

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

In the community setting, advise all patients with symptoms or questions about testing and isolation to contact their **local public health unit** for up-to-date recommendations regarding actions to take based on the symptoms they are experiencing. Remind patients to call ahead to any health-care provider they intend to see regarding any other health-related concern to receive instructions regarding changes in office procedures during the pandemic.

Available data indicates that symptoms and clinical characteristics of COVID-19 may include:^{[1][2][3]}

- Asymptomatic carriage
- Acute mild/moderate illness (80%) – any of the following symptoms alone or in combination:
 - fever (>37.8°C)
 - chills, repeated shaking with chills
 - cough (with or without sputum production)
 - shortness of breath
 - anorexia, headache, malaise, myalgia
 - sore throat
 - new loss of smell and/or taste^{[4][5]}
 - less commonly: conjunctivitis,^{[6][7]} diarrhea, other GI symptoms, rhinorrhea, skin rashes,^{[8][9]} neurological abnormalities
- 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, neurological abnormalities^{[10][11]}

- hyperinflammation syndromes (“cytokine storm”)

Risk factors for symptomatic disease and progression to critical illness:

- age >50 y, substantial risk >70 y
- male
- obesity (BMI \geq 30)
- comorbidities: cardiovascular disease, diabetes, chronic respiratory disease, hypertension, cancer, chronic kidney disease

This chapter provides information/links to guidance for primary care practitioners regarding:

- Prevention measures for COVID-19
- Management of select common symptoms of COVID-19: fever, cough, headache/myalgia
- Experimental treatments being used for COVID-19 in acute-care settings
- Management of special populations and/or patients with comorbidities in the context of the COVID-19 pandemic

Goals of Therapy

- Prevent spread
- Alleviate symptoms
- Prevent complications where possible

Prevention

There is currently no evidence that any pharmacological agent, vitamin or herbal supplement is effective in the prevention of COVID-19. Several prevention trials are ongoing (see [Government of Canada, Vaccines and treatments for COVID-19: List of all COVID-19 clinical trials authorized by Health Canada](#)). Use of any medications for the prevention of COVID-19 outside of a clinical trial or the advice of an infectious disease specialist in an acute-care setting is inappropriate.^[12]

Information on various nonpharmacologic measures 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](#)
- Quarantine and self-isolation: [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](#); [JAMA Patient Page: Masks and coronavirus disease 2019 \(COVID-19\)](#); [Pan-Canadian Public Health Network: Use of non-medical cloth masks or face coverings in community settings](#)
- Personal protective equipment (PPE) for pharmacies: [Canadian Pharmacists Association: Suggested best practices for pharmacies during the COVID-19 pandemic](#)
- Personal protective equipment (PPE) for health professionals: [Health Canada: Coronavirus disease \(COVID-19\): for health professionals](#)
- Skin care while using PPE: [Nurses Specialized in Wound, Ostomy and Continence Canada: Prevention and management of skin damage related to personal protective equipment: update 2020](#)

Therapeutic Choices

Guidance on the treatment of patients with known or suspected COVID-19 can be found through:

- Canadian Medical Association Journal: *Treatment of patients with nonsevere and severe coronavirus disease 2019: an evidence-based guideline*. Published: April 29, 2020.
- Health Canada: *Clinical management of patients with moderate to severe COVID-19 - interim guidance*. Updated: April 9, 2020.
- Infectious Diseases Society of America: *Guidelines on the treatment and management of patients with COVID-19*. Published: April 27, 2020.
- National Institutes of Health (NIH), U.S.: *Coronavirus disease 2019 (COVID-19) treatment guidelines*. Updated: June 16, 2020.
- National Institute for Health and Care Excellence (NICE), U.K.: *Coronavirus (COVID-19): rapid guidelines and evidence summaries*. Date of update varies with each guideline.

Information on the management of select common symptoms of COVID-19, e.g., fever, cough, headache/myalgia, is presented in this chapter. An infographic containing this information for patients is also available: [Managing COVID-19 at home](#).

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 the *Compendium of Therapeutic Choices for Minor Ailments (CTMA)*, Fever.

