Frequently Asked Questions About Drug Therapies for Adults with Severe to Critical COVID-19

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Purpose

This document addresses frequently asked questions (FAQs) about drug therapies for severe to critical COVID-19. This document provides supplemental information to the Ontario Health Recommendations for Antiviral Therapy for Adults with Severe to Critical COVID-19.

Document Development

The information provided in this document is informed by best available evidence retrieved from a systematic literature search conducted between January and April 2025 of peer-reviewed studies, review articles, Canadian guidelines, international guidelines and grey literature. The recommendations were developed by the Ontario Health Infectious Diseases program's guidance development working group with consensus-based feedback and contributions from Ontario Health's Infectious Diseases Advisory Committee (IDAC). This document was reviewed by multidisciplinary clinicians and health care administrators from Ontario Health's Primary Care Program, Systemic Treatment Program (Cancer Care), Regional Clinical Vice-Presidents and the Chief Medical Executive.

This document will be updated as required as new evidence and relevant information becomes available.

Refer to the ***Authorship, Contributors and Acknowledgements*** section for additional information about the authors and contributors of this document.

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1. Pregnancy

Preamble: Drug therapy for pregnant people with COVID-19

Although data on drug therapy of pregnant individuals with COVID-19 is limited, treatment should not be withheld on account of pregnancy.[1] A shared decision-making approach that involves a multidisciplinary team (e.g., an infectious diseases specialist, obstetrician, perinatologist, pharmacist) with suitable expertise in the management of pregnancy and COVID-19 is recommended to evaluate the risks and benefits of drug therapy in pregnant people with COVID-19.[1]

People who are pregnant with symptomatic COVID-19 are at increased risk of maternal death, admission to an intensive care unit (ICU), requiring mechanical ventilation, preeclampsia, eclampsia, thromboembolic disease and caesarean delivery compared with people who are pregnant without COVID-19.[2] Babies of pregnant individuals with COVID-19 are at higher risk of preterm birth and stillbirth.[3] An individualized risk-benefit assessment should be conducted that includes evaluation of the severity of COVID-19, the risk of disease progression based on the pregnant person's medical comorbidities (e.g., pre-existing diabetes mellitus, hypertension, cardiovascular disease) and the safety of the medications used to treat COVID-19 for the fetus and the pregnant person.[1,4]

In addition to the FAQs below, more information on COVID-19 and pregnancy can be found under ***Additional Resources***.

1A. Can dexamethasone be used in pregnant people with COVID-19?

Dexamethasone can be used to treat severe to critical COVID-19 in pregnant people.[1,5,6] Alternative systemic corticosteroid agents (i.e., prednisone, hydrocortisone or methylprednisolone) may be used to treat pregnant patients with COVID 19 who are contraindicated for dexamethasone.[1]

Placental drug transfer

A pharmacokinetic modelling study estimated that 14% of dexamethasone in a pregnant person reaches fetal circulation.[7]

The placental transfer of prednisone, hydrocortisone and methylprednisolone is less than 10%.[8]

Potential adverse pregnancy and/or fetal effects

Although data on the use of dexamethasone in pregnant people with COVID-19 is scarce, dexamethasone has been used to treat other indications during pregnancy.[9] Dexamethasone is considered safe to use in pregnancy with a low risk of fetal adverse effects.[1,5]

Oral clefts (e.g., cleft lips, cleft palates) in children have been reported as a potential adverse effect of dexamethasone and/or systemic corticosteroid antenatal exposure when used to treat non-COVID-19 indications.[10,11] However, observational studies have not shown a consistent association between higher rate of oral clefts in children with antenatal dexamethasone and/or systemic corticosteroid exposure compared to non-exposed children.[11]

In animal studies, an association between the use of antenatal systemic corticosteroid use and adverse effects such as impaired neurodevelopment and a smaller head circumference was reported.[10] However, observational studies in humans have not consistently detected a significant difference in head circumference or impaired neurodevelopment in children who were exposed to a single course of antenatal corticosteroids for non-COVID-19 indications compared to non-exposed children.[12,13]

The potential adverse pregnancy and/or fetal effects listed above are not exhaustive. Refer to the resources related to drug therapy during pregnancy under the ***Additional Resources*** section for more information.

