Chapter 1
COVID-19

Canadian Pharmacists Association
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Information on the rapidly evolving understanding of the epidemiology and pathophysiology of coronavirus disease 2019 (COVID-19), caused by the novel coronavirus SARS-CoV-2, can be found at:

- Public Health Agency of Canada (PHAC)
- World Health Organization (WHO)
- Centers for Disease Control and Prevention (CDC)
- National Institute for Health and Care Excellence (NICE)

**Symptoms and clinical characteristics**

Available data indicates that symptoms and clinical characteristics of COVID-19 may include:[1][2]

- Asymptomatic carriage
- Acute mild/moderate illness (80%) – any of the following symptoms alone or in combination:
  - fever (>37.8°C)
  - cough (with or without sputum production)
  - shortness of breath
  - myalgia, malaise, anorexia, headache
  - loss of smell and/or taste[3]
  - less commonly: conjunctivitis,[4] diarrhea, other GI symptoms, rhinorrhea, sore throat, neurological symptoms
- Acute severe (15%)/critical (5%):
  - two lung phenotypes, probably occurring sequentially
    - atypical viral pneumonitis (hypoxemia with relatively compliant lungs)
    - classic acute respiratory distress syndrome (ARDS) (stiff lungs)
  - nonrespiratory organ dysfunction: renal failure, liver dysfunction, cardiac dysrhythmia
  - hyperinflammation syndromes (“cytokine storm”)

- Risk factors for symptomatic disease and progression to critical illness:
  - age >50 y, substantial risk >70 y
  - male
  - obesity
  - comorbidities: cardiovascular disease, diabetes, chronic respiratory disease, hypertension, cancer, chronic kidney disease

This chapter provides information for primary care practitioners on:
Management of select common symptoms of COVID-19: fever, cough, headache/myalgia
Experimental treatments being used in acute-care settings

**Goals of Therapy**
- Prevent spread
- Alleviate symptoms
- Prevent complications where possible

**Prevention**
Information on various issues related to the prevention of COVID-19 is available as indicated below:
- Handwashing, hygiene, cleaning, physical distancing: Health Canada: Coronavirus disease (COVID-19): prevention and risks
- Homemade or cloth masks: Health Canada: Considerations in the use of homemade masks to protect against COVID-19
- Personal protective equipment (PPE): Canadian Pharmacists Association: Suggested best practices for pharmacies during the COVID-19 pandemic

There is currently no evidence that any pharmacological agent, vitamin or herbal supplement is effective in the prevention of COVID-19. Several prevention trials investigating vaccines and medications are ongoing (see Government of Canada, Vaccines and treatments for COVID-19: List of all COVID-19 clinical trials authorized by Health Canada).

**Therapeutic Choices**
Health Canada guidance on the treatment of patients with COVID-19 can be found at Clinical management of patients with moderate to severe COVID-19 - Interim guidance.

Information on the management of select common symptoms of COVID-19: fever, cough, headache/myalgia is presented in this chapter.

For general information on the management of GI symptoms (less common), see the Compendium of Therapeutic Choices: Nausea in Adults and Diarrhea and the Compendium of Therapeutics for Minor Ailments: Nausea and Vomiting and Diarrhea.

**Fever**
There is no evidence regarding the management of fever due to COVID-19 specifically, but the following information regarding management of patients experiencing fever in general may be helpful. See also Fever.
- Children <6 months of age with a fever should be assessed by an appropriate health-care practitioner.[5]
- In a pregnant patient who is in her first trimester, the goal of antipyresis is protection of the fetus.[6][7]
- There are many arguments against treating a fever:[8][9][10][11][12]
  - Fever is an important defence mechanism; it enhances the immune response.
  - Fever is usually self-limiting and, though sometimes distressing, the associated symptoms of fever (mild dehydration, discomfort, febrile delirium, febrile seizures) are usually not harmful.
Use of antipyretics may impair the use of temperature as an important clinical tool for monitoring the progress of an infection or response to antibiotics.

