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## Neurologic Disorders: Headache in Children

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Headaches occur commonly in children and adolescents. They may occur as a primary disorder such as migraine, or accompany systemic disorders or infectious diseases. In Canada, more than 25% of 12- to 13-year-olds experience headache at least weekly.<sup>1</sup> The prevalence of migraine shows an increase with age, i.e., 2.4% in 12- to 14-year-olds and 5% in 15- to 19-year-olds.<sup>2</sup>

Migraine in children is usually associated with at least one of the following: vomiting, photophobia, family history of migraine.

### Goals of Therapy

- Make an accurate diagnosis of headache<sup>3</sup>
- Relieve or abort pain and associated symptoms
- Prevent further headaches

### Investigations ( [Figure 1 - Investigations Based on Headache Profile](#) )

- The history is the key to the diagnosis of headache and should be obtained from both parent and child with attention to:
  - specific questions such as where pain began, progress, duration, frequency, relieving and aggravating factors (especially sleep loss, excitement, certain foods, relief with activity) and associated symptoms such as vomiting and photophobia
  - specific neurologic symptoms such as seizures, visual disturbances, difficulty with balance, personality change, weakness
  - symptoms suggestive of renal, cardiac, dental or infectious disease
  - degree of interference with school and social life, e.g., pedMIDAS questionnaire<sup>4</sup>
  - analgesic use
  - child's growth and development, behaviour, academic function

*Note:* During the interview, observe interaction between parent and child.

- Physical examination:
  - blood pressure, vital signs, palpation of sinuses, examination of teeth, neck stiffness, examination of optic fundi
  - height, weight, head circumference
  - thorough neurologic examination including cranial nerves, muscle tone, power and reflexes and coordination tests
- Investigations:
  - sinus x-rays if sinusitis suspected
  - CT followed by lumbar puncture with measurement of opening pressure if pseudotumor cerebri suspected based on history of raised intracranial pressure with a negative CT
  - lumbar puncture if infectious process suspected
  - CT and/or MRI if abnormal neurologic examination, decreased visual acuity, recent behaviour change, increasing severity and frequency of headaches, or if headache does not fit a known pattern
- The routine use of any diagnostic study is not indicated when the clinical history has no associated risk factors and the child's examination is normal<sup>5</sup>

## Tension-type Headache

Therapeutic Choices

[Nonpharmacologic Choices](#)

[Pharmacologic Choices](#)

## Therapeutic Choices

### Nonpharmacologic Choices

- Psychological evaluation
- Relaxation therapy
- Biofeedback

### Pharmacologic Choices

- Simple analgesics (**acetaminophen, ASA**) and NSAIDs, such as **ibuprofen** or **naproxen**, are effective for the treatment of acute tension-type headache ([Table 1](#)). Because of the possible association with Reye's syndrome, avoid ASA in children and adolescents for headache or fever associated with viral illness such as influenza or chickenpox.<sup>6</sup>
- **Amitriptyline** ([Table 2](#)) is effective in reducing headache frequency and severity.<sup>7, 8</sup> Preventive therapy may be appropriate when headaches are frequent and significantly disabling and disruptive.

### Medication-overuse Headache

The occurrence of headache induced by chronic use of analgesics, such as acetaminophen and NSAIDs, is now recognized in pediatric patients. Treatment involves education and gradual withdrawal of analgesic drugs. Consider use of a prophylactic agent ([Table 2](#)).<sup>9</sup>

### Migraine

Therapeutic Choices

[Nonpharmacologic Choices](#)

[Pharmacologic Choices](#)

## Therapeutic Choices

### Nonpharmacologic Choices

After exclusion of mass lesion or other causes:

- Provide reassurance and information about the headache condition.
- Discuss triggers of migraine, e.g., lack of sleep, too much sleep, excitement, foods, stress, menstruation.
- Encourage sleep at the time of headache and medication early in the course of the headache.
- Biofeedback and relaxation therapy are effective.