1B. Can remdesivir be used in pregnant people with COVID-19?

Remdesivir can be used to treat COVID-19 in pregnant people.[1]

Placental drug transfer

Placental transfer of remdesivir in humans is unknown, but animal studies showed that remdesivir crossed the placenta into the fetus.[14,15] An ex-vivo pharmacokinetic modelling study estimated that 22% of remdesivir and 16% of the active metabolite of remdesivir (GS-441524) may be transferred from a pregnant person to the fetus.[16]

Potential adverse pregnancy and/or fetal effects

Data from a registry of pregnant people with COVID-19 reported similar maternal outcomes (e.g., placental abruption, pregnancy-related hypertension, venous thromboembolism, death) and neonatal outcomes (e.g., positive SARS-CoV-2 test, stillbirth, neonatal death) in patients treated with remdesivir compared to those who were not treated with remdesivir.[17] Limited data from other observational studies suggest that remdesivir is well-tolerated and associated with a low risk of serious adverse events in individuals across the three trimesters of pregnancy.[1,17–23]

Cases of preterm deliveries and caesarean sections (C-sections) have been reported in pregnant people with COVID-19 post remdesivir exposure.[24] However, it is unknown if these outcomes were due to remdesivir, COVID-19, or a combination of both.[24]

Elevated transaminases (e.g., alanine transaminase [ALT], aspartate transaminase [AST]), are commonly reported in observational studies and post-marketing surveillance studies of pregnant people with COVID-19 treated with remdesivir.[1,17,25] However, severe or medically significant abnormalities are uncommon.[1,17,25] This is consistent with reports that elevated transaminases were observed in non-pregnant people treated with remdesivir for COVID-19.[1,26] COVID-19 and other conditions in pregnancy (e.g., preeclampsia, intrahepatic cholestasis of pregnancy, acute fatty liver of pregnancy, and hemolysis, elevated liver enzymes, and low platelet count [HELLP] syndrome) may also cause transaminase elevations.[27]

The potential adverse pregnancy and/or fetal effects listed above are not exhaustive, refer to the resources related to drug therapy during pregnancy under the ***Additional Resources*** section for more information.

1C. Can tocilizumab be used in pregnant people with COVID-19?

Tocilizumab can be used to treat critical COVID-19 in pregnant people.[1]

Placental drug transfer

It is not known if tocilizumab crosses the placenta to the fetus.[10] However, tocilizumab has a high molecular weight (148,000 daltons) and is not expected to cross the placenta in large amounts.[10] Similar to other immunoglobulin antibodies, the placental transfer of tocilizumab be may be higher during the second and third trimesters compared to the first trimester.[28]

Potential adverse pregnancy and/or fetal effects

There is currently no evidence that tocilizumab is teratogenic or fetotoxic.[29] Case reports and case series have reported good outcomes in pregnant people following tocilizumab use.[30]

There is limited data about the use of tocilizumab in pregnant people with COVID-19.[30] Published reports of individuals with COVID-19 who received tocilizumab during their second or third trimester of pregnancy have not identified an increased risk of adverse drug effects for the pregnant person or the infant.[28] Pregnancy-related problems identified in the case reports (e.g., preterm delivery, C-section, or admission of the newborn to the neonatal intensive care nursery) were believed to be caused by COVID-19 or other underlying medical conditions.[28]