**Nonpharmacologic Choices**

**General** interventions for reduction of fever and associated discomfort include:[5]
- Removal of excess clothing and bedding
- Increased fluid intake to replace insensible water loss during fever
- Maintenance of ambient temperatures around 20–21°C
- Avoidance of physical exertion

**Physical methods** for heat reduction use convection, evaporation or conduction to counteract the body's attempt to maintain a higher temperature set-point (fever). Pharmacologic methods are preferred because they lower the hypothalamic set-point.[13] In the rare instance where core temperatures exceed 41–42°C, physical methods may be used in addition to pharmacologic methods.
- Sponging with tepid or cold water uses evaporation to dissipate body heat. Sponging with alcohol is not recommended as it may be absorbed through the skin, inhaled or accidentally ingested by the patient; it has also been associated with hypoglycemia, intoxication and coma.[14][15]
- Ice packs or cooling (hypothermia) blankets may be applied to the skin to lower body temperature by conduction.
- Circulating fans, sometimes directed over ice before reaching the patient, use convection to transfer heat away from the skin surface.

**Pharmacologic Choices**

The decision to use antipyretics must be individualized. The goal should be reduction of fever rather than “normal” body temperature. Assessment of the patient should not depend solely on the elevation of temperature.
- Acetaminophen is safe and effective in children and adults.[16]
- ASA, ibuprofen and naproxen are also effective antipyretics and may be used in the treatment of fever due to COVID-19, keeping the following in mind:
  - Evidence to date suggests that older people (>60 y) and those with underlying medical conditions are at higher risk of severe COVID-19. As NSAIDs should be used with caution in these populations, it is reasonable to avoid NSAIDs in the elderly and in those with comorbid conditions (e.g., cardiovascular disease, renal disease, chronic respiratory disease). If the use of an NSAID is unavoidable in these patients, it should be at the lowest effective dose and for the shortest duration.[16]
  - ASA is not recommended in children or adolescents because of the potentially increased risk of Reye syndrome.[17]
  - Naproxen is not approved/recommended in children <12 years of age.
- Some clinicians recommend alternating acetaminophen and ibuprofen administration to reduce fever; however, there is insufficient evidence to support this as a routine practice and it is not recommended.[6][18][19] No difference was found in patient discomfort in 2 trials that assessed it.[19] Potential risks of prescribing 2 antipyretics may include confusion and dosing errors with associated toxicity.

For more detailed information on medications used in the management of fever, see Table 2.
Cough

There is no evidence regarding the management of cough due to COVID-19 specifically, but the following general information regarding management of patients experiencing acute cough may be helpful. See also Acute Cough.

Nonpharmacologic Choices

- Avoid exposure to inhaled irritants such as smoke, dust, pollutants and allergens, which can further exacerbate any cough.
- Although evidence is lacking, hydration with oral liquids and humidification of room air may be beneficial. Room humidifiers used as preventive measures should be well cleaned to avoid aerosolizing mould.

Pharmacologic Choices

Overall, there is little evidence for or against the effectiveness of nonprescription cough medicines.[20]

- Nonprescription antitussives act centrally to suppress cough. Antitussives are not recommended when a cough performs a useful function. If used by a patient with a productive cough, more mucus is retained.[21]
  - Dextromethorphan and codeine are commonly used to treat cough related to upper respiratory tract infections, although there is little evidence for efficacy.[20] The American College of Chest Physicians does not recommend centrally acting cough suppressants for cough secondary to upper respiratory tract infections.[22]
- Expectorants are reported to reduce sputum viscosity, permitting more effective removal of secretions from the respiratory tract. There is a lack of evidence to support the efficacy of expectorants: they do not thin sputum nor increase sputum volume, even at doses higher than recommended.[21]
  - Guaifenesin is purported to enhance cough effectiveness by promoting the clearance of airway secretions.[23]
  - Adequate hydration with oral liquids and inhalation of humidified air is perhaps the best protussive or “expectorant” measure.
  - Note that the cough associated with COVID-19 infection has generally been reported as dry in most patients, further limiting the already questionable usefulness of expectorants.
- Various other agents have been used for the management of cough, generally based on limited and/or poor-quality evidence.
  - Honey has demulcent, antioxidant and antibacterial effects. It is proposed that the demulcent effect may act to decrease cough. It may be an effective cough suppressant in children; no studies in adults are available.[23][24]
  - Zinc lozenges have been used to alleviate cough due to the common cold. However, meta-analyses have concluded there is insufficient evidence to recommend zinc preparations.[23] In addition, zinc can be associated with unpleasant taste, mouth irritation and nausea.
  - Anesthetic lozenges containing ingredients such as benzocaine, phenol and menthol may reduce the sensitivity of peripheral nociceptors. They have been used as antitussives, but evidence for efficacy is poor. Rarely observed side effects include tingling or irritation at the site of administration and hypersensitivity reactions.
  - Bronchodilators such as salbutamol or formoterol are recommended only for cough due to obstructive lung disease such as asthma or COPD.[25]

