Covid-19

Chapter 1
COVID-19

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Coronavirus disease 2019 (COVID-19) is caused by the novel coronavirus SARS-CoV-2. The understanding of the epidemiology and pathophysiology of this infection is rapidly evolving. To access the most recent information, consult the following reliable websites:

- Public Health Agency of Canada (PHAC) at www.canada.ca/en/public-health
- Centers for Disease Control and Prevention (CDC) at www.cdc.gov
- World Health Organization (WHO) at www.who.int

In the community setting, advise all patients with symptoms, or those who have questions about COVID-19 testing and isolation, to contact their **local public health unit** for up-to-date recommendations. Remind patients who are planning to see a health-care provider for any other health-related concern during the pandemic to call ahead and confirm instructions about office or clinic procedures.

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

- Prevention of COVID-19
- Outpatient management of acute COVID-19 and long COVID syndrome (*Note*: at the time of writing, the definition and nomenclature for prolonged COVID-19 symptoms have not been standardized; other terms include post-COVID conditions and syndrome.)[1]
- Management of special populations, e.g., pediatric patients

Clinical Presentation

The National Institutes of Health (NIH) defines the spectrum of COVID-19 severities as follows:[2]

- "*Asymptomatic or Presymptomatic Infection:* Individuals who test positive for SARS-CoV-2 using a virologic test (i.e., a nucleic acid amplification test [NAAT] or an antigen test), but who have no symptoms that are consistent with COVID-19." Early in the pandemic, it was estimated this accounted for up to 17–20% of cases.[3][4] With the availability of an effective vaccine combined with newer variants and the changing availability of testing, this number could be much higher than previously estimated.
- "*Mild Illness:* Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who **do not** have shortness of breath, dyspnea, or abnormal chest imaging."
- "*Moderate Illness:* Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have saturation of oxygen (SpO_2) ≥94% on room air at sea level."
- "*Severe Illness:* Individuals who have SpO_2 <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) <300 mmHg, a respiratory rate >30 breaths/min , or lung infiltrates >50%."
- "*Critical Illness:* Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction."

Note: patients may progress quickly from one category to the next and should be advised of the need to seek medical attention when symptoms worsen or progress. Some clinics supply patients with home oxygen monitors to facilitate early detection of clinical deterioration.[5]

The following risk factors increase the likelihood of symptomatic disease and progression to critical illness:[6]

- Unvaccinated persons
- Pregnancy
- Older age (>60 y, with greater incremental risk with increasing decades of life)
- Obesity (BMI ≥40)
- Chronic medical conditions: cardiovascular disease, hypertension, diabetes, respiratory disease, kidney disease, liver disease, dementia, stroke
- Immunocompromised conditions, e.g., cancer or due to immunosuppressive therapies

Goals of Therapy

- Prevent spread
- Alleviate symptoms
- Prevent complications where possible

Community-Based Management

Many patients with mild illness may not contact their primary health-care provider and will only seek symptom alleviation, usually through cough and cold medications available from pharmacies. Sore throat, cough and congestion relief along with triage for more severe symptoms is frequently managed by primary health-care providers and community-practice based pharmacists. For more information on management of mild symptoms, see Acute Bronchitis, Viral Rhinitis and Viral Rhinitis, Influenza, Sinusitis and Pharyngitis. When managing patients in the acute phase of infection, the following criteria may be used to establish suitability for community-based care:[5]

- Stay well hydrated
- Reliably report worsening symptoms (e.g., evaluate language barriers, cognitive status) and carry out their usual activities of daily living
- Have access to appropriate resources and social support for self-isolation
- Be able to manage any comorbidities at home
- Have stable vitals and no signs of respiratory distress or persistent tachypnea
- (If pulse oximetry is available) have an SpO_2 >93% on room air; an SpO_2 of 90–93% on room air may be acceptable if a patient has a pre-existing chronic lung disease

If any of the following red flags are present during patient assessment, consider admission to hospital or assessment by the nearest urgent-care centre:[7]

- Cold, clammy skin
- Confusion
- Decreased urine output
- Difficulty breathing
- Hemoptysis
- Nonblanching rash
- Shortness of breath at rest
- Worsening of respiratory symptoms

Initial Assessment and Follow-Up

Assessment and follow-up after a positive COVID-19 diagnosis includes monitoring for:

- Symptoms:
  - respiratory tract: cough, wheezing, shortness of breath (or change in breathing or activities that cause breathlessness), runny nose, sore throat, sputum
  - thermoregulatory: fever, chills, rigors
  - musculoskeletal: arthralgia, myalgia
  - gastrointestinal: abdominal pain, nausea, vomiting, diarrhea, anorexia
  - neurologic: fatigue, malaise, headache, confusion
  - cardiac: chest pain
  - dermatologic: rash
  - ears, nose, throat (ENT): anosmia, dysgeusia, ear pain
  - ophthalmologic: conjunctivitis
  - psychiatric: anxiety, depression, insomnia
- Signs:
  - oxygen saturation: if a home O_2 saturation monitor is available/provided or on assessment of breathlessness while talking or walking

Based on clinical assessment, patients can continue to be managed at home with regular follow-up at intervals determined by the primary-care provider. For most patients, telehealth visits at days 4, 7 and 10 after onset of symptoms is reasonable. Patients >65 years of age, those with risk factors for more severe disease and those with moderate dyspnea at time of first evaluation may benefit from more frequent follow-up; consideration should be given to scheduling visits within the first 24 hours and every 24–48 hours thereafter, until symptom resolution. If there is evidence of clinical deterioration, follow-up may increase in frequency or arrangements may be made to transfer patient to an acute-care setting (as per the red flags identified above).[5]

Even if mildly ill, **patients at high risk for severe disease** may be eligible for several treatment options. For more information about assessment and treatments, see Therapeutic Choices.

Ongoing follow-up for development of long-COVID or post-COVID syndrome is warranted as these symptoms may manifest weeks after resolution of acute symptoms.[8] See Long-Term Complications of COVID-19.

A number of institutions and health regions, as seen with the COVID tool kit,[7] have established outpatient management algorithms and tools to aid virtual clinical assessment and triage.

Management and Follow-Up of Hospitalized Patients Post-Discharge

Once a patient is medically well and not on oxygen (unless previously on home oxygen), they can be discharged from hospital to an appropriate community setting. When patients are discharged back to their home, either alone or with family, they should have routine follow-up with their primary-care provider or, if available, a dedicated COVID-19 clinic. Discharge from hospital care discussions should take place in collaboration with the primary-care provider and/or community of care as well as the local public health unit.