A study based on data from clinical trials and observational reports of pregnant individuals reported an increased rate of preterm birth in patients exposed to tocilizumab during pregnancy to treat non-COVID-19 indications (e.g., rheumatoid arthritis, Castleman disease, Still's disease) compared to unexposed pregnant patients.[1,31] The same study reported comparable rates of congenital abnormalities among infants following antenatal tocilizumab exposure and infants who were not exposed to tocilizumab.[1,31] A retrospective study of pregnant individuals exposed to tocilizumab at conception or during their first trimester did not find increased rates of congenital abnormalities or spontaneous abortion compared to pregnant individuals in the general population not exposed to tocilizumab.[1,32] The generalizability of the results from the use of tocilizumab to treat non-COVID-19 indications may be limited because repeated doses of the drug are commonly used to treat non-COVID-19 indications, whereas a single dose is recommended to treat COVID-19.[31,32]

Limited data from observational studies of infants born to individuals treated with tocilizumab during pregnancy have not reported any problems with infant development up to 1 year of age.[28]

The potential adverse pregnancy and/or fetal effects listed above are not exhaustive. Refer to the resources related to drug therapy during pregnancy under the ***Additional Resources*** section for more information.

1D. Can baricitinib be used in pregnant people with COVID-19?

The use of baricitinib to treat COVID-19 in pregnant people has not been studied.[6] Tocilizumab is preferred over baricitinib for the treatment of critical COVID-19 in pregnant individuals because its safety profile is better established.[33] Consultation with an infectious diseases specialist and an obstetrician or a perinatologist prior to baricitinib initiation is strongly recommended to determine the most appropriate option for COVID-19 treatment in a pregnant person.

Placental drug transfer

It is not known if baricitinib crosses the placenta to the fetus, but placental transfer is expected to occur based on the drug's low molecular weight (371 daltons).[10]

Potential adverse pregnancy and/or fetal effects

Limited clinical data is available on baricitinib use in pregnancy.[9] A rheumatoid arthritis clinical trials program reported some cases of live births with no fetal abnormalities and some cases of spontaneous fetal loss following baricitinib exposure during pregnancy.[9] In animal studies, doses that were less than 10 times the human dose were not associated with developmental toxicity.[1,10] However, higher doses were associated with embryofetal developmental abnormalities.[10]

The potential adverse pregnancy and/or fetal effects listed above are not exhaustive. Refer to the resources related to drug therapy during pregnancy under the ***Additional Resources*** section for more information.

2. Breastfeeding or Chestfeeding

Preamble: Drug therapy for breastfeeding or chestfeeding patients with COVID-19

Withholding drug therapy for COVID-19 from individuals who are breastfeeding or chestfeeding is not recommended.[1] A shared decision-making approach by a multidisciplinary team (e.g., an infectious diseases specialist, obstetrician, perinatologist, pharmacist) is recommended to evaluate the risks and benefits of breastfeeding/chestfeeding during COVID-19 drug therapy.[1] Examples of factors to consider by the clinical team and the patient include: the postnatal age of the infant, the need for the medication, any underlying risks of exposing the infant to the drug and the potential adverse outcomes of COVID-19.[1]

Breastfeeding or chestfeeding with COVID-19

The available evidence suggests that SARS-CoV-2 is not spread to infants through human breast milk.[34] Breast milk is the recommended source of nutrition for most infants because it contains antibodies and other factors that may provide them with immunological protection.[34] For patients with suspected or confirmed COVID-19 who intend to feed the infant with breast milk, obstetricians and other parental care practitioners should provide counselling on safety precautions to minimize the risk of SARS-CoV-2 transmission through respiratory droplets while in close contact with the infant.[2] These precautions may include hand hygiene, wearing a medical face mask while breastfeeding/chestfeeding, breast milk expression using a dedicated breast pump, proper pump cleaning after each use or having someone who does not have suspected or confirmed COVID-19 infection and is not sick feed the expressed breast milk.[2]

In addition to the FAQs below, more information on COVID-19 and breastfeeding/chestfeeding can be found under ***Additional Resources***.

2A. Can dexamethasone be used in patients with COVID-19 who are breastfeeding or chestfeeding?