- Children <6 months of age with a fever should be assessed by an appropriate health-care practitioner.^[13]
- In a pregnant patient who is in her first trimester, the goal of antipyresis is protection of the fetus.^{[14][15]}
- There are many arguments against treating a fever:^{[16][17][18][19][20]}
 - 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:^[13]

- Removal of excess clothing and bedding
- Increased fluid intake to replace insensible water loss during fever
- Maintenance of ambient temperatures around 20–21°C (68–70°F)
- 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.^[21] 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.^{[22][23]}

- Ice packs (wrapped in cloth, i.e., not touching the skin directly) 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.^[24]
- **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.^[24]
 - ASA is not recommended in children or adolescents because of the potentially increased risk of Reye syndrome.^[25]
 - Naproxen is not approved/recommended in children <12 years of age.
 - For more information on the use of NSAIDs, see the *Compendium of Therapeutic Choices (CTC)*, Osteoarthritis and the *Compendium of Pharmaceuticals and Specialties (CPS)*, Nonsteroidal Anti-inflammatory Drugs (NSAIDs) (CPhA Monograph).
- 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.^{[14][26][27]} No difference was found in patient discomfort in 2 trials that assessed it.^[27] 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 3.

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 the *Compendium of Therapeutic Choices for Minor Ailments (CTMA)*, 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 should be well cleaned to avoid aerosolizing mould.

Pharmacologic Choices

Overall, there is little evidence for or against the effectiveness of nonprescription cough medicines.^[28]

- 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.^[29]
 - **Dextromethorphan** and **codeine** are commonly used to treat cough related to upper respiratory tract infections, although there is little evidence for efficacy.^[28]
- **Expectorants**. Cough associated with COVID-19 infection has generally been reported as dry, but sputum production may be present. Adequate hydration with oral liquids and inhalation of humidified air (e.g., warm showers, cool mist humidifiers) may be helpful in thinning and moving secretions in the respiratory tract. There is a lack of evidence to support the efficacy of products marketed as expectorants (e.g., **guaifenesin**^[30]); they have not been found to thin sputum nor increase sputum volume, even at doses higher than recommended.^[29]
- 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.^{[30][31]}
 - **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.^[30] 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.^[32]

For more detailed information on medications used in the management of cough, see Table 3.

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 (CTMA)* as well as Headache in Adults, Acute Pain and Influenza in the *Compendium of Therapeutic Choices (CTC)*.

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.^[33]
- **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.^[24]

- ASA is not recommended in children or adolescents because of the potentially increased risk of Reye syndrome.^[25]
- Naproxen is not approved/recommended in children <12 years of age.
- For more information on the use of NSAIDs, see the *Compendium of Therapeutic Choices (CTC)*, Osteoarthritis and the *Compendium of Pharmaceuticals and Specialties (CPS)*, Nonsteroidal Anti-inflammatory Drugs (NSAIDs) (CPhA Monograph).
- 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 3.

Experimental therapies for COVID-19

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. Use of any of these medications for these purposes outside of a clinical trial or the advice of an infectious disease specialist in an acute-care setting is inappropriate.^[12]

Information about COVID-19-related clinical trials can be found at:

- Government of Canada: [Vaccines and treatments for COVID-19: list of all COVID-19 clinical trials authorized by Health Canada](#)
- Cochrane Systematic Review Database: [Living mapping and living systematic review of COVID-19 studies](#)
- [Global Coronavirus COVID-19 Clinical Trial Tracker](#)

Information about the rationale for use, dosage, adverse effects, drug interactions and safety during pregnancy or breastfeeding of select trial medications being used in Canada can be found in Table 1.

Table 1: **Select Experimental Therapies for COVID-19**

Drug	Rationale for Use	Dosage	Adverse Effects	Drug Interactions	Safety in Pregnancy and Breastfeeding ^{[38][39][40][41]}
Adenovirus Type 5 Vector (Ad5-nCoV) ^{[42][43]}	Recombinant novel coronavirus vaccine.	“Low” dose and “high” dose single or 2 dose regimens being tested	Not available.	Not available.	Not available.
Azithromycin	Antibacterial. Used as empiric antibiotic therapy for concurrent bacterial infections (e.g., pneumonia).	500 mg on first day then 250 mg daily PO × 4 days	GI upset, rash, cholestatic hepatitis, QT _c interval prolongation. ^[a]	Use cautiously with other drugs that cause QT _c prolongation (e.g., hydroxychloroquine). ^[a] May increase warfarin effect; increased concentrations of substrates of CYP3A4	Pregnancy: considered safe. Breastfeeding: low levels in milk, not expected to cause adverse effects in the infant.