### Pharmacologic Choices

These can be divided into medication given at the time of the headache (symptomatic) and medication to prevent headache (prophylactic).<sup>10</sup>

#### Symptomatic Treatments ([Table 1](#))

##### Analgesics

Intermittent oral analgesics, given as early in the course of the headache as feasible, are the mainstay of pharmacologic management of childhood migraine. **Acetaminophen, ibuprofen** and **ASA** are effective at appropriate doses.<sup>11</sup> As for tension-type headache, avoid ASA in children and adolescents for fever or headache associated with viral illness such as

varicella or influenza. Two evaluations of the evidence for treatment of migraine in children concluded that ibuprofen and acetaminophen are effective.<sup>[10](#), [12](#), [13](#)</sup>

Combination products containing ASA, caffeine and butalbital ± codeine (e.g., Fiorinal) should generally be avoided, but may be appropriate in exceptional circumstances when initial agents fail. These sedating drugs have abuse potential and should be reserved for adolescents (12–18 years) for brief periods only. Take care to avoid unnecessary opioids.

### Antiemetics

Nausea and vomiting occur in up to 90% of young migraine sufferers and besides being disabling, inhibit oral administration of analgesics. Antiemetics alone (e.g., **chlorpromazine**,<sup>[14](#)</sup> **prochlorperazine**, **metoclopramide**) are surprisingly effective in relieving all symptoms including the headache.<sup>[15](#)</sup>

### Ergot Derivatives

Ergotamine compounds have very limited use in pediatrics for the following reasons:

- Auras are uncommon and inconsistent; therefore, warning indicators that trigger the time to treat with ergot are often unreliable.
- Ergots can exacerbate gastrointestinal upset.
- Ergots are contraindicated in complicated migraine syndromes because of the risk of increasing vasospasm.

Oral dihydroergotamine showed no significant difference in headache improvement in a study comparing it with placebo.<sup>[16](#)</sup> In severe intractable headache, dihydroergotamine can be used iv in combination with an antiemetic in the emergency department.<sup>[17](#)</sup>

### Triptans

**Of the 7 agents available in Canada (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan and zolmitriptan), only almotriptan is specifically approved for use in children aged 12–18 years, though several triptans have been shown to be safe in this age group.<sup>[13](#),[18](#),[19](#)</sup> The best evidence exists for nasal sumatriptan, shown to be safe and effective for acute migraine pain in adolescents 12 years and older.<sup>[20](#),[21](#),[22](#)</sup> Consider triptans for use in adolescents with moderate to severe migraine that is unresponsive to conventional analgesics [Evidence: SORT B].<sup>[13](#),[18](#),[19](#)</sup>** Useful Info? Unpleasant taste is a common side effect.

### Prophylactic Agents ([Table 2](#))

A practice parameter on the pharmacologic treatment of childhood migraine examined the evidence for efficacy of several medications.<sup>[10](#)</sup> Although many are in current use and may be effective, only **flunarizine** was deemed probably effective based on evidence. Flunarizine has been shown to significantly reduce headache frequency and severity in children.<sup>[23](#), [24](#)</sup>

Although evidence of its efficacy is lacking, **pizotifen** (pizotyline) may be helpful.

Evidence for **propranolol** is conflicting, although it is commonly used and is effective in some cases.<sup>[25](#)</sup> Propranolol is contraindicated in reactive airway disease, diabetes mellitus and bradyarrhythmias. Symptoms of depression are an under-reported but common side effect in adolescents.

Despite a lack of evidence of efficacy, **cyproheptadine**, an antihistamine with antiserotonergic and calcium channel blocking properties, is widely used as a prophylactic agent. Its use in older children and adolescents is limited by sedation and increased appetite/weight gain.

**Amitriptyline** has shown efficacy in adults; studies in children are limited.<sup>[8](#), [26](#)</sup>

NSAIDs reduce headache frequency and severity in adults, presumably through prostaglandin inhibition. Although evidence of efficacy in children is lacking, **naproxen sodium** can be tried in adolescents as prophylaxis (see Therapeutic Tips).

**Valproic acid** has been studied in children;<sup>[27](#), [28](#)</sup> however, there is insufficient evidence to recommend its use.<sup>[10](#)</sup> Phenobarbital and phenytoin are no longer used.