Breastfeeding/chestfeeding can continue while a patient receives dexamethasone to treat severe or critical COVID-19.[1,5]

Drug transfer into breast milk

Dexamethasone has a low molecular weight (516 daltons) and small amounts of the drug is expected to pass into breast milk.[10,35]

Potential adverse effects for the breastfeeding/chestfeeding patient or child

There is limited data on the use of dexamethasone in breastfeeding/chestfeeding individuals.[1,5,10,36] Some individuals treated with high-dose dexamethasone and/or systemic corticosteroids for non-COVID indications reported a temporary decrease in the volume of breast milk production.[1,36]

There have not been any reports of adverse effects in infants exposed to dexamethasone through breast milk.[1,36]

2B. Can remdesivir be used in patients with COVID-19 who are breastfeeding or chestfeeding?

Breastfeeding/chestfeeding can continue while a patient receives remdesivir therapy for treatment of severe COVID-19.[1,37]

Drug transfer into breast milk

Remdesivir and its active metabolite (GS-441524) are poorly absorbed from the gastrointestinal tract.[37] Infants are unlikely to absorb clinically significant amounts from breast milk.[37] A case report estimated that the relative infant doses of remdesivir and GS-441524 in breast milk as 0.007% and 1.6%, respectively.[37]

Potential adverse effects for the breastfeeding/chestfeeding patient or child

No adverse effects have been reported in infants exposed to remdesivir through breast milk.[14,37]

2C. Can tocilizumab be used in patients with COVID-19 who are breastfeeding or chestfeeding?

Breastfeeding/chestfeeding can continue while a patient receives tocilizumab for critical COVID-19.[1,38]

Drug transfer into breast milk

Less than 1% of the serum concentration of tocilizumab in a breastfeeding/chestfeeding individual has been detected in breast milk.[1,10] However, serum levels of tocilizumab have not been detected in infants who were breastfed by individuals treated with tocilizumab based on data from case reports.[38]

Potential adverse effects for the breastfeeding/chestfeeding patient or child

Limited information is available about the use of tocilizumab in breastfeeding/chestfeeding individuals from case reports of tocilizumab use to treat non-COVID-19 indications (e.g., rheumatoid arthritis, Still's disease, etc).[1,10] No adverse effects have been reported in infants exposed to tocilizumab through breast milk.[28,38]

2D. Can baricitinib be used in patients with COVID-19 who are breastfeeding or chestfeeding?

Baricitinib use in individuals with critical COVID-19 who are breastfeeding/chestfeeding is not recommended outside of a clinical trial setting.[5]

Individuals who are lactating while receiving baricitinib should avoid feeding the breast milk during the course of baricitinib therapy and for four days after the last dose.[1,39] Patients should be encouraged to pump the breast milk during that period to ensure that lactation continues after baricitinib therapy has completed.[1]

Drug transfer into breast milk

It is unknown if baricitinib is excreted in human breast milk.[1,5] However, the drug is expected to pass into breast milk because of its low molecular weight (371 daltons).[9,10] In animal studies, baricitinib was detected in the milk of lactating rats.[1]

Potential adverse effects for the breastfeeding/chestfeeding patient or child

The use of baricitinib in people who are breastfeeding/chestfeeding or the potential adverse effects of baricitinib in infants exposed to the drug through breast milk is unknown because it has not been studied.[1,10,40]

3. For patients who are immunocompromised and were receiving systemic corticosteroid therapy prior to developing severe or critical COVID-19, should the maintenance systemic corticosteroid therapy be continued while the patient is receiving dexamethasone for COVID-19?

