COVID-19 Therapeutics for Long-Term Care

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Land Acknowledgement

We acknowledge the land we are meeting on is the traditional territory of many nations including the Mississaugas of the Credit, the Anishnabeg, the Chippewa, the Haudenosaunee and the Wendat peoples and is now home to many diverse First Nations, Inuit and Métis. We also acknowledge that Toronto is covered by Treaty 13 with the Mississaugas of the Credit.

Disclosures

- None

Overview

1. Components of a COVID Risk Assessment

- Science Table Definitions of Severity
- COVID-19 clinical assessment

2. Algorithm for Eligibility for Therapeutics

3. COVID-19 Therapeutics

- Paxlovid
- Remdesivir
- Budesonide
- Fluvoxamine
- Evusheld**
- Dexamethasone
- Tocizumab**

SLIDO

https://app.sli.do/event/8P2os3YdhmSM4BdQaZ1S9c

COVID-19 in LTC – The Current Numbers

The Current Numbers

- 71 000 residents in 626 long-term care facilities across Ontario
- LTC residents account for <1% of population but >60% of deaths early in pandemic
- Total 31 369 COVID cases and 4542 deaths in LTC residents
- 942 active cases, 90 deaths in past 30d, 3 homes on outbreak
- CFR 2.3% for Wave 6 vs. 31.7% for Wave 1
- Majority have at least 3 doses of vaccine however less likely to have a robust response to vaccination and may have faster waning of immunity

COVID-19 Assessment

Poll

Have you (or someone in your facility) prescribed any COVID-19 therapeutics?

A. Yes, frequently
B. Yes, rarely
C. Yes, but we get a consult from the hospital first
D. No, we send patients to the ED for assessment first

Ontario Science Table Definitions of Severity

SCIENCE TABLE
COVID-19 ADVISORY FOR ONTARIO

Mild	• No new or additional supplemental oxygen from baseline • Asymptomatic or Symptomatic • Most likely to receive care as outpatient or in LTC home
Moderate	• Low-flow supplemental oxygen (e.g. nasal prongs) • May receive care in LTC or in hospital
Severe	• High-flow nasal oxygen, non-invasive ventilation, invasive mechanical ventilation or ECMO • Would require hospital and likely ICU transfer

Risk Assessment

- Age:
- Severity:
- Symptomatic/Not Symptomatic:
- Number of Vaccine Doses:
- Immunocompromise:
- Comorbidities:
- Date of Onset:
- Kidney Function:
- Medications:
- GOC:

Risk Assessment

- Age:
- Severity:
- Symptomatic/Not Symptom
- Number of Vaccine Dose
- Immunocompromise:
- Comorbidities:
- Date of Onset:
- Kidney Function:
- Medications:

- Current Cancer Treatment
- Hematologic malignancies
- Solid Organ Transplant on immunosuppressive therapy
- CAR-T-cell therapy or Hematopoietic Stem Cell Transplant
- Moderate or severe primary immunodeficiency
- Advanced or Untreated HIV
- Steroids with >20mg/day PE for >2 weeks
- Alkylating agents
- Antimetabolites
- Transplant-related immunosuppressive drugs
- Cancer chemotherapeutic agents
- TNF-a inhibitors and other immunosuppressive agents

Risk Assessment

- Age:
- Severity:
- Symptomatic/Not Sym
- Number of Vaccine D
- Immunocompromi
- Comorbidities:
- Date of Onset:
- Kidney Function:
- Medications:

Risk Factors For Progression of Disease

- Obesity (BMI >/= 30kg/m2)
- Diabetes
- Heart Disease, HTN, CHF
- Chronic Respiratory Disease (including CF)
- Cerebral Palsy
- **Intellectual Disability** → ***Not clear if this includes dementia***
- Sickle cell disease
- Moderate to Severe Kidney Disease (eGFR <60 mL/min)
- Moderate or severe liver disease (e.g. CP Class B or C cirrhosis)

Risk Assessment

- Age:
- Severity:
- Symptomatic/Not Symptomatic:
- Number of Vaccine Doses:
- Immunocompromise:
- Comorbidities:
- Date of Onset:
- Kidney Function:
- Medications:
- GOC:

For contraindications, interactions or dose adjustments

Risk Assessment – Mild Disease

- "Higher Risk" if ≥ 3% risk of hospitalization for LTC residents

Ontario Science Advisory Table Drugs and Biologics Clinical Practice Guidelines Working Group, Ontario Science Advisory Table Congregate Care Working Group and LTC+

Therapeutic Management of Residents of Long-term Care Homes with COVID-19

Pharmacologic and non-pharmacologic COVID-19 therapeutic recommendations which incorporates implementation and logistic considerations for long-term care (LTC) home residents.

Risk of Disease Progression

- Higher risk residents are those who have a ≥3% risk of hospitalization if they develop COVID-19. Standard risk residents are those who have a <3% risk of hospitalization
- Despite high rates of COVID-19 vaccination, there continues to be COVID-19-associated morbidity and mortality in LTC home residents due to advanced age, multiple comorbidities and frailty
- Racialized people, particularly those who are Indigenous and Black, may be at increased risk of disease progression due to disparate rates of comorbidities, increased barriers to vaccination, and other social determinants associated with worse health. They should be considered priority populations for access to COVID-19 drugs and therapeutics
- COVID-19 therapeutic management advanced planning should consider goals of care, obtaining needed bloodwork, medication reviews for drug-drug interactions and consent where applicable