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Table 1: **Select Experimental Therapies for COVID-19** (cont'd)

Drug	Rationale for Use	Dosage	Adverse Effects	Drug Interactions	Safety in Pregnancy and Breastfeeding ^{[38][39][40][41]}
Baricitinib	Janus kinase (JAK1 and JAK 2) inhibitor. Predicted to reduce the ability of the virus to infect lung cells.	2 mg daily PO × 10 days	Increased risk of serious infections, malignancy and thrombosis; increased CPK, hypercholesterolemia, pharyngitis, nausea, UTI, hypertension, URTI, headache.	(potent inhibitor), e.g., atorvastatin, carbamazepine, digoxin, lovastatin, simvastatin. Enhanced immunosuppression with other immunosuppressants.	Pregnancy: limited data, ^{[44][45]} animal studies have shown teratogenic effects. ^[46] Breastfeeding: no data available.
Chloroquine	Antimalarial. Under investigation for prevention.	300 mg chloroquine base daily × 4 days followed by 300 mg weekly (low-dose), or 300 mg twice weekly (medium-dose) or 150 mg daily (high-dose) for 3 months	Potentially fatal in overdose. Nonallergic pruritus in African Canadians, nausea, vomiting, headache, bitter taste, QT _c interval prolongation. ^[a] Rare retinal toxicity (patients with underlying macular disease at an increased risk).	Decreased metabolism of beta-blockers. May increase digoxin levels. Increased risk of QT _c prolongation with other QT _c -prolonging agents and strong CYP3A4 inhibitors. ^[a]	Pregnancy: considered safe. Breastfeeding: no information on daily use during breastfeeding but is given directly to infants for malaria prophylaxis.
Colchicine	Antigout therapy. Anti-inflammatory effect may reduce complications due to hyperinflammation (cytokine storm syndrome).	0.5 mg BID × 3 days followed by 0.5 mg daily × 27 days	Abdominal pain and cramps, diarrhea, nausea and vomiting. Possible neuropathy, myopathy, bone marrow suppression.	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. Avoid grapefruit juice.	Pregnancy: generally recommended to avoid unless benefit outweighs risk; however, a systematic review did not show increased risk of malformations or miscarriage. ^[48] 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.
Corticosteroids	Immunomodulator. Studies in sepsis have shown positive effects on	50 mg hydrocortisone IV Q6H × 7 days (or	Fluid retention, hypertension, Cushing syndrome,	Enhanced immunosuppression with other immunosuppressants.	Pregnancy: not associated with increased risk of major

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Table 1: **Select Experimental Therapies for COVID-19** (cont'd)