For patients who are immunocompromised and were treated with a chronic systemic corticosteroid prior to developing severe or critical COVID-19, the maintenance systemic corticosteroid should be discontinued while the patient receives dexamethasone to treat COVID-19.[1] Consult with specialists (e.g., infectious diseases, transplant, oncology, rheumatology, respirology) as required to inform individualized treatment decisions for the treatment of severe or critical COVID-19 in people who have a medical condition where chronic systemic corticosteroid therapy is indicated.[1] Once the individual has recovered from COVID-19 or completed the course of dexamethasone therapy, the maintenance doses of the systemic corticosteroid therapy should resume.[1]

No clinical study has determined the optimal dose of dexamethasone for COVID-19 treatment in immunocompromised patients who were receiving chronic systemic corticosteroid therapy prior to developing severe or critical COVID-19.[1] Dexamethasone 6 mg orally/intravenously daily (or an equivalent dose of another systemic corticosteroid if dexamethasone is not available) for 10 days or until discharge, whichever is sooner, is the minimum recommended dose of systemic corticosteroid to treat severe or critical COVID-19 in this patient population.[1,41]

4. For patients with severe or critical COVID-19 who have clinically improved and no longer require supplemental oxygen or respiratory support but remain hospitalized, can dexamethasone (or equivalent systemic corticosteroid) be discontinued prior to completing 10 days of treatment or prior to hospital discharge?

There is currently insufficient evidence to support routine early discontinuation of dexamethasone (or equivalent systemic corticosteroid) prior to completing 10 days of treatment or prior to hospital discharge. Prescribers should conduct a comprehensive risk-benefit analysis to inform individualized treatment decisions.

In patients with severe or critical COVID-19 who have clinically improved and no longer require supplemental oxygen or respiratory support, the risks and benefits of early discontinuation of dexamethasone (or equivalent systemic corticosteroid) prior to completing 10 days of treatment or prior to hospital discharge have not been evaluated. Consultation with an infectious diseases specialist is recommended to inform individualized treatment decisions.[42] Factors to consider include: COVID-19 disease severity when dexamethasone was initiated, the patient's degree of clinical improvement, and the reason(s) for the patient's continued hospitalization (e.g., medically-related reasons versus non-medically-related for hospitalization).

The recommended duration of dexamethasone therapy for up to 10 days or until hospital discharge, whichever is sooner, is based on the RECOVERY study that established the place in the therapy of dexamethasone for the treatment of COVID-19.[1,43–45] In 2023, a meta-analysis of randomized controlled trials and observational studies of individuals with COVID-19 found similar mortality rates for patients who received a course of systemic corticosteroid therapy with a median duration of 7 days compared to no systemic corticosteroid therapy, and for patients who received a course of systemic corticosteroid therapy with a median duration of greater than 7 days compared to no systemic corticosteroid therapy.[46] However, a major limitation of the study is the lack of direct comparison between systemic corticosteroid courses of 7 days and greater than 7 days. Additional limitations of the meta-analysis include the heterogenous study population, the use of concomitant medications, and the type, dose and duration of systemic corticosteroid therapy.[46]

5. What is the risk of hepatotoxicity secondary to remdesivir use in patients with COVID-19?

Clinical studies of individuals with COVID-19 have not reported any significant difference in the incidence of hepatotoxicity for patients who received remdesivir compared to no remdesivir.[26,47,48] While remdesivir therapy in patients with COVID-19 has been associated with asymptomatic, transient, reversible, mild to moderate elevations in serum aminotransferase levels (e.g., alanine transaminase [ALT], aspartate transaminase [AST]), it has rarely been linked to instances of clinically apparent drug-induced liver injury (DILI).[49–51] The mechanism of remdesivir-induced hepatotoxicity is unknown.[51]

A meta-analysis of randomized controlled trials of individuals with COVID-19 found no significant difference for the rates of medically-significant, severe, or life-threatening liver impairment for patients treated with remdesivir compared to no remdesivir treatment.[47,52] However, a limitation of the meta-analysis was the exclusion of patients with severe hepatic impairment at baseline [e.g., ALT or AST greater than five times the upper limit of normal (ULN)] in many of the trials.[47] Similarly, a retrospective study reported no significant difference in the rates of ALT, AST or bilirubin elevation (e.g., ALT or AST greater than 200 IU, bilirubin greater than 34.2 mmol/L) in individuals with COVID-19 who received remdesivir therapy compared to no remdesivir therapy.[48] An observational study that assessed the incidence of hepatotoxicity secondary to remdesivir therapy for patients with COVID-19 based on the Drug-Induced Liver Injury Network criteria (DILIN) found remdesivir was not associated with a significant increase in moderate or severe hepatotoxicity compared to no remdesivir therapy.[53,54]