**Topiramate** is approved for migraine prophylaxis in adults. While not specifically approved for use in children it is used in adolescents.<sup>[8](#), [29](#), [30](#)</sup>

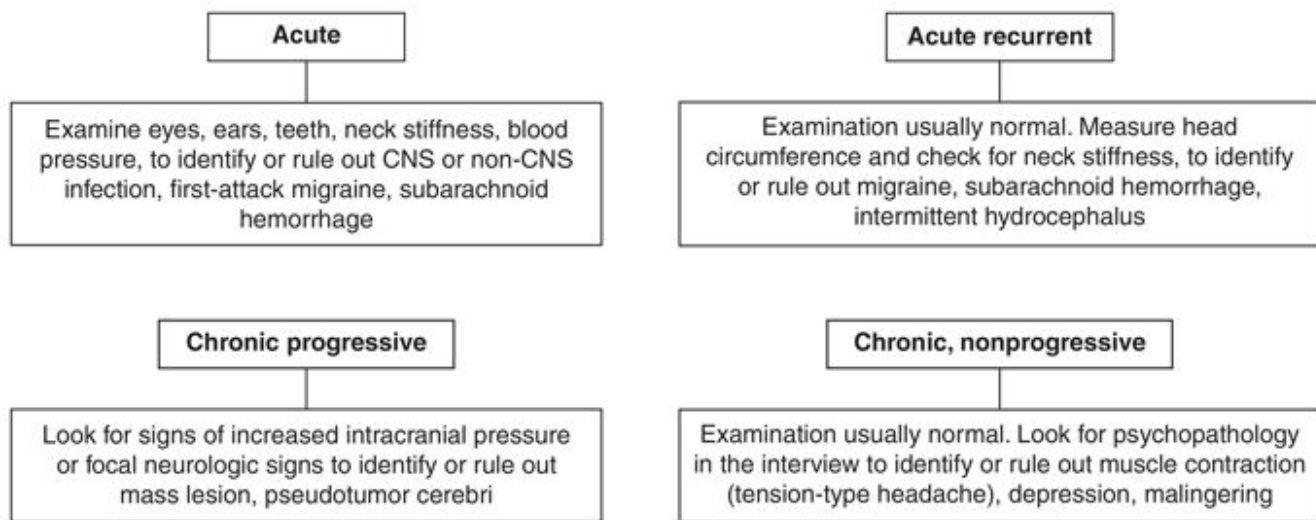
**Riboflavin** 200 mg/day may be effective in reducing migraine frequency and intensity of migraine.<sup>31</sup>

### Therapeutic Tips

- There are very few controlled trials of pharmacologic management of childhood migraine; hence, anecdotal experience prevails. Most young patients with migraine do not require daily medication but need access to reliable analgesia at home and at school.
- Children are debilitated by nausea and vomiting and benefit greatly from antiemetics. Rest and sleep are usually very helpful.
- Consider prophylactic agents for children who cycle through periods of time when they experience such frequency of headache that their lifestyle is disrupted, or when isolated or infrequent events are severe and complex.
- For prophylaxis, consider medications with the fewest side effects first. Cyproheptadine is usually used in *younger children*. For *adolescents*, consider using propranolol, amitriptyline, naproxen sodium or flunarizine.
- A period of 6–12 months is a reasonable trial of prophylactic medication, followed by very gradual tapering and discontinuation to assess ongoing need.
- Calendars/diaries are helpful in identifying triggers, headache patterns, frequency and severity and are invaluable for management and evaluation of response to therapy.
- The prognosis for children with migraine is favourable with 50% of patients reporting improvement within 6 months after medical intervention, regardless of treatment methods used.
- Most children respond to reassurance, general advice and simple remedies for attacks when they occur.

### Algorithm

**Figure 1 - Investigations Based on Headache Profile**



### Drug Tables


**Table 1:** Drug Treatment of Headache in Children

Class	Drug	Dose <sup>a</sup>	Adverse Effects	Drug Interactions	Comments	Cost <sup>b</sup>
Analgesics	<a href="#">acetaminophen</a> <a href="#">Atasol Preparations</a> , <a href="#">Tempra</a> , <a href="#">Tylenol</a> , generics	10–15 mg/kg/dose Q4H prn	GI upset; liver toxicity in overdose.	May enhance anticoagulant effect of warfarin, particularly with doses of >1.3 g/day for >1 wk	Analgesics are the most commonly used abortive medications for headache. Limit use to <15 days per mo to avoid medication-overuse headache.	\$

