypotension, weight gain	Avoid with MAOI, cisapride, clonidine ↑ effects with MAOI, anticholinergics, other CNS depressants ↑ effect with CCBs, SSRIs cimetidine, phenothiazines, cipro (↓ TCA metabolism)	•Central neuromodulator of noradrenaline & serotonin (5HT) system • Start low & titrate up to help ↓ side effects; may give single dose at bedtime (nortriptyline ~2x more potent than amitriptyline) • Caution in elderly ⇒ anticholinergic effects	30-150mg/d 100mg po hs 150mg po hs	21 27
	Nortriptyline AVENTYL /generic (10, 25mg cap)	D	CI •severe cardiac, kidney, liver, prostate or thyroid disease; glaucoma, hypotension •seizures •MAOI use	Nortriptyline ⇒ less drowsiness, dry mouth & weight gain than amitriptyline; but less evidence			10-150mg hs 50mg po hs 100mg po hs	21 33
β-BLOCKERS	Metoprolol LOPRESOR /generic (25 ⁵ , 50 ⁵ , 100 ⁵ mg tab, SR 100, 200mg)	C/D	1st line Can reduce frequency and some effect on intensity and duration	Fatigue, bradycardia, hypotension, coldness of extremities, depression, impotence, sleep disturbance, bronchospasm	↑ levels of rizatriptan (↓ dose of riza to 5mg) ↑ risk of peripheral ischemia with ergots ↑ cardiovascular effects with CCBs, clonidine ↑ levels of β-blocker with cimetidine, fluoxetine Altered hypo-glycemic effect with sulfonylureas	•Modulation of central catecholaminergic system & brain serotonin •May be class effect however β-blockers with intrinsic sympathomimetic activity may not be effective (data from small/poorly designed trials) ⁹ • Timolol 20-30mg/day & nadolol also used • Start low & titrate up •If failure with one → may try another β-blocker •Taper slowly before stopping to prevent rebound	Metopr 50-200mg/d 50mg po bid 100mg SR po od Atenolol 50-150mg/d 100mg po od Propran 80-240mg/d 80mg po bid 120mg LA po od	13 16 20 12 33
	Atenolol (25, 50 ⁵ , 100 ⁵ mg tab)		CI •asthma, heart block or uncompensated heart failure, peripheral vascular disease					
	Propranolol INDERAL /generic (10 ⁵ , 20 ⁵ , 40 ⁵ , 80 ⁵ & 120 ⁵ mg tab; LA 60, 80, 120, 160mg)	C/D						
CCBs	Flunarizine SIBELIUM (5mg cap)	X	Reduce frequency but little effect on intensity or duration CI •CHF, arrhythmias, hypotension (pregnancy with flunarizine) Caution: β-blockers, Parkinsons Verapamil ~1st line option expert opinion	Flunarizine: fatigue, weight gain, depression , parkinson like side effects (EPS) Verapamil: bradycardia, hypotension, constipation , nausea, edema, headache	↑ effect of CNS depressants Verapamil = many DIs ASA, barbs, β-blockers, carbamazepine, cimetidine, digoxin, erythromycin, ketoconazole, lithium, statins & theophylline	•? modulate transmitters rather than vasodilation • Maximum effect may take several months • Overall benefit similar to β-blockers •Flunarizine seldom used; Verapamil used more than flunarizine, but less studied •Verapamil good prophylaxis → cluster headache	5-10mg/d 5mg po hs 10mg po hs starting dose 240-320mg/d 240mg SR po od	26 45 31
	Verapamil ISOPTIN , others (120, 180 ⁵ , 240 ⁵ SR tab/cap)	C						
ANTICONVULSANT	Divalproex (DVA) EPIVAL /generic (125, 250, 500mg EC tab; 1000mg/10ml vial ^x) {may also use valproic acid but more SE's}	D	1st line for severe migraine (↓ severity and duration) but little effect on mild-moderate attacks; •useful for SSRI induced migraine & prolonged atypical migraine aura CI •liver disease Caution: children → hepatotoxicity Monitor: CBC, Platelets, LFT (Level 350-830 umol/l – trough) -see comments column →	Nausea, tremor, weight gain, alopecia, ↑ liver enzymes, diarrhea (transient & can be minimized by starting low & titrating up); polycystic ovary Rare: ↓ platelets (↓ dose helps) & WBC, hepatotoxic , skin rx's, pancreatitis Neural tube defects → spina bifida 1-2%.	↑ ASA & warfarin effect ↑ Valproic acid level by: ASA, cimetidine, erythromycin, fluoxetine, isoniazid & salicylates ↓ Valproic acid level by: carbamazepine, cholestyramine, lamotrigine, phenobarbital, phenytoin, primidone, rifampin & topiramate Valproic acid ↑s levels of: amitriptyline, carbamazepine epoxide (ie. ↑ SE), clonazepam, diazepam, lamotrigine lorazepam, phenobarbital & warfarin	•Modulation of GABA receptors? •Prodrug of valproic acid • Divalproex less GI effects than valproic acid •Monitor LFTs initially: if ↑ enzymes, then ↓ dose; if 2-3x normal → stop drug Lamotrigine (LAMICTAL) – no better than placebo Topiramate (TOPAMAX) 100-200mg/day efficacious ^{10,11} ; although one study not very impressive (28d frequency ↓ from 3.83 to 3.31) ¹² -see drug details from RxFiles charts page 45 or 49	500-1500mg /d 125mg po bid cc 250mg bid-tid cc 500mg po bid cc 500mg po tid cc {cc= with meals}	15 22-28 35 50
	Lamotrigine LAMICTAL Topiramate TOPAMAX							
5HT-2	Pizotiline/pizotifen SANDOMIGRAN (0.5mg, DS = 1 ⁵ mg tab)	C	2nd line (seldom used) CI •?diabetes, heart disease, glaucoma, urinary retention, prostatic hypertrophy, renal/hepatic dysfunction	Weight gain, fatigue, weak anticholinergic effects	Additive effects with: CNS depressants, anticholinergics	•Serotonin-2 receptor antagonist •Somnolence so begin low & dose at bedtime (ie 0.5mg hs)	Start 0.5mg po hs titrate to 0.5mg tid (or 1.5mg po hs) MAX 6 mg/day	20 44 69 (1mg tid)
ERGOTS	Methysergide SANSERT (2mg tab)	X	3rd line - for prevention of severe recurrent migraine unresponsive to other agents (seldom used) CI •hypertension, cardiac, liver, kidney, lung & collagen diseases •thrombophlebitis & pregnancy	Retropuritoneal, cardiac & pulmonary fibrosis ⇒ do not use for >6 months duration without weaning & a 1-2 month drug holiday! Nausea, muscle cramps, weight gain, claudication, hallucinations	• Do NOT use within 24hr of triptans (risk of ↑ vasoconstriction/spasm) ↑ toxicity of ergots with clarithromycin, erythromycin, propranolol & protease inhibitors	•Serotonin-2 receptor antagonist with carotid vasoconstrictor effect •Active metabolite •If no effect after 3 week trial , not likely to help •Taper dose over 2-3 weeks before stopping!	2-8mg/d 2mg po bid cc 2mg po tid cc	62 90