For more detailed information on medications used in the management of cough, see Table 2.
Headache and myalgias

There is no evidence regarding the management of headache and/or myalgia due to COVID-19 specifically, but the following general information regarding management of patients experiencing these symptoms may be helpful. See also Headache in the Compendium of Therapeutics for Minor Ailments as well as Headache in Adults, Acute Pain and Influenza in the Compendium of Therapeutic Choices.

Nonpharmacologic Choices

- Simple measures such as resting in a dark, quiet room and applying a cold cloth/ice pack to the head are helpful for headache, although not evidence-based.

Pharmacologic Choices

The following medications are effective for alleviating headache and myalgia:

- **Acetaminophen** can be used for mild to moderate pain. Compared with full-dose NSAIDs, acetaminophen has fewer adverse effects and drug interactions but is less effective and has no anti-inflammatory action.[26]

- **ASA, ibuprofen and naproxen** are effective anti-inflammatory analgesics. They may be useful for the treatment of headache and myalgia in patients with COVID-19, keeping the following in mind:
  - Evidence to date suggests that older people (>60 y) and those with underlying medical conditions are at higher risk of severe COVID-19. As NSAIDs should be used with caution in these populations, it is reasonable to avoid NSAIDs in the elderly and in those with comorbid conditions (e.g., cardiovascular disease, renal disease, chronic respiratory disease). If the use of an NSAID is unavoidable in these patients, it should be at the lowest effective dose and for the shortest duration.[16]
  - ASA is not recommended in children or adolescents because of the potentially increased risk of Reye syndrome.[17]
  - Naproxen is not approved/recommended in children <12 years of age.

- Headache and myalgia due to COVID-19 seem to respond adequately to acetaminophen or NSAIDs; it is unlikely that stronger analgesics such as opioids would be required.

For more detailed information on medications used in the management of headaches and myalgias, see Table 2.

Experimental therapies for COVID-19

Numerous medications are being used on an experimental basis for the management of COVID-19. Use of any of these medications for the prevention or treatment of confirmed or suspected COVID-19 outside of a clinical trial or acute-care setting on the advice of an infectious disease specialist is inappropriate.[31]

Experimental therapies are being used in the acute-care setting in severely ill patients as well as earlier in the illness or in uninfected patients in attempts to prevent progression or spread of the disease. Information about COVID-19-related clinical trials being conducted in Canada can be found at Government of Canada, Vaccines and treatments for COVID-19: List of all COVID-19 clinical trials authorized by Health Canada. Some treatments are also being used on a compassionate-release basis outside of approved clinical trials.

Information about the rationale for use, dosage, adverse effects, drug interactions and safety during pregnancy or breastfeeding of select trial medications can be found in Table 1.
Table 1: Select Experimental Therapies for COVID-19