Class	Drug	Dose <sup>a</sup>	Adverse Effects	Drug Interactions	Comments	Cost <sup>b</sup>
Analgesics	<a href="#">ASA</a> <a href="#">Aspirin</a> , Coated Aspirin, generics	Age ≥12 y: single dose of 500–650 mg per headache	GI upset (usually the only more common adverse effect when single doses are used to treat acute headache). For a detailed description of adverse effects associated with continuous or frequent NSAID use, see , Table 2.	Warfarin: increased anticoagulant effect.	Because of the concern of Reye's syndrome, ASA should <i>not</i> be used in the context of headache or fever associated with a viral illness; do not use more frequently than Q4–6H.	\$
Analgesics	<a href="#">ibuprofen</a> <a href="#">Advil</a> , <a href="#">Motrin</a> , <a href="#">Motrin Children's</a> , generics	5–10 mg/kg/dose, up to 4 times daily	GI upset (usually the only more common adverse effect when single doses are used to treat acute headache). For a detailed description of adverse effects associated with continuous or frequent NSAID use, see , Table 2.	Warfarin: increased anticoagulant effect.		\$
Analgesics	<a href="#">naproxen sodium</a> <a href="#">Aleve</a> , Anaprox, Maxidol, generics	Age >2 y: 5–7 mg/kg/dose Q8–12H prn	GI upset (usually the only more common adverse effect when single doses are used to treat acute headache). For a detailed description of adverse effects associated with continuous or frequent NSAID use, see , Table 2.	Warfarin: increased anticoagulant effect.		\$
Analgesics, combination	<a href="#">butalbital</a> + ASA + <a href="#">caffeine</a> ± <a href="#">codeine</a> <a href="#">Fiorinal</a> , <a href="#">Fiorinal C1/4</a> , <a href="#">C1/2</a> , generics	Adolescents: 50–100 mg (1–2 tablets) up to 4 times daily	GI upset; dependence and tolerance to barbiturates	Possible additive sedation with other CNS	Should generally be avoided. May be appropriate in exceptional circumstances. Limit use	\$\$

Class	Drug	Dose <sup>a</sup>	Adverse Effects	Drug Interactions	Comments	Cost <sup>b</sup>
			and opioids.	depressants, e.g., alcohol.	to adolescents, no more than 2 days/wk, 7 days/month. Risk of tolerance, addiction and misuse.	
Antiemetics	<a href="#">chlorpromazine</a> generics	Oral/IM: 1 mg/kg to a maximum of 25 mg Q8H IV: 0.1 mg/kg Q10–15 min prn to a maximum of 30 mg	Hypotension.	Possible additive sedation with other CNS depressants, e.g., alcohol.	Can cause hypotension when given iv; used in the emergency department.	\$
Antiemetics	<a href="#">metoclopramide</a> PMS-Metoclopramide, other generics	IV: Adolescents: 0.1– 0.2 mg/kg ( $\leq 10$ mg) single dose May repeat once if necessary; maximum 20 mg	Extrapyramidal dysfunction.	Possible enhanced sedative effect of alcohol.	Use iv in adolescents in the emergency department. See also dihydroergotamine.	\$
Antiemetics	<a href="#">prochlorperazine</a> generics	Oral: 2.5–5 mg BID prn IV: Adolescents: 10 mg	Extrapyramidal dysfunction.	Possible additive sedation with other CNS depressants, e.g., alcohol.	Used iv in adolescents in the emergency department.	\$
Ergot Derivatives	<a href="#">dihydroergotamine injection</a> generics	>6 years: 0.1–0.25 mg/dose iv May repeat Q20 min $\times$ 3  Give metoclopramide 0.2 mg/kg/dose (maximum 20 mg) 30 min prior to iv dihydroergotamine	Flushed feeling, tingling in extremities, nausea and vomiting.	Do not use with potent inhibitors of CYP3A4 such as cimetidine, clarithromycin, efavirenz, erythromycin, itraconazole, ketoconazole and ritonavir.	Useful in patients with severe and prolonged migraine headache; protocol to take place in hospital; contraindicated in complicated migraine, coronary heart disease, abnormal blood pressure, abnormal ECG.	\$\$
Ergot Derivatives	<a href="#">dihydroergotamine nasal spray</a> <a href="#">Migranal</a>	>6 years: 1 spray into each nostril May repeat in 15 min if required	Nausea, taste disturbance, rhinitis.	Do not use with potent inhibitors of CYP3A4 such as cimetidine, clarithromycin, efavirenz, erythromycin, itraconazole, ketoconazole and ritonavir.	Contraindicated in complicated migraine, coronary heart disease, abnormal blood pressure, abnormal ECG.	\$\$
Triptans	<a href="#">almotriptan</a> <a href="#">Axert</a> , generics	$\geq 12$ y: Oral: 6.25 mg at start of headache; if headache returns, dose may be repeated after 2 h;	Chest discomfort, fatigue, dizziness, paresthesias, drowsiness,	All triptans: Do not use with ergotamine-containing products. Caution with	Consider for adolescents 12–18 years unresponsive to conventional analgesics; do not use if any cardiac-like symptoms;	\$\$\$