NON-PHARMACOLOGICAL AGENTS: riboflavin (Vit B2) 400mg/day, magnesium 400-600mg/day, feverfew **TANACET** 125mg/d. •**BOTOX** injection – effective (~q3mons¹³) for some pts •↓ dose for renal dysfunction

PROPHYLACTIC THERAPY should be considered if: •migraines severe enough to impair quality of life or patient has ≥ 3 severe attacks per month which fail to respond to abortive therapy.

TIPS: •use one prophylactic agent at a time •**start low & titrate up**; once effective dose reached, continue for **minimum 3 month trial** to evaluate effectiveness (benefits usually seen after 1-2 months) • efficacy depends on **withdrawal of analgesics** causing rebound or chronic daily headache •if single agent ineffective, may try a **combination** (eg beta blocker + TCA); consider neuro consult if no response •continue effective therapy for **9-12 months; discontinue gradually** to prevent rebound • **Success of prophylaxis** considered to be ↓ in severity or frequency of headache by 50%

CI =contraindication **CNS**=central nervous system **DI**=drug interaction **LFT**=liver function test **SE**=side effect **SR**=sustained release **\$**=total cost Sask. **x**Non-formulary in SK **⊖**EDS status SK **▼**covered NIHB **⊙**not NIHB **⊗**prior NIHB **⊘**=scored tab

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