Drug	Rationale for Use	Dosage	Adverse Effects	Drug Interactions	Safety in Pregnancy and Breastfeeding ^{[38][39][40][41]}
	mortality and resolution of shock.	while in septic shock)	hyperglycemia, adrenal suppression, GI upset, psychiatric effects.	Increased adverse effects/toxicity of corticosteroids with CYP3A4 inhibitors, cyclosporine, diltiazem, estrogens. Decreased effect of corticosteroids with CYP3A4 inducers. May decrease the effect of aldesleukin, caspofungin, cholinesterase inhibitors, isoniazid, salicylates, vaccines. May increase the effect/toxicity of cyclosporine, digoxin (by decreasing serum potassium), warfarin. See Corticosteroids: Systemic (CPhA Monograph).	malformations; possible increased risk of oral cleft. ^[49] 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).
Heparins: low molecular weight (LMWH), unfractionated (UFH)	Anticoagulants (low molecular weight heparins; unfractionated heparin). For treatment of coagulopathy associated with COVID-19.	Various regimens being tested	LMWH: Bleeding; HIT and osteoporosis (less common than with UFH). UFH: Bleeding, HIT, osteoporosis.	LMWH: increased risk of bleeding with other anticoagulants, antiplatelets, NSAIDs. UFH: increased risk of bleeding with other anticoagulants, antiplatelets, NSAIDs. IV nitroglycerin may reduce heparin's anticoagulant effect.	LMWH: Pregnancy: considered safe. Breastfeeding: considered safe. UFH: Pregnancy: considered safe. Breastfeeding: considered safe.
Hydroxychloroquine	Antimalarial. Demonstrated in-vitro activity against SARS-CoV-2 (i.e., COVID-19). Under investigation for prevention; large study did not find benefit for treatment. ^[50]	Pre-exposure prophylaxis: 400–800 mg PO daily × 1–4 days followed by 400 mg weekly Post-exposure prophylaxis: 400–800 mg PO daily × 1–5 days followed by 200–400 mg daily × 7–11 days	Potentially fatal in overdose. Nonallergic pruritus in African-Canadians, nausea, vomiting, headache, bitter taste, QT _c interval prolongation. ^[a] Rare retinal toxicity (patients with underlying macular disease at increased risk).	Decreased metabolism of beta-blockers. May increase digoxin levels. Increased risk of QT _c prolongation with other QT _c -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.
Lopinavir/ritonavir	Antiretroviral. Has activity (in vitro and/or in animal models) against SARS-CoV-1; MERS-CoV.	Treatment: 400/100 mg BID PO × 14 days or until discharge from hospital	GI upset, liver enzyme elevations, hyperlipidemia, and PR and QT _c interval prolongation. ^[a]	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. ^[51]

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Table 1: **Select Experimental Therapies for COVID-19** (cont'd)

Drug	Rationale for Use	Dosage	Adverse Effects	Drug Interactions	Safety in Pregnancy and Breastfeeding ^{[38][39][40][41]}
	Ritonavir is added to lopinavir to increase its half-life through inhibition of CYP450.		Possible increased risk of renal dysfunction.		Breastfeeding: data from use in HIV has not caused concern.
Peg-interferon Lambda-1A	Human recombinant interferon. Stimulates immune responses during viral infections.	Ambulatory cohort: single dose 180 mcg SC at baseline Hospitalized cohort: 180 mcg SC at baseline, second dose on day 7	Preliminary data from studies in other conditions: GI upset, elevated LFTs, flu-like symptoms, musculoskeletal symptoms.	Data not available.	Pregnancy: no data available. Breastfeeding: no data available; other peginterferons (alfa and beta) are considered low risk due to low amounts transferred into breast milk and predicted minimal GI absorption in the infant.
Remdesivir	Antiviral. Has activity in vitro and in animal models against SARS-CoV-1; MERS-CoV.	200 mg IV daily on day 1 followed by 100 mg IV daily for up to 10 days	Generally well-tolerated. GI effects. Aminotransferase elevations.	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.	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. ^[52]
Ruxolitinib	Janus kinase (JAK1 and JAK 2) inhibitor. Theoretically, may reduce complications due to hyperinflammation (cytokine storm syndrome).	10 mg BID × 14 days followed by 5 mg BID × 2 days then 5 mg daily × 1 day	Anemia, thrombocytopenia, neutropenia, bruising, dizziness, headache.	Ruxolitinib exposure may be increased by fluconazole and other strong CYP3A4 inhibitors and decreased by strong CYP3A4 inducers.	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.
Sarilumab	L-6 monoclonal antibody. Theoretically, may reduce complications due to hyperinflammation (cytokine storm syndrome).	Single IV dose ("low" dose vs. "high" dose being studied)	Increased risk of serious infections, injection-site reactions, URTIs, elevated ALT levels.	May decrease the concentration of CYP3A4 substrates by restoring CYP3A4 activity in some patients.	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.