Class	Drug	Dose <sup>a</sup>	Adverse Effects	Drug Interactions	Comments	Cost <sup>b</sup>
		no more than 2 doses in a 24-h period	nausea, throat symptoms.	SSRIs. Do not use a triptan within 24 h after another triptan. Almotriptan: Do not use with MAOIs. Inhibitors of CYP3A4 (e.g., cimetidine, clarithromycin, efavirenz, erythromycin, grapefruit juice, itraconazole, ketoconazole and ritonavir) may increase bioavailability of almotriptan.	contraindicated in ischemic heart disease, sustained hypertension, pregnancy, basilar or hemiplegic migraine; use less than 10 days/mo to avoid medication-overuse headache.	
Triptans	<i>eletriptan</i> <a href="#">Relpax</a> , generics	≥12 y: Oral: 20–40 mg as soon after headache onset as possible; if initial dose is 20 mg and headache returns after ≥2 h, may repeat 20 mg dose; maximum 40 mg in a 24-h period	Chest discomfort, fatigue, dizziness, paresthesias, drowsiness, nausea, throat symptoms.	All triptans: Do not use with ergotamine-containing products. Caution with SSRIs. Do not use a triptan within 24 h after another triptan. Eletriptan: Contraindicated within 72 h of the following inhibitors of CYP3A4: clarithromycin, itraconazole, ketoconazole, nelfinavir and ritonavir, or any potent inhibitor of CYP3A4.	Consider for adolescents 12–18 years unresponsive to conventional analgesics; do not use if <i>any</i> cardiac-like symptoms; contraindicated in ischemic heart disease, sustained hypertension, pregnancy, basilar or hemiplegic migraine; use less than 10 days/mo to avoid medication-overuse headache.	\$\$\$
Triptans	<i>frovatriptan</i> <a href="#">Frova</a>	≥12 y: Oral: 2.5 mg; if headache recurs after initial relief, may repeat in 4–24 h; maximum 5 mg/24 h	Chest discomfort, fatigue, dizziness, paresthesias, drowsiness, nausea, throat symptoms.	All triptans: Do not use with ergotamine-containing products. Caution with SSRIs. Do not use a triptan within 24 h after another triptan. Frovatriptan: Oral contraceptives and propranolol may increase frovatriptan	Consider for adolescents 12–18 years unresponsive to conventional analgesics; do not use if <i>any</i> cardiac-like symptoms; contraindicated in ischemic heart disease, sustained hypertension, pregnancy, basilar or hemiplegic migraine; use less than 10 days/mo to avoid medication-overuse headache.	\$\$\$\$