AGE (Years)	NUMBER OF VACCINE DOSES				RISK FACTORS
	0 doses	1 dose	2 doses	3 or more doses	
40 to 49	**High risk** if ≥1 risk factors	**Standard risk**	**Standard risk**	**Standard risk**	• Obesity (BMI ≥30 kg/m²) • Diabetes • Heart disease, hypertension, congestive heart failure • Chronic respiratory disease, including cystic fibrosis • Cerebral palsy • Intellectual disability • Sickle cell disease • Moderate or severe kidney disease (eGFR <60 mL/min) • Moderate or severe liver disease (e.g., Child Pugh Class B or C cirrhosis)
50 to 69	**High risk**[2]	**High risk** ≥3 risk factors	**Standard risk**	**Standard risk**	
≥70	**High risk**	**High risk** if ≥1 risk factors	**High risk** if ≥1 risk factors[2]	**High risk** ≥3 risk factors	
Severely immunocompromised[1] **individuals of any age**	**High risk:** Therapeutics should always be recommended for immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying immune status, regardless of age or vaccine status.[1]				

1. Examples of immunocompromised or immunosuppressed individuals include receipt of treatment for solid tumors and hematologic malignancies (including individuals with lymphoid malignancies who are being monitored without active treatment), receipt of solid-organ transplant and taking immunosuppressive therapy, receipt of chimeric antigen receptor (CAR)-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy), moderate or severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome, common variable immunodeficiency, Good's syndrome, hyper IgE syndrome), advanced or untreated HIV infection, active treatment with high-dose corticosteroids (i.e., ≥20 mg prednisone or equivalent per day when administered for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor-necrosis factor (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory.
2. Acceptable hospitalization risk of individuals at younger end of age band is at least 1-2%.

Risk Assessment – Mild Disease

- "Higher Risk" if ≥ 5% risk of hospitalization for general population

STEP 1 ▶ Determine the risk of disease progression.

- **Higher risk** individuals are those who have a ≥5% risk of hospitalization if they develop COVID-19. **Standard risk** individuals are those who have a <5% of hospitalization.
- Indigenous people, Black people, and members of other racialized communities may be at increased risk of disease progression due to disparate rates of comorbidity, increased barriers to vaccination, and social determinants of health. They should be considered **priority populations** for access to COVID-19 drugs and therapeutics.

AGE (years)	NUMBER OF VACCINE DOSES			RISK FACTORS
	0 doses	1 or 2 doses	3 doses	
<20[1]	**Higher risk** if ≥3 risk factors[1]	Standard risk[1]	Standard risk[1]	• Obesity (BMI ≥30 kg/m²) • Diabetes • Heart disease, hypertension, congestive heart failure • Chronic respiratory disease, including cystic fibrosis • Cerebral palsy • Intellectual disability • Sickle cell disease • Moderate or severe kidney disease (eGFR <60 mL/min) • Moderate or severe liver disease (e.g., Child Pugh Class B or C cirrhosis)
20 to 39	**Higher risk** if ≥3 risk factors	**Higher risk** if ≥3 risk factors	Standard risk	
40 to 69	**Higher risk** if ≥1 risk factors	**Higher risk** if ≥3 risk factors	Standard risk	
≥70	**Higher risk**	**Higher risk** if ≥1 risk factors	**Higher risk** if ≥3 risk factors	
Immunocompromised[2] individuals of any age	**Higher risk**: Therapeutics should always be recommended for immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying immune status, regardless of age or vaccine status.[1,2]			
Pregnancy	**Higher risk**[3]	Standard risk	Standard risk	

1. Evidence for the safety and efficacy of sotrovimab and nirmatrelvir/ritonavir (Paxlovid) in children <18 years of age is limited. While early evidence on risk factors for moderate and severe COVID-19 in children is emerging, the ability to reliably predict disease progression in children remains very limited, and the frequency of progression is rare. While not routinely recommended in children <18 years of age, the use of these agents may be considered in exceptional circumstances (e.g., severe immunocompromise and/or multiple risk factors, clinical progression) on a case-by-case basis. Multidisciplinary consultation with Infectious Diseases (or Pediatric Infectious Diseases) and the team primarily responsible for the child's care is recommended to review the individual consideration of these medications.
2. Examples of immunocompromised or immunosuppressed individuals include receipt of treatment for solid tumors and hematologic malignancies (including individuals with lymphoid malignancies who are being monitored without active treatment), receipt of solid-organ transplant and taking immunosuppressive therapy, receipt of chimeric antigen receptor (CAR)-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy), moderate or severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome, common variable immunodeficiency, Good's syndrome, hyper IgE syndrome), advanced or untreated HIV infection, active treatment with high-dose corticosteroids (i.e., ≥20 mg prednisone or equivalent per day when administered for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor-necrosis factor (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory. These individuals should have a reasonable expectation for 1-year survival prior to SARS-CoV-2 infection.
3. Therapeutics should always be recommended for pregnant individuals who have received zero vaccine doses.

Example

- Age: 75
- Severity: Mild (No oxygen)

Mild Disease – Standard Risk

- Medications: Metformin, Ramipril, Naproxen

Indications for COVID-19 Therapeutics

Ontario Science Advisory Table Drugs and Biologics Clinical Practice Guidelines Working Group, Ontario Science Advisory Table Congregate Care Working Group and LTC+

Therapeutic Management of Residents of Long-term Care Homes with COVID-19

Pharmacologic and non-pharmacologic COVID-19 therapeutic recommendations which incorporates implementation and logistic considerations for long-term care (LTC) home residents.