SARS-CoV-2 infection commonly affects the liver and serum aminotransferase elevations may present in up to 60% of adults.[50,55,56] The mechanism of COVID-19-related liver injury is not well understood.[57,58] ALT and/or AST elevations are generally mild and less than five times the ULN.[56] Serum aminotransferase elevations are more frequent in people with severe SARS-CoV-2 infection or in people with risk factors associated with more severe COVID-19 outcomes (e.g., older age, diabetes, obesity).[50,59,60]

6. What is the risk of secondary infections following baricitinib therapy compared to tocilizumab therapy in patients with COVID-19?

There is inconsistent evidence with regards to a difference in the rate of secondary infections (e.g., bacterial, fungal or viral infections) for patients with COVID-19 following baricitinib compared with tocilizumab therapy. Patients with critical COVID-19 treated with immunomodulatory agents (e.g., baricitinib or tocilizumab in combination with dexamethasone) should be monitored for secondary infections.[1]

In patients with COVID-19 who required any oxygen supplementation or respiratory support, a meta-analysis of observational studies reported the rate of secondary infections was significantly higher in individuals treated with tocilizumab compared to baricitinib.[61] Another observational study reported similar findings where tocilizumab therapy was associated with a higher rate of hospital-acquired infections compared with baricitinib therapy.[62] However, three other observational studies reported no significant difference in the risk of secondary infections between patients who received baricitinib therapy and those who received tocilizumab therapy.[63–65] Concurrent therapy with a systemic corticosteroid was reported as part of usual care in most of the studies.

A summary of studies that compared the incidence of specific types of secondary infections in patients with COVID-19 is described below.

Secondary Bloodstream Infections

Two observational studies reported no significant difference for the rate of secondary bloodstream infections following treatment with baricitinib compared to tocilizumab in patients with COVID-19.[66,67] Concurrent therapy with a systemic corticosteroid was part of usual care in both studies.[66,67]

Secondary Invasive Fungal Infections

An observational study of patients with COVID-19 who required any oxygen supplementation or respiratory support found no significant difference for the rate of invasive fungal infections (e.g., aspergillosis, mucormycosis) in patients who received baricitinib therapy compared with patients who received tocilizumab therapy.[67] All patients in this study received concurrent therapy with a systemic corticosteroid as part of usual care.[67]

7. In immunocompromised patients with COVID-19, what is the risk of secondary infections following baricitinib or tocilizumab therapy?

No clinical study has evaluated the incidence of secondary infections following baricitinib therapy compared with tocilizumab therapy in immunocompromised patients with COVID-19. Consult with an infectious disease specialist and other specialists (e.g., transplant, oncology, hematology, rheumatology) as needed to inform individualized treatment decisions in immunocompromised individuals with COVID-19. Selection between baricitinib and tocilizumab may also depend on patient-specific factors (e.g., comorbidities, the concurrent use of other immunomodulatory agents, potential drug-drug interactions).[1]

Clinical studies that compared baricitinib or tocilizumab therapy to no baricitinib or tocilizumab therapy reported no significant difference in the rate of secondary infections in this patient population.[68,69] One retrospective study of individuals with COVID-19 who are immunocompromised (e.g., people with hematological malignancies, solid organ transplant recipients, people with primary hypogammaglobulinemia patients, people living with HIV and have CD4 T lymphocyte cell counts equal or less than 200 cells/mm^3, individuals treated with a B-cell depleting agent during the past 12 months or patients on a high-dose long-term corticosteroid treatment) and required any oxygen supplementation or respiratory support did not find any significant difference for the use of antibiotic therapy for patients treated with baricitinib or tocilizumab therapy compared to no baricitinib or tocilizumab therapy.[69] The use of antibiotic therapy as a surrogate measure for secondary infections is a limitation of this study. Another retrospective study of immunocompromised transplant recipients (solid organ transplant or hematopoietic stem transplant) with COVID-19 who required oxygen supplementation or respiratory support reported no significant difference in the incidence of secondary infections for patients who received baricitinib or tocilizumab and those who did not receive baricitinib or tocilizumab.[68] In both retrospective studies, the use of concurrent systemic corticosteroid therapy was over 90%.[68,69]