Ensure that the patient's individual context, including access to transportation, living situation and family/household support, is taken into consideration when deciding when and how to discharge.

Patients diagnosed with COVID-19 are at risk of complications and should have routine follow-up at least 4 weeks after initial recovery or sooner if deemed necessary based on functional status, living arrangements and social supports. Older people are more likely to experience pronounced functional decline and may require coordinated rehabilitation or convalescent care.

Patients who are discharged from hospital on new medications for COVID-19–related complications, such as antithrombotics for pulmonary embolism or deep-vein thrombosis, should be managed as per standard practice. For more information, see Venous Thromboembolism.

Mental Health

Among patients with COVID-19, there may be heightened levels of both new and worsening anxiety (see Anxiety Disorders), depression (see Depression), substance use disorder (see Alcohol-Related Disorders and Opioid-Related Disorders), and PTSD (see Post-traumatic Stress Disorder).

The Centre for Addiction and Mental Health has published resources for health-care providers for self- and patient-centred mental health support that can be accessed at www.camh.ca [search: resources for healthcare workers during COVID-19].

Long-Term Complications of COVID-19

Many patients report long-term health effects that may persist for months after recovering from acute COVID-19. It can also manifest weeks after resolution of acute symptoms.[8] The pathology, epidemiology and risk factors for prolonged COVID-19 symptoms are not fully elucidated, and evidence is still emerging.

Current data suggests that long-COVID symptoms may persist for 4 or more weeks in up to 43% of individuals; in those hospitalized with COVID-19 infection, up to 54% had symptoms lasting ≥4 weeks and 10–12% at 12 weeks post-infection. Since the introduction of COVID-19 vaccinations, this prevalence appears to be decreasing.[11] In those who received 1 or 2 doses of COVID-19 vaccine prior to infection, the risk of developing lingering symptoms at either 4 or 12 weeks post-infection was reduced by approximately 50%. This benefit also extends to those vaccinated after COVID-19 infection and in those with established post-COVID symptoms.[11]

More than 100 symptoms of long-COVID have been reported;[11] the most common ones are:[9][11]

- Respiratory: cough, shortness of breath*
- Cardiac: chest pain, palpitations
- ENT: anosmia, dysgeusia
- Gastrointestinal: abdominal pain, anorexia, diarrhea, nausea, vomiting
- Musculoskeletal: arthralgia, myalgia, reduced mobility
- Neurologic: dizziness, fatigue,* headache, memory problems, cognitive difficulty
- Psychiatric: anxiety,* depression,* insomnia,* post-traumatic stress disorder (PTSD)[12]

* >20% prevalence in patients with long-COVID.[11]

Individuals may complain of 1 or many of these symptoms. It should be noted that this is not an all-inclusive list, and other symptoms that have been less-frequently reported may be present.

Routine follow-up instructions include self-monitoring for any of these symptoms or any symptoms that were not present prior to onset of illness that reflect a less than full return to baseline function. Questions related to return to activities, mobility and independence are important to identify long-term complications of COVID-19. In older patients, potential signs of ongoing symptomatic COVID-19 or long-COVID-19 include descriptions of gradual or ongoing decline in function, persistent

deconditioning, worsening frailty, new or worsening dementia, and loss of interest in eating or drinking.

Supportive or symptomatic management (e.g., headache relief) may be all that is necessary for many of these symptoms, but rehabilitation or referral for further assessment may be required. During follow-up, screening questions for severe hypoxia or significant oxygen desaturation while exercising, chest pain, or severe lung disease will identify individuals who require further assessment. In pediatric patients, symptoms of multisystem inflammatory syndrome should be further investigated. The pathophysiology of this syndrome is unclear at this time. Practitioners are cautioned to avoid dismissing patient complaints or considering them to be predominantly associated with mental health; evidence of organ damage has been described with long-term consequences and is still being explored.

The availability of resources for patients with post-COVID conditions continues to grow and may vary by region. Check with your local public health unit.

Prevention

Vaccination is currently the preferred pharmacologic measure for prevention of COVID-19; see Vaccination against COVID–19. In persons who cannot be vaccinated or specific immunocompromised populations who cannot mount an adequate immune response, pre-exposure prophylaxis with a monoclonal antibody combination may be an option; see Chemoprophylaxis. There is no evidence that any vitamin or herbal supplement is effective in the prevention of the disease. 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* at www.canada.ca/en/health-canada/services/drugs-health-products/covid19-clinical-trials/list-authorized-trials.html#wb-auto-5).

For more information on prevention, see *Health Canada: Coronavirus disease (COVID-19): prevention and risks* at www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/prevention-risks.html. An infographic specifically for patients on the prevention of virus spread has been created by the Canadian Pharmacists Association and is available from www.pharmacists.ca [search: awareness resources > top tips to prevent the spread of viruses].

Vaccination against COVID–19

For a list of available vaccines for the prevention of COVID-19, see Table 1.

COVID-19 immunization for all eligible persons is strongly recommended by public health units in all Canadian jurisdictions. The National Advisory Committee on Immunization (NACI) recommends that individuals with a previous SARS-CoV-2 infection should be vaccinated in order to maximize their immune response.[13] Guidance for time intervals between infection and COVID-19 vaccination (primary or booster doses) in certain populations are also provided.[13] Patients should not seek immunization during an active COVID-19 infection in order to minimize the risk of transmitting the virus at a clinic and to ensure that symptoms are not confused with adverse effects of the vaccine.

Dosing for all vaccines is initiated with a 1- or 2-dose primary schedule. The primary series is followed by booster dose(s) in adults, youth and children ≥5 years of age. Vaccine recommendations are frequently updated and all health-care providers are strongly encouraged to watch for updates from NACI and local public health agencies.[13] See Table 1 and Table 2 for more information.