Class	Drug	Dose <sup>a</sup>	Adverse Effects	Drug Interactions	Comments	Cost <sup>b</sup>
				serum concentrations by 30–60%.		
Triptans	<a href="#">naratriptan</a>  <a href="#">Amerge</a> , generics	≥12 y: Oral: 1 mg at start of headache; if partial response or headache returns, dose may be repeated once after 4 h; maximum dose of 5 mg in a 24-h period	Chest discomfort, fatigue, dizziness, paresthesias, drowsiness, nausea, throat symptoms. Naratriptan may be associated with fewer side effects than the other triptans.	All triptans: Do not use with ergotamine-containing products. Caution with SSRIs. Do not use a triptan within 24 h after another triptan.	Consider for adolescents 12–18 years unresponsive to conventional analgesics; do not use if <i>any</i> cardiac-like symptoms; contraindicated in ischemic heart disease, sustained hypertension, pregnancy, basilar or hemiplegic migraine; use less than 10 days/mo to avoid medication-overuse headache.	\$\$\$
Triptans	<a href="#">rizatriptan</a> <a href="#">Maxalt</a> , <a href="#">Maxalt RPD</a> , generics	≥12 y: Oral: 5–10 mg (tablet or wafer) at start of headache Do not repeat if no relief from first dose; if headache returns 2 h or more after partial or complete relief from an initial 5 mg dose, may repeat 5 mg dose (daily maximum 10 mg)	Chest discomfort, fatigue, dizziness, paresthesias, drowsiness, nausea, throat symptoms.	All triptans: Do not use with ergotamine-containing products. Caution with SSRIs. Do not use a triptan within 24 h after another triptan. Rizatriptan: Do not use with MAOIs. Use with caution in patients taking propranolol (increased bioavailability of rizatriptan).	Consider for adolescents 12–18 years unresponsive to conventional analgesics; do not use if <i>any</i> cardiac-like symptoms; contraindicated in ischemic heart disease, sustained hypertension, pregnancy, basilar or hemiplegic migraine; use less than 10 days/mo to avoid medication-overuse headache. Fastmelt wafers can be taken without water.	\$\$\$\$
Triptans	<a href="#">sumatriptan</a> <a href="#">Imitrex Nasal Spray</a> , <a href="#">Imitrex DF</a> , generics	≥12 y: 25 mg tablet or 20 mg nasal spray at start of headache Do not repeat if no relief from first dose; if headache returns 2 h or more after first dose, may repeat dose (daily maximum 2 doses)	Chest discomfort, fatigue, dizziness, paresthesias, drowsiness, nausea, throat symptoms. Nasal spray may cause taste disturbance.	All triptans: Do not use with ergotamine-containing products. Caution with SSRIs. Do not use a triptan within 24 h after another triptan. Sumatriptan: Do not use with MAOIs.	Consider for adolescents 12–18 years unresponsive to conventional analgesics; do not use if <i>any</i> cardiac-like symptoms; contraindicated in ischemic heart disease, sustained hypertension, pregnancy, basilar or hemiplegic migraine; use less than 10 days/mo to avoid medication-overuse headache. Faster onset with nasal spray than with oral formulations.	\$\$\$
Triptans	<a href="#">zolmitriptan</a> <a href="#">Zomig</a> , <a href="#">Zomig Rapimelt</a> , <a href="#">Zomig Nasal Spray</a> ,	≥12 y: 2.5–5 mg (tablet, orally dispersible tablet or nasal spray) at start of headache	Chest discomfort, fatigue, dizziness, paresthesias,	All triptans: Do not use with ergotamine-containing products.	Consider for adolescents 12–18 years unresponsive to conventional analgesics; do not use if <i>any</i> cardiac-like	\$\$\$



Class	Drug	Dose <sup>a</sup>	Adverse Effects	Drug Interactions	Comments	Cost <sup>b</sup>
	generics	Do not repeat if no relief from first dose; if headache returns 2 h or more after first dose, may repeat dose (daily maximum 2 doses)	drowsiness, nausea, throat symptoms. Nasal spray may cause taste disturbance.	Caution with SSRIs. Do not use a triptan within 24 h after another triptan. Zolmitriptan: Do not use with MAOIs. Maximum dose of 5 mg/24 h if also taking fluvoxamine or cimetidine.	symptoms; contraindicated in ischemic heart disease, sustained hypertension, pregnancy, basilar or hemiplegic migraine; use less than 10 days/mo to avoid medication-overuse headache. Zolmitriptan orally dispersible tablets can be taken without water.	

<sup>a</sup>. Not to exceed maximum adult dose.

<sup>b</sup>. Cost per dose, based on 20 kg body weight; includes drug cost only.




Dosage adjustment may be required in renal impairment; see [Appendices: Dosage Adjustment in Renal Impairment](#).