People who are immunocompromised are a heterogeneous group.[1] Individuals with immunocompromising conditions (e.g., hematological malignancies, solid organ transplants, HIV, rheumatic diseases) or are receiving immunosuppressive medications (e.g., T cell-depleting or T cell-suppressing agents, B cell-depleting agents) have a higher risk of severe COVID-19 outcomes, compared to the general population, but not all immunocompromising conditions carry the same risk.[1,70]

8. What is the risk of gastrointestinal perforation in patients with COVID-19 following baricitinib therapy compared to tocilizumab therapy?

Limited available evidence suggests the risk of gastrointestinal perforation is similar between baricitinib and tocilizumab as a potential adverse drug effect following their use to treat patients with COVID-19.

One observational study found no significant difference in the rate of gastrointestinal perforation in individuals with COVID-19 following baricitinib therapy compared to tocilizumab therapy.[63] The concurrent use of systemic corticosteroids was not reported for this study and patient enrollment for this study began approximately two months before the results of the RECOVERY trial was released and dexamethasone became a part of usual care.[47,63] The lack of information about the concurrent use of systemic corticosteroids is a limitation of the study because immunosuppressive agents (e.g., systemic corticosteroids, baricitinib, tocilizumab) may potentially impair gastrointestinal tissue repair and lead to an increased risk of gastrointestinal perforation.[71]

Gastrointestinal perforation is an uncommon, but serious complication of COVID-19.[72] Safety data about gastrointestinal perforation following baricitinib or tocilizumab therapy for COVID-19 from clinical trials are scarce. Individuals with a high risk of gastrointestinal perforation (e.g., patients with a history of gastrointestinal ulceration of diverticulitis) were often excluded from clinical trials of baricitinib and tocilizumab because gastrointestinal perforation is a less common, but known potential adverse effect of the drugs.[1,39,73]

Patients with COVID-19 treated with immunosuppressive drugs (i.e., baricitinib, tocilizumab, systemic corticosteroids) should be monitored for gastrointestinal perforations as a potential adverse effect.[74] Clinicians should be aware that the immunosuppressive effects of these drugs may mask potential signs and symptoms of gastrointestinal perforation (e.g., abdominal pain and/or tenderness, fever, tachycardia, tachypnea).[72]

9. What is the risk of venous thromboembolism in patients with COVID-19 following baricitinib therapy compared to tocilizumab therapy?

There is inconsistent evidence with regards to a difference for the risk of venous thromboembolism (VTE) in patients with COVID-19 following baricitinib compared with tocilizumab therapy. Consult with specialists (e.g., infectious disease, hematology) as required to inform individualized treatment decisions in patients with COVID-19 who may be at an increased risk of VTE.

Two observational studies reported an association between tocilizumab therapy and a significantly higher rate of VTE compared to baricitinib therapy in patients with COVID-19.[75,76] However, five other observational studies of patients with COVID-19 found no significant difference in VTE rates between patients who received baricitinib therapy compared to tocilizumab therapy.[63,64,66,77,78] Most patients in the observational studies received concurrent systemic corticosteroid therapy for COVID-19. VTE is a potential, albeit uncommon, adverse effect of systemic corticosteroid therapy.[79,80]

COVID-19 is associated with an increased risk of VTE due to SARS-CoV-2-induced endotheliopathy and systemic inflammation.[81,82] In addition, people with severe to critical COVID-19 commonly have other risk factors for VTE (e.g., previous VTE, obesity, age greater than 60 years old).[81,83]

Refer to the supplementary information on thromboprophylaxis for patients hospitalized with COVID-19 in the ***Additional Resources*** section for more information.