Table 1: COVID-19 Vaccines Available For Use in Canada[a]

Vaccine[b]	Dose and Schedule[b][c][d]	Adverse Effects	Comments
Adenovirus vector			
COVID-19 vaccine (ChAdOx1-S [recombinant]) Vaxzevria (AstraZeneca), Covishield	**Primary series** ≥18 y: 0.5 mL IM x 2 doses given 4–12 wk apart[e] Moderately to severely immunocompromised individuals:[f] 3-dose series consisting of 2 doses followed by 1 mRNA dose, all given at least 4–8 wk apart[13] **Booster doses**: see criteria for eligibility in Table 2	Pain, redness or swelling at injection site. Fatigue, headache, muscle or joint pain, low fever, chills.[g] Very rare: serious blood clots associated with thrombocytopenia (VIPIT/VITT; occurring 4–28 days after vaccination),[13][16] capillary leak syndrome (CLS),[13] Guillain-Barre Syndrome (GBS; occurs more frequently in males and persons ≥50 y).[13] For more information, see Product Monograph.	An mRNA vaccine is the preferred second dose for individuals who received a first dose of AstraZeneca/ COVISHIELD vaccine. This mixed vaccine schedule has the potential to elicit a better immune response and will mitigate the potential risk of VIPIT associated with viral vector vaccines.[13] If thrombocytopenia or GBS symptoms develop within 42 days of vaccination, advise patient to seek immediate medical attention.[13]
COVID-19 vaccine (Ad26.COV2.S [recombinant]) JCOVDEN (Janssen)	**Primary series** ≥18 y: 0.5 mL IM x 1 dose Moderately to severely immunocompromised individuals[f]: 2–dose series consisting of 1 initial dose followed by 1 mRNA dose given at least 4–8 wk apart[13] **Booster doses**: see criteria for eligibility in Table 2	See COVID-19 vaccine (ChAdOx1-S [recombinant]) .	If thrombocytopenia or GBS symptoms develop within 42 days of vaccination, advise patient to seek immediate medical attention.[13]

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Table 1: **COVID-19 Vaccines Available For Use in Canada**[a] *(cont'd)*

Vaccine[b]	Dose and Schedule[b][c][d]	Adverse Effects	Comments
mRNA spike protein			
elasomeran mRNA vaccine, elasomeran/imelasomeran mRNA vaccine Spikevax (Moderna), Spikevax Bivalent (Moderna; original and Omicron [BA.1])[b]	*Note*: In patients 5–29 y, Comirnaty (Pfizer-BioNTech) is preferred over the Moderna product due to the risk of myocarditis/pericarditis in this population; Spikevax (Moderna) may be offered as an alternative[13] **Primary series** 6 months–5 y: 0.25 mL (25 mcg) IM x 2 doses given 28 days apart[14][e] 6–11 y: 0.25 mL (50 mcg) IM x 2 doses given 28 days apart[13][e] ≥12 y: 0.5 mL (100 mcg) IM x 2 doses given 28 days apart[e] Moderately to severely immunocompromised individuals ≥6 months:[f] 3-dose primary series; each dose given at least 4–8 wk apart[13] **Booster doses**: see criteria for eligibility in Table 2 Dose: ■ 12–69 y: 0.25 mL (50 mcg) IM ■ adults ≥70 y, moderately to severely immunocompromised adults or adults living in congregate settings: 0.5 mL (100 mcg) IM	Pain, redness or swelling at injection site. Fatigue, headache, muscle or joint pain, low fever, chills. Rare: myocarditis or pericarditis. Cases occur after vaccination more often after the second dose, usually within a wk of vaccination, more often in adolescents and young adults under 30 y and more often in males than females. Symptoms include shortness of breath, chest pain, and sensation of rapid or abnormal heart rhythm.[13][17] Advice and management recommendations for individuals presenting with these symptoms are available.[18]	**Multiple products are available:** ■ Original product, 0.1 mg/mL: vial with a royal blue cap ■ Original product, 0.2 mg/mL: vial with a red cap ■ Bivalent product, 0.1 mg/mL: vial with a royal blue cap and green label. Only approved as a booster in those ≥18 y; however, NACI states that it may be offered (off-label) to those 12–17 y who are moderately to severely immunocompromised[f][15] Note: dosing in children 6 months to 5 y should only use the product with a royal blue cap (0.1 mg/mL).
COVID-19 mRNA vaccine, tozinameran Comirnaty (Pfizer-BioNTech), Comirnaty Bivalent (Pfizer-BioNTech; original and Omicron BA.4/BA.5)[b]	*Note*: In patients 5–29 y, Comirnaty (Pfizer-BioNTech) is preferred over the Moderna product due to the risk of myocarditis/pericarditis in this population; Spikevax (Moderna) may be offered as an alternative[13] **Primary series** 6 months–4 y: 0.2 mL (3 mcg/0.2 mL product) IM x 3 doses given at 0, 3 and 11 wk (i.e., 8 wk after second dose) Children 5–11 y: 0.2 mL (10 mcg/0.2 mL product) IM x 2 doses given 21 days apart[13][e] Adults and adolescents ≥12 y: 0.3 mL (30 mcg/0.3 mL product) IM x 2 doses given 21 days apart[e] Moderately to severely immunocompromised individuals ≥5 y:[f] 3-dose primary series; each dose given at least 4–8 wk apart[13] **Booster doses**: see criteria for eligibility in Table 2 Dose: age-specific; use same dose as listed above for primary series	See elasomeran mRNA vaccine/elasomeran/imelasomeran mRNA vaccine. Very rare: reports of Bell palsy following vaccination.[19]	**Multiple products are available:** ■ Original product, 6 month-4 y formulation (3 mcg/0.2 mL): maroon cap and label border (must be diluted) ■ Original product, 5–11 y formulation (10 mcg/0.2 mL): orange cap and label border (must be diluted) ■ Original product, adolescent and adult formulation (30 mcg/0.3 mL): purple cap and label border (must be diluted) or grey cap and label border (do *not* dilute) ■ Bivalent product, adolescent and adult formulation (30 mcg/0.3 mL): grey cap and label border (do *not* dilute) Note: original and bivalent product have grey cap and label border; read vial *carefully* to ensure that the appropriate product is administered.