Legend: \$ < \$1    \$\$ \$1-5    \$\$\$ \$5-10    \$\$\$\$ \$10-15

**Table 2:** Drugs Used for Prophylaxis of Headache in Children

Class	Drug <sup>a</sup>	Dose	Adverse Effects	Drug Interactions	Comments	Cost <sup>b</sup>
Antiepileptic Drugs	<i>topiramate</i> <a href="#">Topamax</a> , generics	Adolescents: Start at 25 mg daily, increase by 25 mg daily at weekly intervals to 100 mg/day in 1 or 2 divided doses	Most common: somnolence, anorexia, weight loss, paresthesias. Less common: psychomotor slowing, metabolic acidosis.	Avoid use with alcohol or other CNS depressants.	Used in adolescents.	\$\$\$
Antihistamines	<i>cyproheptadine</i> generics	Age 2-6 y: 2 mg Q8-12H (maximum 12 mg/day)  Age 7-14 y: 4 mg Q8-12H (maximum 16 mg/day)	Drowsiness, weight gain.	Possible additive sedation with other CNS depressants, e.g., alcohol.	More useful in younger children; use in older children and adolescents limited by sedation and increased appetite/weight gain.	\$\$
Beta <sub>1</sub> -adrenergic Antagonists	<i>propranolol</i> generics	Oral: 0.6-1.5 mg/kg/day in 2-3 divided doses	Fatigue, bradycardia, hypotension, depression.	Antacids may decrease absorption.	Contraindicated in asthma, diabetes, heart block, bradyarrhythmias, pregnancy; avoid abrupt withdrawal.	\$
Calcium Channel Blockers	<i>flunarizine</i> generics	Oral: 5 mg/day	Bradycardia, hypotension, depression,	Additive sedation with other CNS depressants.	May take several weeks to be effective; do not	\$\$

Class	Drug <sup>a</sup>	Dose	Adverse Effects	Drug Interactions	Comments	Cost <sup>b</sup>
			drowsiness.		use in depressed patients or those with extrapyramidal disorders.	
NSAIDs	<a href="#">naproxen sodium</a>  <i>Aleve</i> , Anaprox, Maxidolgenerics	Adolescents: 220–550 mg twice daily	For a detailed description of adverse effects associated with continuous NSAID use, see , Table 2.	Warfarin: increased anticoagulant effect. Antihypertensives (diuretics, beta-blockers, ACE inhibitors, alpha-blockers): possible reduction in antihypertensive effect; may require additional antihypertensive therapy.  Lithium may interfere with sodium/water balance. Monitor lithium levels when NSAID added.	Used in adolescents.	<i>Aleve</i> NonRx: \$\$ Rx: \$\$
Tricyclic Analgesics (TCAs)	<a href="#">amitriptyline</a> Elavil	10–150 mg/day	Weight gain, drowsiness; anticholinergic symptoms such as dry mouth and constipation.	Possible additive sedation with other CNS depressants, e.g., alcohol; metabolized by cytochrome P450 enzyme system —clearance may be affected by inhibitors (e.g., erythromycin, fluoxetine, fluvoxamine, isoniazid, itraconazole, ketoconazole, paroxetine, valproic acid), inducers (e.g., phenobarbital, carbamazepine, phenytoin, rifampin) or other substrates of these enzymes.	Contraindicated in significant cardiac disease or hypotension.	\$
Serotonin Antagonists	<a href="#">pizotifen</a> Sandomigran/ Sandomigran DS	Oral: 0.5–1.5 mg/day in divided doses	Sedation and weight gain.	Possible additive sedation with other CNS depressants including alcohol.	Start medication slowly and increase over 1– 3 wk.	\$\$-\$\$\$

<sup>a</sup>. Not to exceed maximum adult dose.

<sup>b</sup>. Cost of 30-day supply based on 20 kg body weight; includes drug cost only.



Dosage adjustment may be required in renal impairment; see [Appendices: Dosage Adjustment in Renal Impairment](#).

Abbreviations: NonRx=nonprescription; Rx=prescription product

Legend: \$ < \$10    \$\$ \$10–20    \$\$\$-\$\$\$\$ \$10–30    \$\$\$\$ \$20–30

### Suggested Readings

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