Mild Disease

SEVERITY OF ILLNESS	RECOMMENDATIONS
Mild COVID-19 Disease Residents who do not require new or additional supplemental oxygen from their baseline status	▶ **Pharmacological therapy is recommended for mildly-symptomatic residents at higher risk of disease progression and should be considered for nirmatrelvir/ritonavir (Paxlovid) or remdesivir. The choice of drug depends on availability, contraindications, ease of administration and goals of care.** ● Nirmatrelvir/ Ritonavir (Paxlovid) **is recommended** at a dose of 300 mg nirmatrelvir and 100 mg ritonavir given together PO BID x 5 days. Dose-adjust to 150/100mg PO BID x 5 days if eGFR 30-59 mL/min. Not recommended if eGFR <30 mL/min. *(Order Creatinine prior to administration if no recent results available (< 30 days). If results available within 30 days, can start therapy and order a repeat Creatinine as soon as possible).* • Indicated for mild COVID-19 throughout (not requiring new or increased oxygen) meeting eligibility criteria within **5 days** of symptom onset • Lack of efficacy and side effect data in the LTC population • High potential for drug-drug interactions due to ritonavir; requires a pharmacist review for drug-drug interactions prior to prescribing • Cannot be crushed, limiting administration in some LTC residents • Consider whether goals of care are in line with life-prolonging treatment of acute medical conditions ● Remdesivir **is recommended** at a dose of 200 mg IV on day 1, then 100 mg IV per day on days 2-3. Contraindicated in residents with renal dysfunction (eGFR <30 mL/min), ALT>5x upper limit of normal. *(Order Creatinine and ALT prior to administration if no recent results available (< 30 days). If results available within 30 days, can start therapy and order a repeat Creatinine and ALT as soon as possible).* • Indicated for mild COVID-19 throughout (not requiring new or increased oxygen) meeting eligibility criteria within **7 days** of symptom onset • Need for IV access, and daily infusion x 3 make the logistics of administering remdesivir challenging for some LTC homes unless performed by an external provider • Consider whether goals of care are in line with life-prolonging treatment of acute medical conditions ▶ **Pharmacological therapy for mildly symptomatic residents in LTC, regardless of risk** ▲ Budesonide **may be considered** at a dose of 800 mcg inhaled BID for 14 days. • Evidence of reduction in duration of symptoms (very low certainty evidence) • Low risk of harm • Can be considered in addition to other COVID-19 therapies when residents have bothersome respiratory symptoms • May be a class effect; other inhaled steroids that can be administered via an aerochamber (e.g., ciclesonide) rather than a turbuhaler may also be considered ▲ Fluvoxamine **may be considered** at a dose of 50 mg PO daily, titrated up to 100 mg **PO BID for 10-15 days**. *(If the drug is well tolerated, increase the dose to 100 mg PO BID on day 2. If the drug is less well tolerated, consider a dose of 50 mg PO BID on day 2, and increase the dose to 100 mg PO BID on day 3).* • Indicated for mild COVID-19 throughout (not requiring new or increased oxygen) within **7 days** of symptom onset and not receiving Paxlovid or remdesivir • Evidence of benefit is not very strong. Not believed to be a class effect • Side effect profile of high dose fluvoxamine and high potential for drug-drug interactions makes this treatment challenging for most LTC residents, recommend pharmacist review for drug-drug interactions prior to prescribing • Limited clinical experience in LTC population • Older adults may experience fluvoxamine concentrations that are 2- to 3-fold higher than younger adults • **Risks in this population may outweigh the benefits** ◆ There is currently insufficient evidence to make a recommendation around aspirin or anticoagulation for mildly ill residents ■ The following therapies **are not recommended** for mildly ill residents: dexamethasone, tocilizumab, sarilumab and baricitinib ▶ **Supportive therapy** **Fluids** Consider fluid intake as LTC residents with COVID-19 are at risk of volume depletion. For those with decreased oral intake, encourage oral fluids or consider initiating hypodermoclysis as a temporary measure, as needed, through the acute illness. *(Hypodermoclysis up to a rate of approximately 50 cc/hour using an isotonic solution (e.g., normal saline)).*

CURRENTLY NOT RECOMMENDED*

There is insufficient evidence to support the use of the following therapies in the treatment of COVID-19 outside of clinical trials or where other indications would justify its use:

- ◆ Colchicine
- ◆ Interferon (with or without lopinavir-ritonavir and ribavirin)
- ◆ Vitamin D

** Applies to residents with any severity of illness*

RECOMMENDED AGAINST*

The following therapies are not recommended for treatment of COVID-19 due to lack of benefit, potential harm, and system implications of overuse:

- ■ Antibiotics (azithromycin)
- ■ Casirivimab-imdevimab

due to lack of neutralizing activity against the Omicron variant

Poll

Have you prescribed/administered Paxlovid or Remdesivir at your facility?

A. Paxlovid only
B. Remdesivir only
C. Both Paxlovid and Remdesivir
D. Neither Paxlovid or Remdesivir, but have prescribed either Fluvoxamine or Budesonide
E. Have not used any therapeutics for mild disease

Moderate Disease

Moderate COVID-19 Disease

Patients newly requiring low-flow supplemental oxygen or having an increase in oxygen requirements if on chronic oxygen therapy

- Patients with moderate COVID-19 will need to have a clinical assessment and decision made around need for transfer to hospital
- The following therapies may be offered to residents in homes where moderate COVID-19 can be managed
- These therapies may also be offered to residents who do not wish to be transferred to acute care, in accordance with their goals of care

▶Pharmacologic therapy

🟢 **Dexamethasone is recommended** at a dose of 6 mg PO daily for 10 days (IM dexamethasone 10 mg per day or SC dexamethasone 6 mg per day may be alternative options for people with poor swallowing).