(cont'd)

Table 1: COVID-19 Vaccines Available For Use in Canada[a] *(cont'd)*

Vaccine[b]	Dose and Schedule[b][c][d]	Adverse Effects	Comments
Recombinant plant-based virus-like particles			
COVID-19 vaccine (plant-based virus-like particles [VLP], recombinant, adjuvanted) Covifenz (Medicago)	**Primary series** 18–64 y: 0.5 mL (3.75 mcg) IM x 2 doses given 21 days apart[e] **Booster doses**: see criteria for eligibility in Table 2	Pain, redness or swelling at the injection site. Fatigue, fever, chills, headache, muscle/joint aches, nasal congestion.	Has not been evaluated in a primary series of mixed vaccines. Covifenz has not been authorized as a booster dose in Canada.
Recombinant protein subunit			
COVID-19 vaccine (recombinant protein, adjuvanted) Nuvaxovid (Novavax)	**Primary series** ≥18 y: 0.5 mL (5 mcg) IM x 2 doses given 21 days apart[e] **Booster doses**: see criteria for eligibility in Table 2	Pain, redness or swelling at the injection site. Fatigue, headache, muscle pain.	May be offered as a booster dose (off-label) to individuals who are unable or unwilling to receive an mRNA vaccine.[13]

NACI = National Advisory Committee on Immunization; VIPIT = vaccine-induced prothrombotic immune thrombocytopenia; VITT = vacine-induced thrombotic thrombocytopenia

[a] To report adverse effects related to COVID-19 vaccination, visit www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting/vaccine.html.
[b] For more information, see the individual product monographs for each vaccine, available from https://cps.pharmacists.ca.
[c] In patients ≥5 y, NACI recommends that COVID-19 vaccines may be given at the same time as, or any time before or after, other live, non-live, adjuvanted or unadjuvanted vaccines.[13] In children <5 y, NACI recommends waiting ≥14 days between the administration of COVID-19 and other vaccines.[14]
[d] Actual dosing schedules may vary depending on vaccine availability, NACI recommendations, local epidemiology and timing of a recent COVID-19 infection.
[e] NACI recommends that the optimal interval between doses is ≥8 wk;[13][14] however, in patients who are moderately to severely immunocompromised, an interval of 4–8 wk between doses is recommended.[13][14]
[f] NACI statement includes list of conditions that can reduce immune response.[13]
[g] Acetaminophen or ibuprofen may be used in the management of pain or fever occurring after vaccination.[13]

Table 2: Booster Dose Recommendations[a][13]

Age Group	First Booster Criteria[a][b]	Subsequent Booster Criteria (regardless of number of booster doses previously received)[a][c][d][20]
6 months to 5 y	Not currently recommended.	Not currently recommended.
5–11 y[e][f]	Recommended if patient has underlying medical condition that increases the risk of severe illness due to COVID-19.[g] May be offered to all other patients. Consider risk vs. benefit, epidemic conditions, time since last vaccine/infection, etc.[g]	Not currently recommended.
12–17 y[e][f]	Should be offered to patients with an underlying medical condition that increases the risk of severe illness due to COVID-19,[g] to residents of congregate living settings (shelters, group homes, etc.) and to those who belong to racialized and/or marginalized communities disproportionately affected by COVID-19.[13] May be offered to all other patients based on epidemiological risk.[13]	Recommended if patient has underlying medical condition that increases the risk of severe illness due to COVID-19[g] and in residents of congregate living settings (shelters, group homes, etc.). May be offered to all other patients.

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Table 2: **Booster Dose Recommendations**[a][13] *(cont'd)*

Age Group	First Booster Criteria[a][b]	Subsequent Booster Criteria (regardless of number of booster doses previously received)[a][c][d][20]
18–64 y[f]	Recommended in all patients.	Recommended if patient is at increased risk of severe illness due to COVID-19, e.g., underlying medical condition,[g] resident of congregate living settings (shelters, group homes, etc.), individual who belongs to racialized and/or marginalized communities disproportionately affected by COVID-19 (e.g., people living with disabilities) and where infection can have disproportionate consequences (e.g., First Nations, Métis, or Inuit communities), residents of congregate living settings for the elderly. May be offered to all other patients.
≥65 y	Recommended in all patients.	Recommended in all patients.

[a] Criteria for booster dose recommendations are evolving; consult the COVID-19 section of the Canadian immunization guide available from: www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-26-covid-19-vaccine.html and/or confirm patient eligibility with local public health unit.

[b] For all individuals eligible to receive a first booster, NACI recommends administering 1 dose of mRNA vaccine ≥6 months after the primary series has been completed.[13] In patients ≥12 years of age, the bivalent booster is recommended.[20] In patients unable or unwilling to receive an mRNA vaccine, the Nuvaxovid vaccine may be administered; however, this is an off-label use.[13]

[c] For all individuals eligible to receive a subsequent booster, NACI recommends administering 1 dose of mRNA bivalent vaccine ≥6 months after the last booster (or COVID-19 infection); however, in the context of heightened epidemiological risk, a 3-month interval may be warranted.[20]

[d] Subsequent booster doses are currently considered off-label.[13]

[e] Comirnaty (Pfizer-BioNTech) is the only product authorized as a booster in the pediatric population. The original formulation is indicated as a booster in children ≥16 years of age.[13] The bivalent formulation (original plus Omicron BA.4/BA.5) is approved as a booster in children ≥12 years of age. [20]

[f] In patients 5–29 y, Comirnaty (Pfizer-BioNTech) is preferred over the Moderna product due to the risk of myocarditis/pericarditis in this population.[13]

[g] For more information, see www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-first-booster-dose-pfizer-biontech-comirnaty-covid-19-vaccine-children-5-11-years.html.

Health Canada's website is an up-to-date resource for information on COVID-19 vaccines approved for use in Canada (available from www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/vaccines.html). Vaccine efficacy and effectiveness may be impacted as variants of concern emerge and circulate globally.

Other helpful resources include:

- Recommendations on the use of COVID-19 vaccines from the National Advisory Committee on Immunization (NACI), available from www.canada.ca/en/public-health
- COVID-19 Vaccine in the Canadian Immunization Guide, available from www.canada.ca/en/public-health/services/canadian-immunization-guide.html (Part 4 active vaccines > COVID-19 vaccine)
- Administration of COVID-19 vaccine in allergic or immunosuppressed patients from the Canadian Pharmacists Association, available from www.pharmacists.ca
- Frequently asked questions: COVID-19 booster doses from Focused COVID Communication, available from https://uwaterloo.ca/pharmacy/sites/ca.pharmacy/files/uploads/files/covid-19-boosters-faq.pdf
- Immunize Canada, available from www.immunize.ca/covid-19
- Working with vaccine-hesitant parents: an update [MacDonald N, Desai S, Gerstein B; Canadian Paediatric Society, 2018]: evidence-based guidance for health-care practitioners who are initiating discussions with vaccine-hesitant parents

Patients and caregivers may have questions about the difference between COVID-19 vaccines, their expected side effects and other risks. Many excellent resources for frequently asked questions are available on provincial and regional websites (e.g., Ottawa Public Health's Frequently asked questions about COVID-19 vaccination available from www.ottawapublichealth.ca [search: COVID-19 vaccine

FAQs]). Some resources address questions about vaccinating children (e.g., COVID-19 vaccines from the Hospital for Sick Children available from www.aboutkidshealth.ca [search: vaccinating children]).