<table>
<thead>
<tr>
<th>Drug</th>
<th>Rationale for Use</th>
<th>Dosage</th>
<th>Adverse Effects</th>
<th>Drug Interactions</th>
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<tbody>
<tr>
<td>Azithromycin</td>
<td>Used in combination with hydroxychloroquine for a potential synergistic antiviral effect and to prevent concurrent bacterial infections (e.g., pneumonia).</td>
<td>500 mg on first day then 250 mg daily PO x 4 days</td>
<td>GI upset, rash, cholestatic hepatitis, QTc interval prolongation.</td>
<td>Use cautiously with other drugs that cause QTc prolongation (e.g., hydroxychloroquine). May increase warfarin effect; increased concentrations of substrates of CYP3A4 (potent inhibitor), e.g., atorvastatin, carbamazepine, digoxin, lovastatin, simvastatin. Pregnancy: considered safe. Breastfeeding: low levels in milk, not expected to cause adverse effects in the infant.</td>
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<tr>
<td>Baricitinib</td>
<td>Janus kinase (JAK1 and JAK 2) inhibitor predicted to reduce the ability of the virus to infect lung cells.</td>
<td>2 mg daily PO x 10 days</td>
<td>Increased risk of serious infections, malignancy and thrombosis; increased CPK, hypercholesterolemia, pharyngitis, nausea, UTI, hypertension, URTI, headache.</td>
<td>Enhanced immunosuppression with other immunosuppressants. Pregnancy: limited data, animal studies have shown teratogenic effects. Breastfeeding: no data available.</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>Unpublished Chinese trials suggest benefit in reducing exacerbations of pneumonia, shortening disease course and decreasing viral load.</td>
<td>Adults ≥50 kg: 500 mg BID PO x 7 days Adults &lt;50 kg: 500 mg BID PO x 2 days followed by 500 mg daily PO x 5 days</td>
<td>Nonallergic pruritus in African Canadians, nausea, vomiting, headache, bitter taste, QTc interval prolongation. Rare retinal toxicity (patients with underlying macular disease at an increased risk).</td>
<td>Decreased metabolism of beta-blockers. May increase digoxin levels. Increased risk of QTc prolongation with other QTc-prolonging agents and strong CYP3A4 inhibitors. Pregnancy: considered safe. Breastfeeding: no information on daily use during breastfeeding but is given directly to infants for malaria prophylaxis.</td>
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<tr>
<td>Colchicine</td>
<td>Anti-inflammatory effect may reduce complications due to hyperinflammation (cytokine storm syndrome).</td>
<td>0.5 mg BID x 3 days followed by 0.5 mg daily x 27 days</td>
<td>Abdominal pain and cramps, diarrhea, nausea and vomiting. Possible neuropathy, myopathy, bone marrow suppression.</td>
<td>May increase levels of HMG Co-A reductase inhibitors; monitor for statin myotoxicity (muscle pain, weakness). Monitor for colchicine toxicity (GI symptoms, fever, leukopenia) if also taking known inhibitors of CYP3A4 (e.g., antiretroviral drugs, clarithromycin, erythromycin, itraconazole, ketoconazole, verapamil) or Pgp (e.g., cyclosporine). Fatalities have been reported with clarithromycin, which inhibits both CYP3A4 and Pgp. Pregnancy: generally recommended to avoid unless benefit outweighs risk; however, a systematic review did not show increased risk of malformations or miscarriage. Breastfeeding: no adverse effects reported in infants. Highest milk levels occur 2–4 h after dosing; delay breastfeeding until 4 h postdose or take dose immediately after nursing.</td>
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(cont’d)
Table 1: Select Experimental Therapies for COVID-19 (cont’d)

<table>
<thead>
<tr>
<th>Drug</th>
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<tbody>
<tr>
<td><strong>Corticosteroids</strong></td>
<td>Studies in sepsis have shown positive effects on mortality and resolution of shock.</td>
<td>50 mg hydrocortisone IV Q6H x 7 days (or while in septic shock)</td>
<td>Fluid retention, hypertension, Cushing syndrome, hyperglycemia, adrenal suppression, GI upset, psychiatric effects.</td>
<td>Avoid grapefruit juice.</td>
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<td>Pregnancy: not associated with increased risk of major malformations; possible increased risk of oral cleft.[41] Breastfeeding: no data on transfer of hydrocortisone into milk, though not expected to be present in levels harmful to the infant. There is more evidence of safety for other systemic corticosteroids (e.g., methylprednisolone).</td>
</tr>
<tr>
<td><strong>Hydroxychloroquine</strong></td>
<td>Demonstrated potent in-vitro activity against SARS-CoV-2 (i.e., COVID-19).</td>
<td>Pre-exposure prophylaxis: 400–800 mg PO daily x 1–4 days followed by 400 mg weekly Post-exposure prophylaxis: 400–800 mg PO daily x 1–5 days followed by 200–400 mg daily x 7–11 days Treatment: various doses under investigation</td>
<td>Nonallergic pruritus in African-Canadians, nausea, vomiting, headache, bitter taste, QTc interval prolongation.[a] Rare retinal toxicity (patients with underlying macular disease at increased risk).</td>
<td>Decreased metabolism of beta-blockers. May increase digoxin levels. Increased risk of QTc prolongation with other QTc-prolonging agents (e.g., azithromycin) and strong CYP3A4 inhibitors; QT monitoring may be required.[a] Increased risk of hypoglycemia with blood glucose-lowering agents. Pregnancy: limited data do not indicate significant risk; CDC considers it safe for the prevention of malaria. Breastfeeding: low levels in milk; no adverse effects reported.</td>
</tr>
<tr>
<td><strong>Lopinavir/ritonavir</strong></td>
<td>Has activity (in vitro and/or in animal models) against SARS-CoV-1; MERS-CoV. Ritonavir is added to lopinavir to increase its half-life</td>
<td>Treatment: 400/100 mg BID PO x 14 days or until discharge from hospital</td>
<td>GI upset, liver enzyme elevations, hyperlipidemia, and PR and QTc interval prolongation.[a] Possible</td>
<td>Numerous serious drug interactions; consult a reputable drug interaction checker or resource. Pregnancy: registry data for use in pregnant women with HIV has not shown increased risk of malformations.[42]</td>
</tr>
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</table>
Table 1: **Select Experimental Therapies for COVID-19 (cont’d)**