- Monitor closely for delirium (including hypoactive delirium); consider early discontinuation if harms outweigh the benefits for the resident after considering their goals of care
- Monitor blood glucose in all residents with diabetes
- No reason to withhold dexamethasone regardless of the administration of remdesivir

🟢 **Remdesivir is recommended** at a dose of 200 mg IV on day 1, then 100 mg IV per day for 4 days. Contraindicated in patients with renal dysfunction (eGFR<30 mL/min) or ALT>5x upper limit of normal. *(Order Creatinine and ALT prior to administration if no recent results available (< 30 days). If results available within 30 days, can start therapy and order a repeat Creatinine and ALT as soon as possible).*

- Need for IV access, and daily infusion x5 make the logistics of administering remdesivir challenging for some LTC settings unless performed by an external provider
- Consider whether goals of care are in line with life-prolonging treatment of acute medical conditions

🟡 **Anticoagulation** – therapeutic dose anticoagulation with low molecular weight heparin (LMWH) **may be considered**.

- Therapeutic dose anticoagulation with LMWH for residents not already anticoagulated who are felt to be at low risk of bleeding
- Residents on therapeutic doses of anticoagulation (regardless of type) for other pre-COVID-19 reasons should continue to take anticoagulation as previously prescribed
- If residents have a bleeding risk, consider no anticoagulation or prophylactic dose LMWH

🟢 **Tocilizumab is recommended** at a dose of 400 mg one time IV.

- For residents on supplemental oxygen, only given if they have not shown improvement with dexamethasone after 24-48 hours and their CRP>75
- Illness severity, need for evaluation of CRP, IV route of admission, and drug availability make tocilizumab administration very challenging in LTC, and so would require acute care transfer if consistent with goals of care

🔴 Currently **not recommended** – SARS-CoV-2 neutralizing antibodies and nirmatrelvir/ ritonavir (Paxlovid)

▶Supportive therapies

Fluids

Consider fluid intake as LTC residents with COVID-19 are at risk of volume depletion. For those with decreased oral intake, encourage oral fluids or consider initiating hypodermoclysis as a temporary measure as needed, through the acute illness.

(Hypodermoclysis up to a rate of approximately 50 cc/hour using an isotonic solution (e.g., normal saline)).

Oxygen – supplemental oxygen up to 5L/min via nasal prongs.

Target SpO2 > 92% (unless prior chronic lung disease, where lower SpO2 levels could be targeted)

🔴 Hydroxychloroquine or chloroquine

🔴 Ivermectin

🔴 Lopinavir/ritonavir

🔴 Sotrovimab due to reduced neutralizing activity against Omicron BA.2 subvariant

** Applies to residents with any severity of illness*

Poll

Have you prescribed/administered Dexamethasone or Remdesivir for moderate disease your facility?

A. Dexamethasone only
B. Remdesivir only
C. Both Dexamethasone and Remdesivir
D. Have not used any therapeutics for moderate disease

Prescribing and Monitoring COVID-19 Therapeutics

Paxlovid (Nirmatrelvir/Ritonavir)

Mechanism

- Nirmatrelvir (protease inhibitor) and Ritonavir (booster)

Benefits

- EPIC-HR: 88% reduction in hospitalization or death for unvaccinated high risk patients with mild COVID (NNT 18)

Target Population

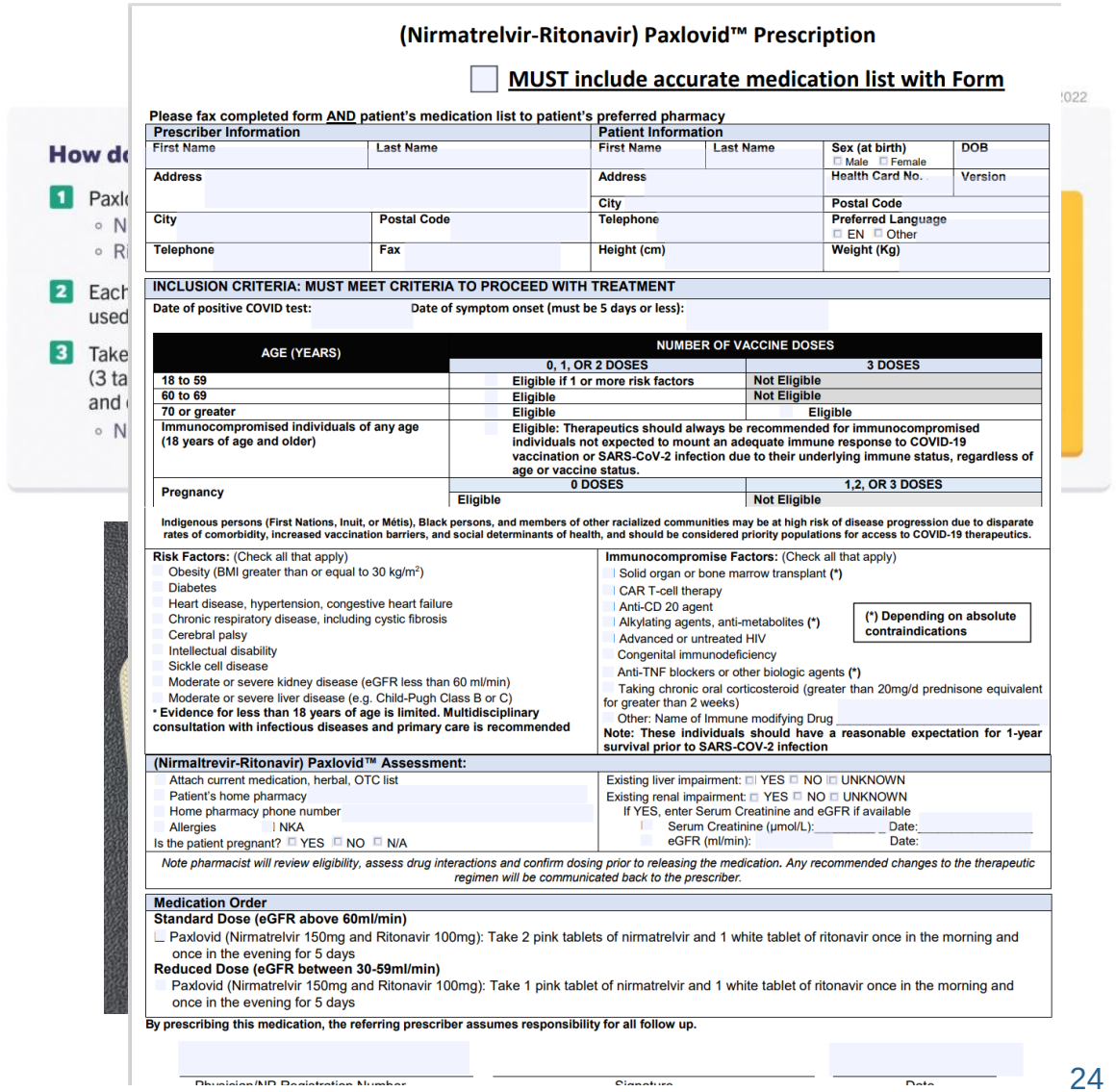
- Patients at *elevated risk* with *confirmed COVID-19* who are *mildly ill* (not on oxygen) but *symptomatic* and *within 5 days of symptom onset*