Chemoprophylaxis

When vaccination is not an option, some individuals may be eligible for pre-exposure prophylaxis with a combination therapy of **tixagevimab/cilgavimab**, 2 long-acting monoclonal antibodies (mAbs). Target candidates are those who have been advised that they should not receive a COVID-19 vaccination or are immunocompromised and unlikely to mount an adequate immune response to the vaccine. Furthermore, patients must be ≥12 years of age, weigh ≥40 kg and have no known recent exposure to a person infected with SARS-CoV-2. **Tixagevimab** 150 mg and **cilgavimab** 150 mg are sequentially administered by IM injection for a total dose of 300 mg. A higher dose of 600 mg (i.e., 300 mg/300 mg) may be recommended depending on efficacy against current circulating strains of the SARS CoV-2 virus. If uncertain of recommended dose, consult the local public health guidelines. The combination therapy has an extended half-life of approximately 90 days. See also Table 3.

Therapeutic Choices

Guidance on the treatment of patients with known or suspected COVID-19 is available from:

- AMMI Canada: *Practice point: treatments for adults with COVID-19 in 2021–2022*
- Health Canada: *Clinical management of patients with moderate to severe COVID-19 - interim guidance*
- Centre for Effective Practice: *Primary-care assessment and testing for COVID-19*
- Infectious Diseases Society of America: *Guidelines on the treatment and management of patients with COVID-19*
- National Institute for Health and Care Excellence (NICE), U.K.: *Coronavirus (COVID-19): rapid guidelines and evidence summaries*

In the outpatient setting, treatment for patients with mild to moderate COVID-19 symptoms is usually supportive and based on the provider's assessment of the patient's clinical condition. For patients being cared for or recovering at home, standard treatment for cold-like symptoms and influenza-like illness is recommended. For management of fever and pain, both **acetaminophen** and **nonsteroidal anti-inflammatory drugs (NSAIDs)** are equally effective and considered safe choices.[21] Similarly, patients who regularly take an NSAID or acetylsalicylic acid may continue to do so as previously directed.

Recommendations for nonpharmacologic and pharmacologic management of specific COVID-19 symptoms can found in:

- Fever: see Fever
- Cough: see Acute Bronchitis
- Headache: see Headache in Adults
- Myalgias: there is no evidence for the management of myalgia due to COVID-19 specifically, but the following general information related to management of patients experiencing these symptoms may be helpful; see Acute Pain and Influenza
- GI symptoms (less common): see Nausea and Vomiting and Diarrhea

An infographic from the Canadian Pharmacists Association, *Managing COVID-19 at home*, containing this information for patients is also available from www.pharmacists.ca [search: awareness resources].

In any setting (community, hospital, congregate care), mildly ill patients who are considered to be at high risk for severe disease may be eligible for oral, IV or inhaled therapies. The degree of disease risk is assessed by determining if the patient:[22][23]

- Is immunosuppressed
- Is vaccinated (for COVID-19), unvaccinated or had a previous SARS-CoV-2 infection
- Has comorbid or chronic conditions[22]
- Is elderly[22]
- Is at increased risk of disease progression due to social determinants of health (e.g., Indigenous people, members of other racialized communities)

Choice of therapy for symptomatic mildly ill patients at high risk for severe disease will depend on the availability, contraindications, ease of administration of agents, and timing of a molecular or rapid antigen test relative to symptom onset. Several options are now being considered in Canadian jurisdictions:[22][23]

- **Nirmatrelvir**, a 3CL protease inhibitor that stops the replication of SARS-CoV-2, is approved by Health Canada to treat mild to moderate COVID-19 in adults who are at high-risk for progression to severe COVID-19. Low-dose **ritonavir** is coadministered with nirmatrelvir to slow the metabolism of the protease inhibitor.[24][25] In vitro studies have shown nirmatrelvir to be effective against earlier variants of concern (i.e., Alpha, Beta, Delta, Gamma, Lambda and Mu) as well as the Omicron variant.[25] In placebo-controlled clinical trials, **nirmatrelvir/ritonavir** demonstrated an 89% reduction in risk of hospitalization or death related to COVID-19 when this agent was started within 3 days of symptom onset and 85% risk reduction if started within 5 days of symptom onset.[25]

  Nirmatrelvir 300 mg (2 x 150 mg tablets) in combination with 1 tablet of ritonavir 100 mg is administered PO twice daily for 5 days. Dose adjustments are required if patients have moderate renal impairment. Patient eligibility for this treatment is defined by a number of factors:

  – a positive COVID-19 test (molecular or rapid-antigen tests are acceptable)
  – treatment initiation within 3–5 days of symptom onset
  – a thorough review of patient's drug profile to identify any potential contraindicated therapies, i.e., CYP3A inducers or inhibitors; consult the Paxlovid product monograph or a reputable drug interaction resource for a complete list of drug-drug interactions[25]
  – access to the drug in the patient's region or jurisdiction
- **Sotrovimab**, an anti-SARS-CoV-2 spike protein monoclonal antibody, is authorized under Health Canada's COVID-19 interim order. It is indicated for the treatment of adults and adolescents (≥12 years weighing ≥40 kg) with mild to moderate COVID-19 who are at high risk for hospitalization or death. If patients present within 7 days of symptom onset, they may be candidates for a single IV infusion of sotrovimab 500 mg over 60 minutes.
- **Remdesivir** is a nucleotide analogue antiviral approved for the treatment of COVID-19 in hospitalized adults and adolescents with pneumonia requiring supplemental oxygen and in nonhospitalized adults who are at risk for progression to severe disease. The benefit of a 3-day course was demonstrated in nonhospitalized patients who were at risk of progression to severe disease in a 2021 randomized clinical trial.[26] Several jurisdictions now include remdesivir as a potential treatment for mildly ill patients who are at higher risk of severe disease.[22][23] If patients present within 7 days of symptom onset, an IV infusion of remdesivir 200 mg can be given on day 1, followed by an infusion of 100 mg daily for 2 days.
- When patients are not eligible for infusion therapies or oral nirmatrelvir/ritonavir due to contraindications, drug interactions, limited drug availability, etc., off-label treatment with oral **fluvoxamine** or inhaled **budesonide** may be offered.[22][23] Several studies have demonstrated the efficacy of the SSRI antidepressant **fluvoxamine** in preventing disease progression and hospitalization in outpatients with COVID-19[27][28][29] and more studies are underway.[30] Fluvoxamine has known anti-inflammatory properties; however, its role in preventing clinical