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<tr>
<td><strong>Remdesivir</strong></td>
<td>Has activity in vitro and in animal models against SARS-CoV-1; MERS-CoV.</td>
<td>200 mg IV daily on day 1 followed by 100 mg IV daily for up to 10 days</td>
<td>Generally well-tolerated. GI effects. Aminotransferase elevations.</td>
<td>Remdesivir effect possibly decreased by CYP3A4 inducers: dexamethasone (at high doses or for prolonged duration), rifabutin, rifampicin, carbamazepine, phenobarbital, phenytoin, primidone, St. John’s Wort.</td>
</tr>
<tr>
<td><strong>Ruxolitinib</strong></td>
<td>Janus kinase (JAK1 and JAK 2) inhibitor: Theoretically, may reduce complications due to hyperinflammation (cytokine storm syndrome).</td>
<td>10 mg BID x 14 days followed by 5 mg BID x 2 days then 5 mg daily x 1 day</td>
<td>Anemia, thrombocytopenia, neutropenia, bruising, dizziness, headache.</td>
<td>Ruxolitinib exposure may be increased by fluconazole and other strong CYP3A4 inhibitors and decreased by strong CYP3A4 inducers.</td>
</tr>
<tr>
<td><strong>Sarilumab</strong></td>
<td>IL-6 monoclonal antibody: Theoretically, may reduce complications due to hyperinflammation (cytokine storm syndrome).</td>
<td>Single IV dose (“low” dose vs. “high” dose being studied)</td>
<td>Increased risk of serious infections, injection-site reactions, URTIs, elevated ALT levels.</td>
<td>May decrease the concentration of CYP3A4 substrates by restoring CYP3A4 activity in some patients.</td>
</tr>
</tbody>
</table>

Breastfeeding: data from use in HIV has not caused concern. Pregnancy: no data, weigh benefit vs. risk. Breastfeeding: transfer into milk is unknown; there is a single case report of direct use in an infant with Ebola without adverse effects.[43]

Pregnancy: no data, weigh benefit vs. risk. Breastfeeding: no data available. Highly protein bound: milk levels predicted to be low. Manufacturer recommends not to breastfeed until 2 wk after last dose. Pregnancy: no data, weigh benefit vs. risk. Breastfeeding: no data available. Large protein molecule: milk levels predicted to be low and any ingested drug expected to be destroyed in infant’s GI tract.
### Table 1: Select Experimental Therapies for COVID-19 (cont’d)