Paxlovid (Nirmatrelvir/Ritonavir)

[Nirmatrelvir 300mg + Ritonavir 100mg] BID x 5 days

- Pharmacies associate with LTC should be dispensing Paxlovid
- Other outpatient pharmacies:
  - COVID-19 treatments | COVID-19 (coronavirus) in Ontario
  - Paxlo_Pharmacy - Google My Maps
- COVID Assessment Centre

- Optional Paxlovid Prescribing Form



(Nirmatrelvir-Ritonavir) Paxlovid™ Prescription

☐ **MUST include accurate medication list with Form**

Please fax completed form AND patient's medication list to patient's preferred pharmacy

Prescriber Information		Patient Information			
First Name	Last Name	First Name	Last Name	Sex (at birth) ☐ Male ☐ Female	DOB
Address		Address		Health Card No.	Version
		City		Postal Code	
City	Postal Code	Telephone		Preferred Language ☐ EN ☐ Other	
Telephone	Fax	Height (cm)		Weight (Kg)	

INCLUSION CRITERIA: MUST MEET CRITERIA TO PROCEED WITH TREATMENT

Date of positive COVID test: Date of symptom onset (must be 5 days or less):

AGE (YEARS)	NUMBER OF VACCINE DOSES	
	0, 1, OR 2 DOSES	3 DOSES
18 to 59	Eligible if 1 or more risk factors	Not Eligible
60 to 69	Eligible	Not Eligible
70 or greater	Eligible	Eligible
Immunocompromised individuals of any age (18 years of age and older)	Eligible: Therapeutics should always be recommended for immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying immune status, regardless of age or vaccine status.	
Pregnancy	0 DOSES	1,2, OR 3 DOSES
	Eligible	Not Eligible

Indigenous persons (First Nations, Inuit, or Métis), Black persons, and members of other racialized communities may be at high risk of disease progression due to disparate rates of comorbidity, increased vaccination barriers, and social determinants of health, and should be considered priority populations for access to COVID-19 therapeutics.

Risk Factors: (Check all that apply)
- ☐ Obesity (BMI greater than or equal to 30 kg/m²)
- ☐ Diabetes
- ☐ Heart disease, hypertension, congestive heart failure
- ☐ Chronic respiratory disease, including cystic fibrosis
- ☐ Cerebral palsy
- ☐ Intellectual disability
- ☐ Sickle cell disease
- ☐ Moderate or severe kidney disease (eGFR less than 60 ml/min)
- ☐ Moderate or severe liver disease (e.g. Child-Pugh Class B or C)

* **Evidence for less than 18 years of age is limited. Multidisciplinary consultation with infectious diseases and primary care is recommended**

Immunocompromise Factors: (Check all that apply)
- ☐ Solid organ or bone marrow transplant (*)
- ☐ CAR T-cell therapy
- ☐ Anti-CD 20 agent
- ☐ Alkylating agents, anti-metabolites (*)
- ☐ Advanced or untreated HIV
- ☐ Congenital immunodeficiency
- ☐ Anti-TNF blockers or other biologic agents (*)
- ☐ Taking chronic oral corticosteroid (greater than 20mg/d prednisone equivalent for greater than 2 weeks)
- ☐ Other: Name of Immune modifying Drug _____

(*) Depending on absolute contraindications

Note: These individuals should have a reasonable expectation for 1-year survival prior to SARS-COV-2 infection

(Nirmaltrevir-Ritonavir) Paxlovid™ Assessment:
- ☐ Attach current medication, herbal, OTC list
- Patient's home pharmacy
- Home pharmacy phone number
- Allergies ☐ NKA
- Is the patient pregnant? ☐ YES ☐ NO ☐ N/A
- Existing liver impairment: ☐ YES ☐ NO ☐ UNKNOWN
- Existing renal impairment: ☐ YES ☐ NO ☐ UNKNOWN
- If YES, enter Serum Creatinine and eGFR if available
- ☐ Serum Creatinine (µmol/L): _____ Date: _____
- ☐ eGFR (ml/min): Date:

Note pharmacist will review eligibility, assess drug interactions and confirm dosing prior to releasing the medication. Any recommended changes to the therapeutic regimen will be communicated back to the prescriber.