deterioration is not well understood.[30] In a systematic review and meta-analysis of 3 placebo-controlled trials, the authors concluded that fluvoxamine has a moderate effect on preventing COVID-19 hospitalizations and may be a potential option for high-risk outpatients who do not have access to other treatments.[31] Fluvoxamine can interact with other drug treatments and some foods (e.g., caffeine); a careful review of the patient's drug profile is required before initiating treatment.

- For more information about dosing considerations or limitations for all these therapies, see Table 4.

Dexamethasone (or an equivalent corticosteroid) is *not* indicated for patients with COVID-19 who are not admitted to hospital, unless indicated for another condition (e.g., asthma exacerbation). Corticosteroid therapy is routinely indicated for patients admitted to hospital with COVID-19 who require supplemental oxygen. Dexamethasone is administered IV or PO at doses of 6 mg in adults or 0.15 mg/kg (up to 6 mg) in children for 10 days or until discharge, whichever is sooner.[22]

For hospitalized patients, continuation of prophylactic antithrombotics postdischarge for COVID-19 is not recommended. Furthermore, antithrombotic therapy has not demonstrated benefit in outpatient management of COVID-19.

Investigation of other pharmacological options is ongoing and the reader is directed to refer to a reliable source of frequently updated information such as *Health Canada: Drug and vaccine authorizations for COVID-19: List of authorized drugs, vaccines and expanded indications*.

Approved and Experimental Therapies for Acute COVID–19

Information, including links to product monographs, for those agents approved in Canada for the management of COVID-19 can be found on the Health Canada's list of authorized drugs, vaccines and expanded indications.

A few antivirals or monoclonal antibodies have received Emergency Use Authorization and may be considered based on clinical circumstances and availability (e.g.,**bamlanivimab**, **casirivimab/imdevimab**, **remdesivir**, **sotrovimab**). Due to its lack of effectiveness against the Omicron variant, **casirivimab/imdevimab** is not currently recommended.[22] Recommendations and evidence-based decisions on place in therapy for these agents will change as new data emerges. It is important to identify reliable, evidence-based guidelines for the management of acute COVID-19 in outpatient and inpatient settings. Many such provincial and regional evidence-based resources exist (e.g., Ontario COVID-19 Science Advisory Table, BC Centre for Disease Control Clinical Resources for Health Professionals).

Tocilizumab is an interleukin-6 inhibitor marketed in Canada. Although it does not have an indication for the treatment of COVID-19, it is frequently used based on international clinical trial data.[32]

Other experimental therapies have been used to prevent progression or spread of the disease in severely ill patients in the acute-care setting, in mild or moderate illness, or in uninfected patients. Any use of these medications for these purposes outside of a clinical trial or the advice of an infectious disease specialist is inappropriate.

Information about COVID-19–related clinical trials can be found on the following web pages:

- Government of Canada: *Drugs and vaccines for COVID-19: List of authorized clinical trials*
- Cochrane Systematic Review Database: *Living mapping and living systematic review of COVID-19 studies*
- *COVID-19 Clinical TrialsTracker*

The following agents have not demonstrated clinically significant benefit in the prevention or treatment of COVID-19: azithromycin, chloroquine, colchicine, hydroxychloroquine, interferons, ivermectin lopinavir/ritonavir, rifampin, vitamin C, vitamin D and zinc.

Special Populations

Pediatrics

Most children with COVID-19 can be managed at home with supportive care.[33]

Some pediatric populations may be at higher risk for severe COVID-19 and therefore may require hospitalization in order to monitor for deterioration. This includes children who:

- Are ≤1 year of age
- Have obesity
- Are on home ventilation
- Have been diagnosed with:
  - comorbid cardiac or lung disease, e.g., asthma, cystic fibrosis
  - severe genetic, metabolic, neurological or neuromuscular disorders
  - other chronic conditions, e.g., diabetes, sickle cell disease, chronic kidney disease, immunosuppressive conditions such as post-transplant

For treatment of fever in pediatric patients, see Fever.

Long-Term Complications of COVID-19 in Children

As discussed in Long-Term Complications of COVID-19, some pediatric patients will experience a post COVID condition. In children, this most frequently presents as a multisystem inflammatory syndrome (MIS-C). After initial recovery from acute COVID-19, pediatric patients should be assessed for the emergence of signs and symptoms of long COVID-19 in order to ensure appropriate management.[34]

Important signs and symptoms of MIS-C include the following:

- Thermoregulatory: fever that lasts ≥3 days
- Cardiac: tachycardia
- Gastrointestinal: abdominal pain, vomiting, diarrhea
- Immune-mediated: skin rash; redness or swelling of the lips/tongue or hands/feet
- Neurologic: fatigue, headache, dizziness or lightheadedness
- Ophthalmologic: conjunctivitis
- Respiratory: tachypnea
- Other: lymphadenopathy

Immediate medical attention is needed if the child is experiencing any of the following signs or symptoms: severe abdominal pain, difficulty breathing, cyanosis of lips/face, neurologic findings of confusion, or altered level of consciousness.