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<tr>
<th>Drug</th>
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<th>Dosage</th>
<th>Adverse Effects</th>
<th>Drug Interactions</th>
<th>Safety in Pregnancy and Breastfeeding[32][33][34][35]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tocilizumab</td>
<td>IL-6 monoclonal antibody: theoretically, may reduce complications due to hyperinflammation (cytokine storm syndrome).</td>
<td>8 mg/kg (up to max of 800 mg) x 1 dose IV, repeated once prn if symptoms worsen or show no improvement</td>
<td>Infusion reactions (very severe reactions resulting in death have been reported rarely), serious infections, GI perforation, increased neutrophils, decreased platelets, neutropenia, elevated ALT, increased lipids.</td>
<td>May increase CYP450 enzyme activity—monitor concurrent therapy with drugs metabolized by CYP450.</td>
<td>Pregnancy: limited data have not shown increased risk of major defects. Breastfeeding: limited data show small amounts in milk. Case reports have not reported adverse effects in infants.</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>Has been studied with respect to lessening organ dysfunction secondary to sepsis based on experimental evidence of anti-inflammatory and antioxidant properties.</td>
<td>50 mg/kg Q6H IV x 4 d</td>
<td>Diarrhea, increased risk of renal stones in predisposed individuals.</td>
<td>Urinary acidifier in large doses, the excretion of drugs that are weak acids or bases may be decreased or increased respectively. May reduce the effect of warfarin, cyclosporine, amphetamines, bortezomib.</td>
<td>Pregnancy: data limited, crosses the placenta, possibly resulting in above-normal levels in fetus. Upper tolerable limit 2000 mg/day during pregnancy.[44] Breastfeeding: no data on high-dose IV use. Milk levels predicted to be high and predispose infant to kidney stones. If used, avoid breastfeeding for 12–24 h after dose.</td>
</tr>
</tbody>
</table>

*Abbreviations: ACE2 = angiotensin-converting enzyme 2; ALT = alanine transaminase; ARB = angiotensin receptor blocker; ARDS = acute respiratory distress syndrome; CDC = Centers for Disease Control and Prevention; CPK = creatine phosphokinase; CYP = cytochrome P; GI = gastrointestinal; IL = interleukin; MERS-CoV = Middle East respiratory syndrome coronavirus; NSAID = nonsteroidal anti-inflammatory drug; Pgp = p-glycoprotein; SARS-CoV = severe acute respiratory syndrome coronavirus; URTI = upper respiratory tract infection; UTI = urinary tract infection.*

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**Choices during Pregnancy and Breastfeeding**

**Management of COVID-19 during pregnancy**

General information on what is known thus far with respect to COVID-19 and pregnancy can be found on the Society of Obstetricians and Gynecologists of Canada website.

**Fever, headache, myalgia:** acetaminophen is considered the drug of choice. ASA and NSAIDs may be considered as alternatives during the first or second trimester, but are not recommended in the third trimester.[32]

**Cough:** codeine has the most evidence of safety during pregnancy and dextromethorphan can be considered as an alternative.[32] Available data do not support an association between guaifenesin use during pregnancy and congenital defects. Liquid products containing guaifenesin may contain high alcohol content. Products with high alcohol content should be avoided during pregnancy.[45] Honey is safe to consume during pregnancy. **Zinc** is considered safe in pregnancy, provided the recommended...
daily maximum zinc intake (40 mg)\[^{[46]}\] is not exceeded. The safety of other ingredients in any zinc-based lozenges must also be assessed.

Experimental therapies: see Table 1.

**Management of COVID-19 during breastfeeding**

General information on breastfeeding and COVID-19 can be found through the Canadian Paediatric Society, the PHAC and the WHO. Continuation of breastfeeding is recommended, as breast milk is considered an insignificant route of transmission for other respiratory viruses. If the mother is infected, wearing a mask, respiratory etiquette and hand hygiene are recommended.\[^{[47]}\]

*Fever, headache, myalgia:* acetaminophen is considered the drug of choice. Anti-inflammatory doses of ASA are not recommended during breastfeeding due to possible excretion of salicylic acid into breast milk and risk of Reye syndrome. NSAIDs have been shown to be present in breast milk in small amounts and are considered safe to use. The use of short-acting drugs, such as ibuprofen, may be preferred over those with a longer half-life, such as naproxen.\[^{[48]}\]

*Cough:* the transfer of dextromethorphan and guaifenesin into breast milk is unknown. It is unlikely that usual maternal doses would harm a nursing infant, especially in those over 2 months of age; however, liquid products containing dextromethorphan or guaifenesin may contain high alcohol content. Products with high alcohol content should be avoided while breastfeeding.\[^{[34]}\][[^{45}]] Use codeine with caution at the lowest effective dose for a maximum of 2–3 days in a breastfeeding mother. If codeine is used, monitor the infant for increased sleepiness, difficulty breastfeeding, breathing difficulties and limpness.\[^{[33]}\] Honey is safe to consume during breastfeeding. Zinc is considered safe in breastfeeding, provided the recommended daily maximum zinc intake (40 mg)\[^{[46]}\] is not exceeded. The safety of other ingredients in any zinc-based lozenges must also be assessed.