Medication Order

Standard Dose (eGFR above 60ml/min)

☐ Paxlovid (Nirmatrelvir 150mg and Ritonavir 100mg): Take 2 pink tablets of nirmatrelvir and 1 white tablet of ritonavir once in the morning and once in the evening for 5 days

Reduced Dose (eGFR between 30-59ml/min)

☐ Paxlovid (Nirmatrelvir 150mg and Ritonavir 100mg): Take 1 pink tablet of nirmatrelvir and 1 white tablet of ritonavir once in the morning and once in the evening for 5 days

By prescribing this medication, the referring prescriber assumes responsibility for all follow up.

Physician/NP Registration Number | Signature | Date

Paxlovid (Nirmatrelvir/Ritonavir)

Special Populations

- HIV Positive: Can be used if HIV suppressed. Do not use if inadequately controlled or untreated
- Renal Impairment: Not recommended for eGFR <30 or dialysis. Reduced dose 150mg/100mg for eGFR 30-59
- Hepatic Impairment: Not recommended for Child Pugh C cirrhosis.

Paxlovid (Nirmatrelvir/Ritonavir)

DRUG INTERACTIONS

- Nirmatrelvir and Ritonavir: CYP3A4 substrates
- Ritonavir: CYP3A4 Inhibitor

- Recommend Pharmacist Consult

Resources:

- Paxlovid - What Pharmacists and Prescribers Need to Know (with Appendix) February 23, 2022 (covid19-sciencetable.ca)
- Paxlovid for a Patient on a DOAC (covid19-sciencetable.ca)
- Liverpool COVID-19 Interactions (covid19-druginteractions.org)

Nirmatrelvir/Ritonavir (*Paxlovid*) Drug Interactions:

This is not an exhaustive list. Consultation with a pharmacist who can obtain a complete medication, recreational, and natural health product history from the patient is recommended prior to prescribing nirmatrelvir/ritonavir.

Symbol	Severity	Recommendation	Rationale
▲	Contraindicated	Use alternative COVID agent. **Do not use nirmatrelvir/ritonavir.**	Stopping the drug will not mitigate the interaction (e.g., prolonged half-life, narrow therapeutic index, prolonged enzyme-inducing effects which may decrease effectiveness of nirmatrelvir/ritonavir). Do not coadminister due to risk of serious toxicity.
◬	Contraindicated (use within past 14 days)		
●	Do not coadminister	Hold and restart 2 days after completing nirmatrelvir/ritonavir.	Significant ↑ in drug concentrations expected. Do not coadminister due to risk of serious toxicity.
◆	Caution	Therapy modification required (see Appendix).	Significant ↑/↓ in drug concentrations expected, which may lead to serious toxicity or impaired efficacy. Only coadminister if the interacting drug can be safely held or dose-adjusted and closely monitored (see Appendix). Expert consultation may be useful.
✔	Drug interaction not likely to be clinically relevant	Continue with standard dosing.	Although mentioned in the monograph, clinically relevant interaction is not anticipated (e.g., minimal impact on certain metabolic pathways, wide therapeutic index, and short course of nirmatrelvir/ritonavir).