Choices during Pregnancy and Breastfeeding

COVID-19 Infection in Pregnancy

Although pregnant individuals are not at higher risk for COVID-19, the risk of developing severe disease is greater compared to nonpregnant patients of the same age.[35][36] In general, most babies of patients who have COVID-19 are born healthy at term; however, there is an increased risk of

preterm delivery, low birth weight and admission to a neonatal intensive care unit.[35][37][38] Risk factors for severe COVID-19 disease in pregnancy include asthma, diabetes, obesity, advanced maternal age, hypertension and heart disease.[35]

Vertical transmission of COVID-19 is a rare event.[39][40] There is, however, a risk of person-to-person transmission to the newborn;[36] therefore, all babies born to patients with confirmed COVID-19 should be tested for SARS CoV-2 within 24 hours of delivery.[41]

COVID-19 Infection in Breastfeeding

Although current information is limited, it is unlikely that COVID-19 is transmitted via breast milk.[36] It is recommended that individuals with suspected or confirmed COVID-19 continue to breastfeed their infant if they are able, taking appropriate precautions while doing so.[42][43] If an individual is too ill to breastfeed, they may choose to use a breast pump.[42] Appropriate precautions include:[41]

- Washing hands prior to holding the baby
- Washing hands before handling bottles, breast pump or other equipment
- Wearing a mask while holding or feeding the baby
- While holding or feeding the baby, coughing and sneezing away from the baby
- Good breast and skin cleaning practices prior to holding or feeding the baby
- Ensuring breast pumps, bottles and any other supplies are clean and not shared with others

Prevention of COVID-19

Pregnant or breastfeeding individuals should be offered vaccination against COVID-19 (primary series and/or booster doses) at any time during pregnancy if they are eligible and no other contraindications exist.[13][44] As with all patients, informed consent of the pregnant individual should include a discussion of the risks and symptoms of adverse events associated with COVID-19 vaccines.[13] Enrolment in COVID-19 vaccine registries is encouraged for anyone who receives these vaccines during pregnancy.[13]

COVID-19 vaccination is safe in pregnancy and during breastfeeding. The rates of local and systemic adverse effects to mRNA COVID-19 vaccines are the same as those in the general population. No increase in adverse birth outcomes (e.g., miscarriage, stillbirth, low birth weight, preterm birth, NICU admission) have been observed. Vaccination of the breastfeeding individual did not affect milk production or excretion.[38]

More studies are needed to determine if tixagevimab/cilgavimab can be safely used during pregnancy or while breastfeeding. The drug should be used only if the potential benefit outweighs the potential risks to patient and fetus or the breastfeeding infant.

Treatment of COVID-19

Information on the safety of approved and investigational therapies is listed below:[45][46][47][48]

- Dexamethasone is standard of care for patients admitted to hospital with COVID-19. No major malformations are associated with use of dexamethasone in pregnancy, but a possible increased risk of cleft palate has been described.[49] There is no data on the transfer of dexamethasone into breast milk, though it is not expected to reach levels that are harmful to the infant.
- Remdesivir is an antiviral that has been approved for the treatment of hospitalized patients with severe COVID-19 and nonhospitalized patients at risk of severe COVID-19. There is no data on the use of remdesivir in pregnancy, and the benefit versus risk must be weighed for each individual. Similarly, in breastfeeding, transfer into breast milk is unknown but there is a single case report of direct use in an infant with Ebola without adverse effects.[50]

- There is no human data available on the risk of birth defects, miscarriage or adverse fetal or maternal outcomes associated with the use of **nirmatrelvir** during pregnancy. Nirmatrelvir/ritonavir should not be used in this population unless the potential benefits outweigh the potential risks to the fetus.[25] There is no data available on the presence of nirmatrelvir in human milk and limited published data report that ritonavir is present. For both of these drugs, the effects on the breastfed infant, or the effects on milk production are unknown.
- Sotrovimab should be used in pregnancy only if the expected benefit to the patient will outweigh the potential risk to the fetus. Data is lacking for its effects on human pregnancy and during breastfeeding. Although sotrovimab is a large protein molecule and the amount found in human milk is expected to be very low, caution is advised while breastfeeding, particularly when the infant is newborn or preterm.
- There is limited data on the use of fluvoxamine during pregnancy, and its safety has not been established. Most documented cases of fluvoxamine use while breastfeeding were uneventful; diarrhea and vomiting occurred in 1 exposed infant.[51]
- Bamlanivimab is the only other agent currently approved for the management of COVID-19. This monoclonal antibody does have potential for placental transfer, and the risk to the fetus is unknown. Exposure in breast milk is expected to be limited due to the size of the molecule; however, there is no human data and therefore the benefit to the patient and the risk to the infant must be weighed.
- There is limited data with use of **tocilizumab** in pregnancy, and available data does not demonstrate an increased risk of major defects. There is potential for placental transfer risk, which increases as pregnancy progresses; therefore, fetal risk cannot be ruled out. A small amount of tocilizumab may be transferred into breast milk, but no adverse effects in infants have been reported to date.

For information on the treatment of:

- Cough in pregnancy and breastfeeding, see Acute Bronchitis
- Fever in pregnancy and breastfeeding, see Fever
- Headache in pregnancy and breastfeeding, see Headache in Adults
- Myalgia in pregnancy and breastfeeding, see Acute Pain and Influenza

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

Table 3: Pre-exposure Prophylaxis of COVID-19 Disease in Immunocompromised Individuals

Class	Drug	Dosage	Adverse Effects	Drug Interactions	Comments	Cost
Monoclonal Antibodies	*tixagevimab/ cilgavimab* Evusheld	**Immunocompromised adults and adolescents (≥12 y weighing ≥40 kg):** tixagevimab 150 mg IM injection + cilgavimab 150 mg IM injection administered separately and sequentially Administer at different injection sites; one in each gluteal muscle is recommended A higher dose, i.e., tixagevimab 300 mg + cilgavimab 300 mg, may be recommended depending on its efficacy against the current circulating virus strain.	Injection site reaction. Consider the risks and benefits of using this drug in patients at high risk for cardiovascular or thromboembolic events.	No drug interaction studies conducted. Not excreted renally, not metabolised by CYP P450 enzymes.	Eligible individuals: ■ Must not have a SARS-CoV-2 infection ■ Have no known recent exposure to persons infected with SARS-CoV-2 ■ Are unlikely to mount an adequate immune response to COVID-19 vaccination OR vaccination is not recommended	Consult provincial distribution plans for access.