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Table 1: **Select Experimental Therapies for COVID-19** (cont'd)

Drug	Rationale for Use	Dosage	Adverse Effects	Drug Interactions	Safety in Pregnancy and Breastfeeding ^{[38][39][40][41]}
Tocilizumab	IL-6 monoclonal antibody. Theoretically, may reduce complications due to hyperinflammation (cytokine storm syndrome).	8 mg/kg (up to max of 800 mg) × 1 dose IV, repeated once prn if symptoms worsen or show no improvement	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.	May increase CYP450 enzyme activity—monitor concurrent therapy with drugs metabolized by CYP450.	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.
Vitamin C	Vitamin. Has been studied with respect to lessening organ dysfunction secondary to sepsis based on experimental evidence of anti-inflammatory and antioxidant properties.	50 mg/kg Q6H IV × 4 days	Diarrhea, increased risk of renal stones in predisposed individuals.	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, borteozomib.	Pregnancy: data limited, crosses the placenta, possibly resulting in above-normal levels in fetus. Upper tolerable limit 2000 mg/day during pregnancy. ^[53] 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.

^a See Canadian Heart Rhythm Society guideline on antimicrobial drug-induced ventricular arrhythmia with COVID-19.^[47]

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; HIT = heparin-induced thrombocytopenia; IL = interleukin; LFT = liver function test; 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

Choices during Pregnancy and Breastfeeding

Management of COVID-19 during pregnancy

See Table 2 for suggested resources providing general information with respect to COVID-19 and pregnancy.

For the treatment of *fever, headache, myalgia*:

- **Acetaminophen** is considered the drug of choice during pregnancy.
- **ASA and NSAIDs** may be considered as alternatives during the first or second trimester, but are not recommended in the third trimester.^[38]

For the treatment of *cough*:

- **Codeine** has the most evidence of safety during pregnancy.^[38]

- **Dextromethorphan** can be considered as an alternative.^[38]
- 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.^[54]
- **Honey** is safe to consume during pregnancy.
- **Zinc** is considered safe in pregnancy, provided the recommended daily maximum zinc intake (40 mg)^[55] is not exceeded. The safety of other ingredients in any zinc-based lozenges must also be assessed.

For information on the safety of *experimental therapies*: see Table 1.

Management of COVID-19 during breastfeeding

See Table 2 for suggested resources providing general information with respect to COVID-19 and breastfeeding. 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 and practicing respiratory etiquette and hand hygiene are recommended.^[56]

For the treatment of *fever, headache, myalgia*:

- **Acetaminophen** is considered the drug of choice during breastfeeding.
- Anti-inflammatory doses of **ASA** are not recommended 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**.^[57]

For the treatment of *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 >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.^{[40][54]}
- 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.^[39]
- **Honey** is safe to consume during breastfeeding.
- **Zinc** is considered safe in breastfeeding, provided the recommended daily maximum zinc intake (40 mg)^[55] is not exceeded. The safety of other ingredients in any zinc-based lozenges must also be assessed.

For information on the safety of *experimental therapies*, see Table 1.

A discussion of general principles on the use of medications in these special populations can be found in CPS Clin Info: Drug use During Pregnancy and Drug use During Breastfeeding. Other specialized reference sources are also provided in these appendices.

Resources for the Management of Special Populations/Comorbidities

Guidance/information is available to address the concerns of health-care practitioners managing patients in special population groups and/or with various disease states with respect to prevention and treatment of COVID-19:

Table 2: **Resources for the Management of Special Populations/Comorbidities**

Special population/ comorbidity	Resources
Anticoagulation/ thrombosis	The Anticoagulation Forum: Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the Anticoagulation Forum Canadian Medical Association Journal: Coagulopathy associated with COVID-19 CHEST Guideline and Expert Panel Report: Prevention, diagnosis, and treatment of VTE in patients with COVID-19 Thrombosis Canada: Managing anticoagulation during the COVID-19 pandemic
Asthma	Canadian Thoracic Society: Inhaled salbutamol shortage - mitigation strategy for asthma Canadian Thoracic Society: Position statement: addressing therapeutic questions to help Canadian physicians optimize asthma management for their patients during the COVID-19 pandemic Global Initiative for Asthma (GINA): COVID-19: GINA answers to frequently asked questions on asthma management
Breastfeeding	B.C. Centre for Disease Control/B.C. Ministry of Health: Guideline for lactation for women/individuals who are confirmed or suspect cases of COVID-19 Canadian Paediatric Society: Breastfeeding when mothers have suspected or proven COVID-19 Centers for Disease Control and Prevention (CDC): Care for breastfeeding women, interim guidance on breastfeeding and breast milk feeds in the context of COVID-19 Health Canada: Pregnancy, childbirth and caring for newborns: advice for mothers during COVID-19 The Provincial Council for Maternal and Child Health: Maternal-neonatal COVID-19 general guideline Public Health Agency of Canada (PHAC): Updated: public health management of cases and contacts associated with coronavirus disease 2019 (COVID-19) Safely Fed Canada: COVID-19 infant feeding resources World Health Organization (WHO): Breastfeeding advice during the COVID-19 outbreak
Cardiovascular conditions	American College of Cardiology: COVID-19 clinical guidance for the cardiovascular care team Canadian Cardiovascular Society and the Canadian Heart Failure Society: COVID-19 and concerns regarding use of cardiovascular medications, including ACEi/ARB/ARNi, low-dose ASA and nonsteroidal anti-inflammatory drugs (NSAIDs)
Chronic obstructive pulmonary disease	Canadian Thoracic Society: Position statement: addressing therapeutic questions to help Canadian health care professionals optimize COPD management for their patients during the COVID-19 pandemic Canadian Thoracic Society: Inhaled salbutamol shortage - mitigation strategy for COPD Global Initiative for Chronic Obstructive Lung Disease (GOLD): GOLD COVID-19 guidance
Contact lens care	British Contact Lens Association: The COVID-19 pandemic: important considerations for contact lens practitioners
Dermatological conditions	Canadian Dermatology Association: Patient information: COVID & systemics
Diabetes	Diabetes Canada: COVID-19 (coronavirus) and diabetes Diabetes Canada: Sick-day medication list European Society of Endocrinology: COVID-19 and endocrine diseases. A statement from the European Society of Endocrinology
Drug adverse effects and interactions specific to COVID-19	Canadian Heart Rhythm Society: Guidance on minimizing the risk of antimicrobial drug-induced ventricular arrhythmia during treatment of COVID-19 University of Liverpool: COVID-19 Drug Interactions, Interaction Checker
Endocrine conditions	European Society of Endocrinology: COVID-19 and endocrine diseases. A statement from the European Society of Endocrinology

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Table 2: **Resources for the Management of Special Populations/Comorbidities** (cont'd)

Special population/ comorbidity	Resources
Exercise/return to sports	American College of Cardiology, Sports and Exercise Cardiology Council: A game plan for the resumption of sport and exercise after coronavirus disease 2019 (COVID-19) infection
Feeding infants and young children	Safely Fed Canada: COVID-19 infant feeding resources Unicef, Global Nutrition Cluster, Global Technical Assistance Mechanism for Nutrition: Infant and young child feeding in the context of COVID-19
Geriatrics	GeriMedRisk: COVID-19 resources for clinicians
Heart Failure	Canadian Cardiovascular Society and the Canadian Heart Failure Society: COVID-19 and concerns regarding use of cardiovascular medications, including ACEi/ARB/ARNi, low-dose ASA and nonsteroidal anti-inflammatory drugs (NSAIDs)
Human immunodeficiency virus	U.S. Department of Health and Human Services, AIDSinfo: Interim guidance for COVID-19 and persons with HIV
Hypertension	Canadian Cardiovascular Society and the Canadian Heart Failure Society: COVID-19 and concerns regarding use of cardiovascular medications, including ACEi/ARB/ARNi, low-dose ASA and nonsteroidal anti-inflammatory drugs (NSAIDs)
Inflammatory bowel disease	American Gastroenterological Association (AGA): AGA clinical practice update on management of inflammatory bowel disease during the COVID-19 pandemic British Society of Gastroenterology: Guidance for management of inflammatory bowel disease during the COVID-19 pandemic
Medications requiring regular monitoring (e.g., lithium, warfarin)	National Health Service (NHS), Specialist Pharmacy Service: Guidance on the management of drugs requiring monitoring during COVID-19
Mental health	Canadian Psychological Association: Psychology works for COVID-19. Psychologists giving back to front line service providers Centre for Addiction and Mental Health: Mental health and the COVID-19 pandemic Free Apps for the public: Wellness Together Canada: Mental health and substance use support (Wellness Together Canada) WellCan: Free mental health digital resource for all Canadians (Morneau Shepell) SilverCloud (Shopper's Drug Mart; free access with code SHOPPERS)
Multiple sclerosis	MS Society of Canada: Disease-modifying treatment (DMT) guidelines for coronavirus (COVID-19)
Pediatrics	Canadian Paediatric Society: COVID-19 information and resources for paediatricians
Pregnancy	Health Canada: Pregnancy, childbirth and caring for newborns: advice for mothers during COVID-19 The Provincial Council for Maternal and Child Health: Maternal-neonatal COVID-19 general guideline The Society of Obstetricians and Gynecologists of Canada: Updated SOGC committee opinion – COVID-19 in pregnancy
Rehabilitation/after-care	Alberta Health Services: COVID-19 Scientific Advisory Group rapid evidence report National Health Service (NHS): After-care needs of inpatients recovering from COVID-19
Rheumatic diseases	American College of Rheumatology: Guidance for the management of adult patients with rheumatic disease during the COVID-19 pandemic
Return to work	Alberta Health Services: COVID-19 return to work guide for healthcare workers