Additional Resources

Supplementary Information on Pregnancy and Breastfeeding/Chestfeeding

- Public Health Agency of Canada: COVID-19 – Pregnancy, Childbirth and Caring for a Newborn
- The Society of Obstetricians and Gynaecologists of Canada: COVID-19 Resources
- American College of Obstetricians and Gynecologists: COVID-19 FAQs for Obstetrician-Gynecologists, Obstetrics
- Australian Guidelines for the Clinical Care of People with COVID-19: refer to the individual COVID-19 drug therapy sections for pregnant and breastfeeding people
- Organization of Teratology Information Specialists: Mother to Baby Drug Fact Sheets
- United States Centers for Disease Control and Prevention: COVID-19 and Breastfeeding
- United States National Institute of Child Health and Human Development: Drugs and Lactation Database
- United States National Institutes of Health: refer to the Pregnancy, Lactation and COVID-19 Therapeutics section

Supplementary Information for Treating COVID-19 in Transplant Recipients

- American Society of Transplantation: COVID-19 Resources
- European Society for Bone and Marrow Transplantation: COVID-19 Information and Resources
- International Society of Heart and Lung Transplant: COVID-19 Information for Transplant Professionals

Supplementary Information on Thromboprophylaxis for Patients Hospitalized with COVID-19

- Thrombosis Canada: Primary Thromboprophylaxis for Patients Hospitalized with COVID-19

Authorship, Contributions, Acknowledgments

Ontario Health Infectious Diseases Program

Guidance Development Working Group

Anna Lee, Senior Advisor, Infectious Diseases
Fatima Jaffer, Pharmacist, Infectious Diseases
Nirooya Sivapalan, Lead, Infectious Diseases
Dr. Gerald Evans, Clinical Lead, Infectious Diseases and Chair, Infectious Diseases Advisory Committee

Program Leadership

Dr. Christopher Simpson, Executive Vice President, Clinical Institutes and Quality Programs and Chief Medical Executive
Scott Gavura, Director, Provincial Drug Reimbursement Programs

Infectious Diseases Advisory Committee (IDAC)

About IDAC

The Ontario Health Infectious Diseases Advisory Committee (IDAC) provides Ontario Health with timely evidence-based clinical and health system guidance on infectious diseases matters. It is a multidisciplinary committee comprised of health care professionals practising throughout Ontario who specialize or have a focus in treating infectious diseases in the hospital or community setting.

Members

Carol-Ann Agnihotri, primary care nurse practitioner, Blind River District Health Centre
Dr. Lucas Castellani, internal medicine and infectious disease physician, Sault Area Hospital
Kelly Grindrod, pharmacist and associate professor, University of Waterloo School of Pharmacy
Dr. Charles Hui, infectious diseases specialist, Children's Hospital of Eastern Ontario
Elizabeth Leung, infectious diseases clinical pharmacist, Unity Health (St. Michael's Hospital)
Dr. Michaeline McGuinty, infectious diseases specialist and clinical scientist, University of Ottawa
Dr. Santiago Perez-Patrigeon, infectious diseases physician, Kingston Health Sciences Centre
Sumit Raybardhan, infectious diseases pharmacist, antimicrobial stewardship program co-lead, North York General Hospital
Dr. Kevin Schwartz, infectious diseases physician (St. Joseph's Health Centre) and antimicrobial stewardship program co-medical director (Unity Health Toronto)
Dr. Brent Wolfrom, family physician, Queen's University

Ex-Officio Members

Daniel Warshafsky, Associate Chief Medical Officer of Health, Ontario

Disclosures

Ontario Health Infectious Diseases Program staff and IDAC members must disclose conflicts of interest. Depending on the nature of the disclosure, Ontario Health will develop and implement a mitigation plan with strategies to address the disclosure.

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