Experimental therapies: see Table 1.

A discussion of general principles on the use of medications in these special populations can be found in and . Other specialized reference sources are also provided in these appendices.
## Table 2: Treatment of symptoms associated with COVID-19

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>Dosage</th>
<th>Adverse Effects</th>
<th>Drug Interactions</th>
<th>Comments</th>
<th>Cost[^a]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antipyretic/ Analgesic</strong></td>
<td>acetaminophen</td>
<td>Children: 10–15 mg/kg Q4–6H PO/PRN for symptom management; maximum 75 mg/kg/day; do not exceed the adult dose. Adults: 325–650 mg Q4–6H PO/PRN; maximum 4000 mg/day</td>
<td>Uncommon with infrequent use and recommended dose. Hypersensitivity, agranulocytosis, anemia (rare). Chronic use and overdose associated with hepatotoxicity, nephropathy. Potential for toxicity enhanced if concurrent dehydration, prolonged fasting, diabetes mellitus, obesity, concomitant viral infection or family history of hepatotoxic reaction.</td>
<td>Increased risk of hepatotoxicity with alcohol and isoniazid. Decreased acetaminophen levels with enzyme inducers, e.g., barbiturates, carbamazepine, phenytoin. Acetaminophen has been reported to increase INR in warfarin-treated patients.[27] Check INR if acetaminophen ≥2 g/day is used for ≥3 consecutive days. Adjust warfarin dosage as required.</td>
<td>Use with caution in patients with liver dysfunction or active liver disease. Rectal administration results in erratic absorption and should be used under HCP supervision. Available as oral drops, tablets, chewable tablets, suppositories and suspension. Acetaminophen may be associated with exacerbation of wheezing in febrile children.[28] Many nonprescription products contain acetaminophen in combination with other drugs. Advise patients/caregivers to check labels carefully to avoid inadvertent administration of excessive doses.</td>
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<tr>
<td>ASA</td>
<td>Aspirin, Coated Aspirin, generics</td>
<td>Children &lt;18 y: not recommended; avoid use. Adults: 325–650 mg Q4–6H PO PRN; maximum 4000 mg/day</td>
<td>GI upset. Avoid in patients with renal failure, peptic ulcer disease, heart failure and ASA-sensitive asthma.</td>
<td>Increased risk of GI pain/ulceration with alcohol, corticosteroids. Antagonism of hypotensive effects of ACE inhibitor, beta-blockers, diuretics. Increased risk of bleeding with anticoagulants, SSRIs.</td>
<td>Avoid if ClCr &lt;10 mL/min. Enteric-coated products will have delayed onset of action. Evidence to date suggests that older people (&gt;60 y) and those with underlying medical conditions are at higher risk of severe COVID-19. As NSAIDs</td>
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<tr>
<td>Class</td>
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<td>ibuprofen</td>
<td>Children &lt;6 months: 5 mg/kg Q8H PO PRN; maximum 40 mg/kg/day; do not exceed the adult dose Children &gt;6 months: 5–10 mg/kg Q6–8H PO PRN for symptom management; maximum 40 mg/kg/day; do not exceed the adult dose Adults: 200–400 mg Q4–6H PO PRN; maximum for self-care 1200 mg/day; maximum if supervised by HCP: 2400 mg/day</td>
<td>Uncommon with infrequent use and recommended dose. GI intolerance and bleeding, allergic reactions, tinnitus, visual disturbances, nephropathy. Sodium and water retention. Dehydration enhances risk of renal toxicity. Platelet dysfunction can result in increased bleeding risk.</td>
<td>Increased risk of GI pain/ulceration with alcohol, corticosteroids. Antagonism of hypotensive effects of ACE inhibitor, beta-blockers, diuretics. Increased risk of bleeding with anticoagulants, SSRIs. Increased levels of cyclosporine (and risk of nephrotoxicity) with methotrexate, lithium. Possible reduction of ASA antiplatelet effects when combined with some NSAIDs, lithium. ASA may decrease therapeutic effect of uricosuric agents, e.g., probenecid, sulfinpyrazone.</td>
<td>should be used with caution in these populations, it is reasonable to avoid NSAIDs in the elderly and in those with comorbid conditions (e.g., cardiovascular disease, renal disease, chronic respiratory disease). If the use of an NSAID is unavoidable in these patients, it should be at the lowest effective dose and for the shortest duration.</td>
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Chapter 1: COVID-19