(cont'd)

Table 2: **Resources for the Management of Special Populations/Comorbidities** (cont'd)

Special population/ comorbidity	Resources
Substance Use	Canadian Centre on Substance Use and Addiction: Impacts of COVID-19 on substance use
Vaccine scheduling	Canadian Pharmacists Association: COVID-19: Disruption of immunization schedules during the pandemic. Is a delay a problem? PHAC: Canadian immunization guide

Table 3: Treatment of symptoms associated with COVID-19



Class	Drug	Dosage	Adverse Effects	Drug Interactions	Comments	Cost ^[a]
Antipyretic/ Analgesic	acetaminophen Atasol Preparations, Tempra, Tylenol, generics	Children: 10–15 mg/kg Q4–6H PO/PR PRN for symptom management; maximum 75 mg/kg/day; do not exceed the adult dose Adults: 325–650 mg Q4–6H PO/PR PRN; maximum 4000 mg/day	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.	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. ^[34] Check INR if acetaminophen ≥2 g/day is used for ≥3 consecutive days. Adjust warfarin dosage as required.	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. ^[35] Many nonprescription products contain acetaminophen in combination with other drugs. Advise patients/ caregivers to check labels carefully to avoid inadvertent administration of excessive doses.	\$
	ASA Aspirin, Coated Aspirin, generics	Children <18 y: not recommended; avoid use Adults: 325–650 mg Q4–6H PO PRN; maximum 4000 mg/day	GI upset. Avoid in patients with renal failure, peptic ulcer disease, heart failure and ASA-sensitive asthma.	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.	Avoid if ClCr <10 mL/min. Enteric-coated products will have delayed onset of action. 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	\$

Class	Drug	Dosage	Adverse Effects	Drug Interactions	Comments	Cost ^[a]
				<p>Increased levels of cyclosporine (and risk of nephrotoxicity) with methotrexate,^[b] lithium.</p> <p>Possible reduction of ASA antiplatelet effects when combined with some NSAIDs.^[36]</p> <p>ASA may decrease therapeutic effect of uricosuric agents, e.g., probenecid, sulfinpyrazone.</p>	<p>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.^[24]</p>	
	<p><i>ibuprofen</i> Advil, Advil (Children's), Advil Liqui-Gels, Motrin, Motrin (Children's), Motrin Liquid Gels, generics</p>	<p>Children <6 months: 5 mg/kg Q8H PO PRN; maximum 40 mg/kg/day; do not exceed the adult dose</p> <p>Children >6 months: 5–10 mg/kg Q6–8H PO PRN for symptom management; maximum 40 mg/kg/day; do not exceed the adult dose</p> <p>Adults: 200–400 mg Q4–6H PO PRN; maximum for self-care 1200 mg/day; maximum if supervised by HCP: 2400 mg/day</p>	<p>Uncommon with infrequent use and recommended dose.</p> <p>GI intolerance and bleeding, allergic reactions, tinnitus, visual disturbances, nephropathy.</p> <p>Sodium and water retention.</p> <p>Dehydration enhances risk of renal toxicity.</p> <p>Platelet dysfunction can result in increased bleeding risk.</p>	<p>Increased risk of GI pain/ulceration with alcohol, corticosteroids.</p> <p>Antagonism of hypotensive effects of ACE inhibitor, beta-blockers, diuretics.</p> <p>Increased risk of bleeding with anticoagulants, SSRIs.</p> <p>Increased levels of cyclosporine (and risk of nephrotoxicity) with methotrexate,^[b] lithium.</p> <p>Possible reduction of ASA antiplatelet effects when combined with some NSAIDs.^[36]</p>	<p>Renal dysfunction: no adjustment required; however, should be avoided in renal dysfunction due to effects of prostaglandin inhibition on renal function.</p> <p>Do not give if dehydration is present; ensure patient has adequate intake of fluids.</p> <p>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</p>	\$