Table 4: Therapies for Adults with Mild COVID-19 at Moderate or Higher Risk for Severe Disease

Class	Drug	Dosage	Adverse Effects	Drug Interactions	Comments	Cost[a]
Antiviral, Nucleotide Analogue	*remdesivir* Veklury	**Nonhospitalized high-risk adults:**[22] 200 mg IV infusion on day 1, 100 mg IV infusion on days 2 and 3 Discontinue if eGFR falls to <30 mL/min	Elevated transaminase levels, headache, nausea, rash.	Chloroquine and hydroxychloroquine may diminish the therapeutic effect of remdesivir. Studies have not been conducted on potential interactions between remdesivir and inhibitors or inducers of the hydrolytic pathway, CYP2C8, 2D6 or 3A4. A loss of efficacy may occur in drugs with a narrow therapeutic index that are CYP1A2 or CYP3A4 substrates when coadministered with remdesivir.	Initiate treatment within 7 days of symptom onset. **Severe renal impairment** (eGFR <30 mL/min): not recommended. **Hepatic impairment**: Do not initiate or continue treatment in patients with ALT ≥5 × ULN. Also approved for hospitalized adults and adolescents with pneumonia requiring supplemental oxygen. See product monograph for dosing recommendations.	Distribution limited to specialized facilities.

(cont'd)

Table 4: Therapies for Adults with Mild COVID-19 at Moderate or Higher Risk for Severe Disease *(cont'd)*

Class	Drug	Dosage	Adverse Effects	Drug Interactions	Comments	Cost[a]
Antiviral, Protease Inhibitor	*nirmatrelvir/ritonavir* Paxlovid	**Nonhospitalized high-risk adults:**[24] 2 tabs nirmatrelvir 150 mg plus 1 tab ritonavir 100 mg PO BID × 5 days If eGFR ≥30 to <60 mL/min: 150/100 mg BID PO × 5 days	Mostly mild: altered sense of taste, elevated blood pressure, GI effects (diarrhea, vomiting), headache, muscle pain. Hepatotoxicity has been reported in patients receiving ritonavir long term.	Numerous potential drug interactions; consult a reputable drug interaction resource or the Paxlovid product monograph.[25] Nirmatrelvir and ritonavir are CYP3A substrates. Some CYP3A inducers (e.g., carbamazepine, dexamethasone, phenytoin, rifampin, St. John's wort) may decrease plasma concentrations of both agents and are contraindicated.[b] Ritonavir, a CYP3A inhibitor, may increase plasma levels of drugs that are extensively metabolized by CYP3A (e.g., alfuzosin, ranolazine, amiodarone, colchicine, lurasidone, lovastatin, simvastatin, sildenafil, triazolam). [c]	Not approved for use in pediatric patients (<18 y). Initiate treatment only after diagnosis with a positive viral test and within 3–5 days of symptom onset. Can be taken with or without food. Tablets should be swallowed whole; do not chew, break or crush. Pharmacist consultation is important to mitigate significant drug–drug interactions. **Severe renal impairment** (eGFR <30 mL/min): not recommended. **Hepatic impairment**: Mild-moderate: no dose adjustment. Severe: not recommended.	Consult provincial distribution plans for access.
Corticosteroids, Inhaled	*budesonide* Pulmicort Turbuhaler, Pulmicort Nebuamp, generics	**Moderate to higher risk adults:**[22] 800 mcg inhaled BID × 14 days	Cough, sore mouth, sore throat, dysphonia (hoarseness), oral candidiasis (thrush).	Strong CYP3A4 inhibitors, e.g., ritonavir, azole antivirals, can increase systemic exposure to budesonide.	**Off-label use.** To reduce adverse effects with inhaled corticosteroids, advise patients to rinse mouth with water after each dose, clean dentures, or use with a spacer device, where appropriate.	Turbuhaler: $$$$$ Nebules: $$$$

Class	Drug	Dosage	Adverse Effects	Drug Interactions	Comments	Cost[a]
Monoclonal Antibodies	*sotrovimab* Sotrovimab for Injection	**Nonhospitalized high-risk patients:**[22] 500 mg IV infusion (over 60 min) × single dose	Diarrhea, injection site pain, bleeding, swelling. Rare: anaphylaxis, infusion-related reactions.	Not renally excreted or metabolized by CYP enzymes. No formal drug interaction studies have been performed.	Authorized by Health Canada's COVID-19 interim order. Approved for use only in certain adults or adolescents (≥12 y weighing ≥40 kg). Initiate treatment within 7 days of symptom onset.	Distribution limited to specialized facilities.
Selective Serotonin Reuptake Inhibitors (SSRIs)	*fluvoxamine* Luvox, generics	**Moderate to higher risk adults:**[22] 50 mg PO daily, titrated up to 100 mg PO BID for a total of 15 days	CNS effects: highly sedating, anxiety, agitation, insomnia, headache, extrapyramidal effects. Significant GI effects: nausea, vomiting, diarrhea, constipation, increased risk of upper GI bleeding. Others: dry mouth, increased sweating, sexual dysfunction, SIADH with hyponatremia.	Numerous potential drug interactions; consult a reputable drug interaction checker or resource. Strong inhibitor of CYP1A2, CYP2C19. It can also affect CYP2C9 and CYP3A4 to a lesser degree. Contraindicated with MAO inhibitors, pimozide, tizanidine, thioridazine, ramelteon. Use discouraged in patients taking lansoprazole, omeprazole, clopidogrel. Can potentiate the effects of alcohol and increase plasma levels of caffeine.	**Off-label use.** Consult local guidelines. **May be considered** in some mildly ill patients presenting within 7 days of symptom onset who are: ■ at moderate risk of severe disease OR ■ at higher risk of severe disease when nirmatrelvir/ritonavir is not available or contraindicated Pharmacist consultation and outpatient follow-up is important to avoid significant drug-drug interactions.	$

[a] Cost of inhaled agents is per unit (1 inhaler); cost of nebules or oral medication is per course of adult treatment; includes drug cost only.

[b] Contraindicated with potent CYP3A inducing drugs that can reduce the plasma concentration of nirmatrelvir/ritonavir, causing potential loss of virologic response and potential resistance.

[c] Contraindicated with drugs that can cause serious or life-threatening reactions in elevated concentrations and are highly dependent on CYP3A for clearance.

Dosage adjustment may be required in renal impairment; see Appendix I.

Abbreviations:
ALT = alanine aminotransferase; CNS = central nervous system; CYP = cytochrome P450; eGFR = estimated glomerular filtration rate; GI = gastrointestinal; MAO = monoamine oxidase inhibitor; SIADH = syndrome of inappropriate antidiuretic hormone; ULN = upper limit of normal

Legend: $ < $15 $$ $15–30 $$$ $30–45 $$$$ $45–60 $$$$$ $60–75

Suggested Readings

Centers for Disease Control and Prevention. *Post-COVID conditions: information for healthcare providers* [internet]. July 9, 2021. Available from: www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/post-covid-conditions.html.

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