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### Treatment of symptoms associated with COVID-19 (cont'd)

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>Dosage</th>
<th>Adverse Effects</th>
<th>Drug Interactions</th>
<th>Comments</th>
<th>Cost(a)</th>
</tr>
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<tbody>
<tr>
<td>comorbid conditions (e.g., cardiovascular disease, renal disease, chronic respiratory disease). If the use of an NSAID is unavoidable in these patients, it should be at the lowest effective dose and for the shortest duration.</td>
<td>naproxen sodium&lt;br&gt;Aleve, Anaprox, Naproxen Sodium, other generics&lt;br&gt;Children &lt;12 y: not recommended&lt;br&gt;Adults: 220 mg Q8–12H PO PRN; maximum 440 mg/day</td>
<td>See ibuprofen.</td>
<td>See ibuprofen.</td>
<td>See ibuprofen.</td>
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<tr>
<td>Class</td>
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<td>Antitussives</td>
<td>codeine</td>
<td>Adults: 10–20 mg Q4–6H PO; maximum 120 mg/day. Health Canada recommends against the use of codeine and other opioids in children &lt;18 y. For combination products, consult label for additional ingredients; follow directions on label.</td>
<td>Drowsiness, sedation, nausea, vomiting, constipation.</td>
<td>CNS depressants, including alcohol, enhance CNS side effects. MAOIs: risk of serotonin syndrome. CYP2D6 inhibitors (e.g., fluoxetine, paroxetine) may inhibit conversion of codeine to its active metabolite and reduce clinical effect.</td>
<td>Causes less sedation than hydrocodone. Metabolized to morphine. Potential for dependence/addiction. Nonprescription codeine products always contain other ingredients.</td>
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<td>dextromethorphan</td>
<td>Adults and children ≥12 y: 10–20 mg Q4H PO or 30 mg Q6–8H PO; maximum 120 mg/day. Children 6–11 y: 5–10 mg Q4H PO or 15 mg Q6–8H PO; maximum 60 mg/day. For combination products, consult label for additional ingredients; follow directions on label.</td>
<td>Generally well-tolerated. Occasional dizziness, drowsiness, nausea.</td>
<td>Modulators of serotonin: risk of serotonin syndrome, e.g., SSRIs, linezolid, MAOIs (including moclobemide), sibutramine. CYP2D6 inhibitors (e.g., fluoxetine, paroxetine) may inhibit DM metabolism, resulting in increased DM levels and potential for adverse effects.</td>
<td>Causes less sedation than codeine and other opioids. DM has been abused for its euphoric effects.</td>
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<td></td>
<td>honey</td>
<td>Adults: 15 mL daily to TID. Children 1–18 y: 2.5–10 mL HS.</td>
<td>Side effects are rare; nervousness, insomnia, hyperactivity.</td>
<td>No known interactions.</td>
<td>Only use pasteurized honey due to the risk of botulism. Due to this risk, avoid in children &lt;1 y, patients who are immunocompromised or those who have structural abnormalities of the GI tract. Avoid in patients allergic to pollen. Do not use honey made from</td>
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<tr>
<td>Class</td>
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<td><strong>Expectorants</strong></td>
<td>gualfenesin</td>
<td>Adults and children ≥12 y: 200–400 mg Q4H PO; maximum 2.4 g/day</td>
<td>Side effects are rare; dizziness, drowsiness, headache, nausea and vomiting have been reported at high doses.</td>
<td>No known interactions.</td>
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Rhododendron (e.g., *R. ponticum*, *R. flavum*, *R. luteum*) due to risk of grayanotoxin, which is poisonous.

- Cost per day; includes drug cost only.
- More likely to occur with antineoplastic doses of methotrexate.
- Dosage adjustment may be required in renal impairment; see Appendix I.

**Abbreviations**

ACE = angiotensin-converting enzyme; ClCr = creatinine clearance; CNS = central nervous system; DM = dextromethorphan; GI = gastrointestinal; HCP = health-care provider; INR = international normalized ratio; MAOI = monoamine oxidase inhibitor; NSAID = nonsteroidal anti-inflammatory drug; SSRI = selective serotonin-reuptake inhibitor

Legend: $ < $1
Suggested Readings


References