(cont'd)

Table 3: **Treatment of symptoms associated with COVID-19** (cont'd)

Class	Drug	Dosage	Adverse Effects	Drug Interactions	Comments	Cost ^[a]
	<i>naproxen sodium</i> Aleve, Anaprox, Naproxen Sodium, other generics	Children <12 y: not recommended Adults: 220 mg Q8–12H PO PRN; maximum 440 mg/day	See ibuprofen.	See ibuprofen.	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. See ibuprofen.	\$

Class	Drug	Dosage	Adverse Effects	Drug Interactions	Comments	Cost ^[a]
Antitussives	<i>codeine</i>  Combination products: Robitussin AC, generics	Adults: 10–20 mg Q4–6H PO; maximum 120 mg/day Health Canada recommends against the use of codeine and other opioids in children <18 y ^[37] For combination products, consult label for additional ingredients; follow directions on label	Drowsiness, sedation, nausea, vomiting, constipation.	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.	Causes less sedation than hydrocodone. Metabolized to morphine. Potential for dependence/addiction. Nonprescription codeine products always contain other ingredients.	\$
	<i>dextromethorphan</i>  Balminil DM, Benylin DM; Combination products: Robitussin DM, others	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	Generally well-tolerated. Occasional dizziness, drowsiness, nausea.	Modulators of serotonin: risk of serotonin syndrome, e.g., SSRIs, linezolid, MAOIs (including moclobemide). CYP2D6 inhibitors (e.g., fluoxetine, paroxetine) may inhibit DM metabolism, resulting in increased DM levels and potential for adverse effects.	Causes less sedation than codeine and other opioids. DM has been abused for its euphoric effects.	\$
	<i>honey</i>	Adults: 15 mL daily to TID Children 1–18 y: 2.5–10 mL HS	Side effects are rare; nervousness, insomnia, hyperactivity.	No known interactions.	Only use pasteurized honey due to the risk of botulism. Due to this risk, avoid in children <1 y, patients who are immunocompromised or those who have structural abnormalities of the GI tract. Avoid in patients allergic to pollen. <i>Do not</i> use honey made from <i>Rhododendron</i> (e.g.,	\$


(cont'd)

Table 3: Treatment of symptoms associated with COVID-19 (cont'd)

Class	Drug	Dosage	Adverse Effects	Drug Interactions	Comments	Cost ^[a]
					<i>R. ponticum</i> , <i>R. flavum</i> , <i>R. luteum</i>) due to risk of grayanotoxin, which is poisonous.	
Expectorants	<i>guaifenesin</i> Robitussin Mucus & Phlegm, generics	Adults and children ≥12 y: 200–400 mg Q4H PO; maximum 2.4 g/day Children ≥6 y: 12 mg/kg/day in divided doses Q4H PO; maximum 1.2 g/day For combination products, consult label for additional ingredients; follow directions on label	Side effects are rare; dizziness, drowsiness, headache, nausea and vomiting have been reported at high doses.	No known interactions.		\$

^a Cost per day; includes drug cost only.

^b 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

- International Pharmaceutical Federation. *COVID-19: guidelines for pharmacists and the pharmacy workforce* [PDF file]. Updated March 26, 2020. Available from: www.fip.org/files/content/priority-areas/coronavirus/COVID-19-Guidelines-for-pharmacists-and-the-pharmacy-workforce.pdf.
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