- ◆ Abemaciclib (*Verzenio*)
- ● Alfuzosin (*Xatral*)
- ◆ Alprazolam (*Xanax*)
- ▲ Amiodarone
- ✔ Amitriptyline
- ◆ Amlodipine (*Norvasc*)
- ◬ Apalutamide (*Erleada*)
- ◆ Apixaban (*Eliquis*)
- ◆ Aripiprazole (*Abilify*), oral
- ◆ Atorvastatin (*Lipitor*)
- ✔ Atovaquone
- ▲ Bosentan (*Tracleer*)
- ● Bosutinib (*Bosulif*)
- ◆ Brexpiprazole (*Rexulti*)
- ✔ Budesonide
- ✔ Bupropion
- ◆ Buspirone (*Buspar*)
- ◬ Carbamazepine (*Tegretol*)
- ◆ Ceritinib (*Zykadia*)
- ● Cisapride
- ✔ Citalopram
- ✔ Clarithromycin
- ✔ Clomipramine
- ● Clonazepam
- ◆ Clopidogrel (*Plavix*)
- ● Clorazepate
- ▲ Clozapine (*Clozaril*)
- ● Cobimetinib (*Cotellic*)
- ● Colchicine in renal/hepatic impairment
- ◆ Cyclosporine (*Neoral*)
- ◆ Dabigatran
- ◬ Dabrafenib (*Tafinlar*)
- ◆ Dasatinib (*Sprycel*)
- ◆ Dexamethasone, high dose
- ● Diazepam (*Valium*)
- ◆ Digoxin
- ◆ Diltiazem (*Tiazac, Cardizem*)
- ✔ Divalproex
- ● Dofetilide
- ✔ Dronabinol
- ▲ Dronedarone (*Multaq*)
- ◆ Edoxaban (*Lixiana*)
- ◆ Elagolix (*Orilissa*)
- ◆ Encorafenib (*Braftovi*)
- ◬ Enzalutamide
- ● Ergot alkaloids (e.g., dihydroergotamine, ergonovine)
- ◬ Eslicarbazepine
- ✔ Ethinyl estradiol
- ● Everolimus (*Certican*)
- ◆ Felodipine
- ▲ Fentanyl (*Duragesic*)
- ▲ Flecainide
- ✔ Fluoxetine
- ● Flurazepam
- ✔ Fluvoxamine
- ◆ Fostamatinib (*Tavalisse*)
- ✔ Fusidic acid, topical
- ● Glecaprevir/Pibrentasvir (*Maviret*)
- ◆ Hydrocodone
- ● Ibrutinib (*Imbruvica*)
- ✔ Imipramine
- ✔ Itraconazole
- ✔ Ketoconazole
- ✔ Lamotrigine
- ● Lomitapide (*Juxtapid*)
- ◬ Lorlatinib (*Lorbrena*)
- ● Lovastatin
- ▲ Lurasidone (*Latuda*)
- ✔ Maprotiline
- ✔ Maraviroc
- ● Meperidine (*Demerol*)
- ✔ Methamphetamine
- ✔ Metoprolol
- ● Midazolam, oral
- ◬ Mitotane (*Lysodren*)
- ◆ Modafinil
- ● Neratinib (*Nerlynx*)
- ◆ Nifedipine
- ◆ Nilotinib (*Tasigna*)
- ● Nitrazepam (*Mogadon*)
- ✔ Nortriptyline
- ◬ Oxcarbazepine
- ◆ Oxycodone (*Percocet, OxyNEO*)
- ✔ Paroxetine
- ◬ Phenobarbital
- ◬ Phenytoin (*Dilantin*)
- ▲ Pimozide
- ◬ Primidone
- ▲ Propafenone
- ◆ Quetiapine (*Seroquel*)
- ▲ Quinidine
- ● Quinine
- ✔ Raltegravir
- ▲ Ranolazine (*Corzyna*)
- ◆ Rifabutin
- ◬ Rifampin
- ◬ Rifapentine
- ◆ Risperidone (*Risperdal*), oral
- ▲ Risperidone, long-acting injection (*Risperdal Consta*)
- ● Rivaroxaban (*Xarelto*)
- ◆ Rosuvastatin (*Crestor*)
- ● Salmeterol (*Serevent, Advair*)
- ✔ Sertraline
- ◆ Sildenafil for ED† (*Viagra*)
- ▲ Sildenafil for PAH‡ (*Revatio*)
- ● Silodosin (*Rapaflo*)
- ● Simvastatin
- ● Sirolimus (*Rapamune*)
- ▲ Sonidegib (*Odomzo*)
- ◬ St. John's wort (*Hypericum perforatum*)
- ● Tacrolimus (*Prograf, Advagraf, Envarsus*)
- ◆ Tadalafil for ED† (*Cialis*)
- ▲ Tadalafil for PAH‡ (*Adcirca*)
- ● Tamsulosin (*Flomax*)
- ▲ Tepotinib (*Tepmetko*)
- ✔ Theophylline
- ● Ticagrelor (*Brilinta*)
- ✔ Timolol
- ◆ Tramadol
- ● Triazolam (*Halcion*)
- ✔ Trimipramine
- ● Vardenafil (*Levitra*) for ED†
- ▲ Vardenafil (*Levitra*) for PAH‡
- ▲ Venetoclax (*Venclexta*)
- ✔ Venlafaxine
- ◆ Verapamil
- ◆ Vinblastine
- ◆ Vincristine
- ✔ Voriconazole
- ◆ Warfarin
- ◆ Ziprasidone (*Zeldox*)
- ◆ Zolpidem (*Sublinox, Ambien*)
- ◆ Zopiclone (*Imovane*)

Click here for the Liverpool COVID-19 Interaction Checker

Or visit: https://www.covid19-druginteractions.org/.

†ED = erectile dysfunction ‡PAH = pulmonary arterial hypertension

Paxlovid (Nirmatrelvir/Ritonavir)

Side Effects:

- Dysgeusia
- Diarrhea
- HTN
- Myalgias

Rebound

- Case reports of viral rebound and recurrence of symptoms after completing Paxlovid
- Frequency, mechanism, clinical implication not yet clear

Remdesivir

Mechanism

- Inhibits RNA-dependent RNA polymerase

Benefits

- PINETREE: 87% reduction in COVID-19 related hospitalization or death in unvaccinated patients with mild COVID and risk factors for progression
- Multiple RCTs (ACTT-1, CATCO, DisCoVeRy) in moderate illness with disparate results
  - meta-analysis of >7000 showed reduction in mortality with NNT of 44
  - Reduced mechanical ventilation and time to recovery

Target Population

- Patients at *elevated risk* with *confirmed COVID-19* who are *mildly ill* (not on oxygen) *within 7 days of symptom onset*
- Patients with *confirmed COVID-19* who are *moderately ill* (on low flow oxygen)
- (Can be considered for critically ill patients on high flow oxygen or NIV)

Remdesivir

How to Prescribe:

- Mild Disease: 200mg IV x 1 on day 1, then 100mg IV daily for 2 days
- Moderate Disease: 200mg IV x 1 on day 1, then 100mg IV daily for 4 days

Special Populations

- Kidney Dysfunction: Limited data. Generally not recommended for eGFR <30 or dialysis. 2 observational studies did not suggest increased risk.
- Hepatic Dysfunction: Contraindicated if ALT>5x ULN

Access:

- For Long-Term Care Facilities: Contact Nurse-Led Outreach Team to facilitate
- Some jurisdictions may have their own processes

Remdesivir

Side Effects:

- Nausea
- Elevated liver enzymes
- Hypersensitivity Reactions
- Increase PT

Monitoring

- Consider baseline Cr, liver enzymes, PT
- Repeat as clinically indicated

Budesonide

Mechanism

- Targeted anti-inflammatory effects on the lungs

Benefits: Low quality evidence

- Budesonide: STOIC showed possible reduction in need for urgent care or ED visit. PRINCIPLE found reduced time to self-reported recovery but no impact on hospitalization or death
- Ciclesonide: 2 small trials. 1 trial with no difference in symptom improvement, 1 trial with no difference in time to recovery but reduction in ED visits/hospitalizations

Target Population

- *May be considered* for patients with *symptomatic COVID-19* who are *mildly ill* (not on oxygen) and not candidates for other therapies

Budesonide

How to Prescribe:

- Budesonide 800mcg inh BID x 14 days

Interactions

- Use with CYP3A4 inhibitor may increase systemic absorption

Fluvoxamine

Mechanism

- Binds sigma-1 receptor resulting in reduced production of inflammatory cytokines and may reduce COVID-19 associated inflammation

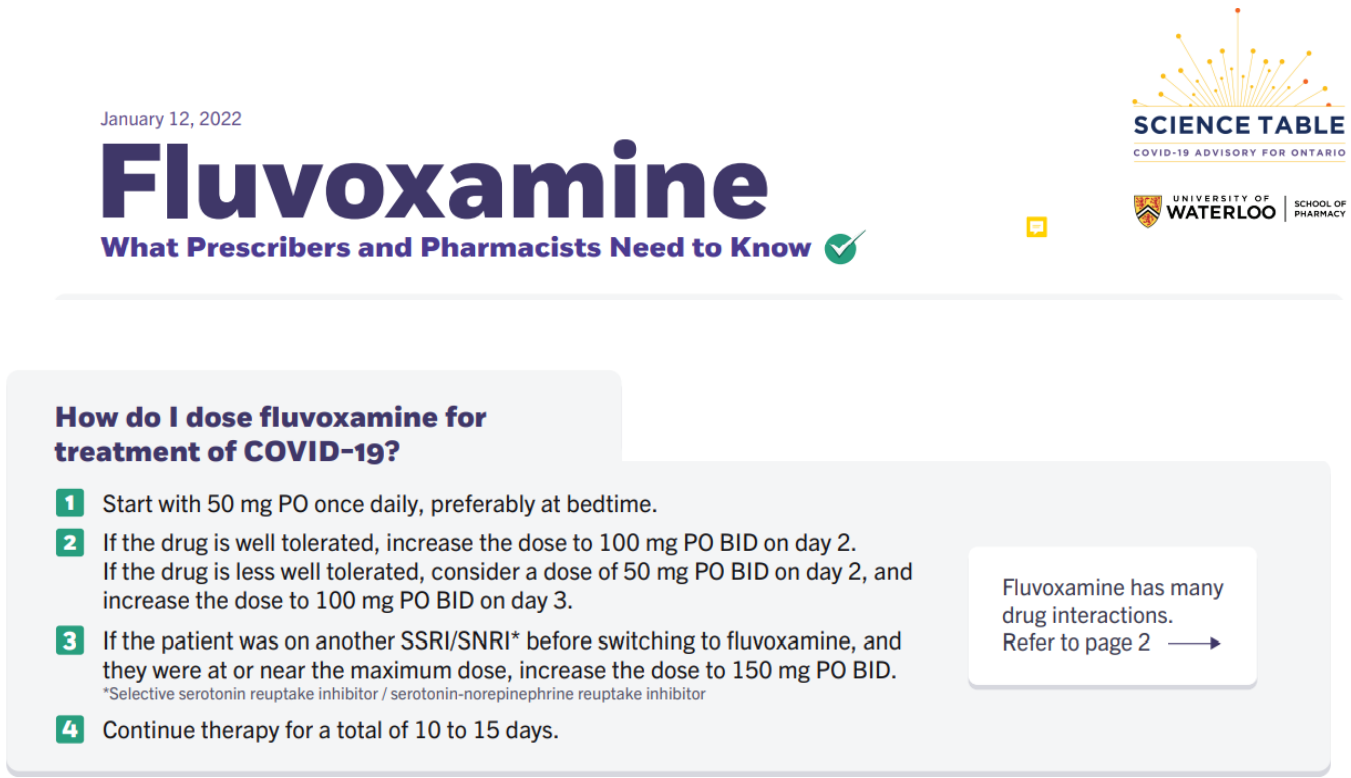
Benefits

- STOP COVID showed reduction in clinical deterioration but STOP COVID 2 stopped early for futility
- TOGETHER: Reduction in composite outcome of admission to hospital or stay in ED >6hrs but not difference in mortality

Target Population

- *May be considered* in patients with *confirmed COVID-19* who are *mildly ill* (not on oxygen) but *symptomatic* and *within 7 days of symptom onset,* preferentially those *with risk factors for progression*, who are *not candidates for other therapies*

Fluvoxamine



January 12, 2022

Fluvoxamine

What Prescribers and Pharmacists Need to Know

SCIENCE TABLE
COVID-19 ADVISORY FOR ONTARIO

UNIVERSITY OF WATERLOO | SCHOOL OF PHARMACY

How do I dose fluvoxamine for treatment of COVID-19?

1. Start with 50 mg PO once daily, preferably at bedtime.
2. If the drug is well tolerated, increase the dose to 100 mg PO BID on day 2.
   If the drug is less well tolerated, consider a dose of 50 mg PO BID on day 2, and increase the dose to 100 mg PO BID on day 3.
3. If the patient was on another SSRI/SNRI* before switching to fluvoxamine, and they were at or near the maximum dose, increase the dose to 150 mg PO BID.
   *Selective serotonin reuptake inhibitor / serotonin-norepinephrine reuptake inhibitor
4. Continue therapy for a total of 10 to 15 days.

Fluvoxamine has many drug interactions.
Refer to page 2 →

Resources:

[Fluvoxamine: What Prescribers and Pharmacists Need to Know - Ontario COVID-19 Science Advisory Table (covid19-sciencetable.ca)]

Special Populations:

- Patients with history of Bipolar disorder or mania: May trigger manic or hypomanic episode
- Patients or other psychiatric medications:
  - Non-sertraline SSRI/SNRI: switch to fluvoxamine then switch back OR can add fluvoxamine if original drug is low dose
  - Sertraline: Switch to fluvoxamine then switch back. Do not add.
  - MAOI Inhibitors: Do not use Fluvoxamine

Fluvoxamine

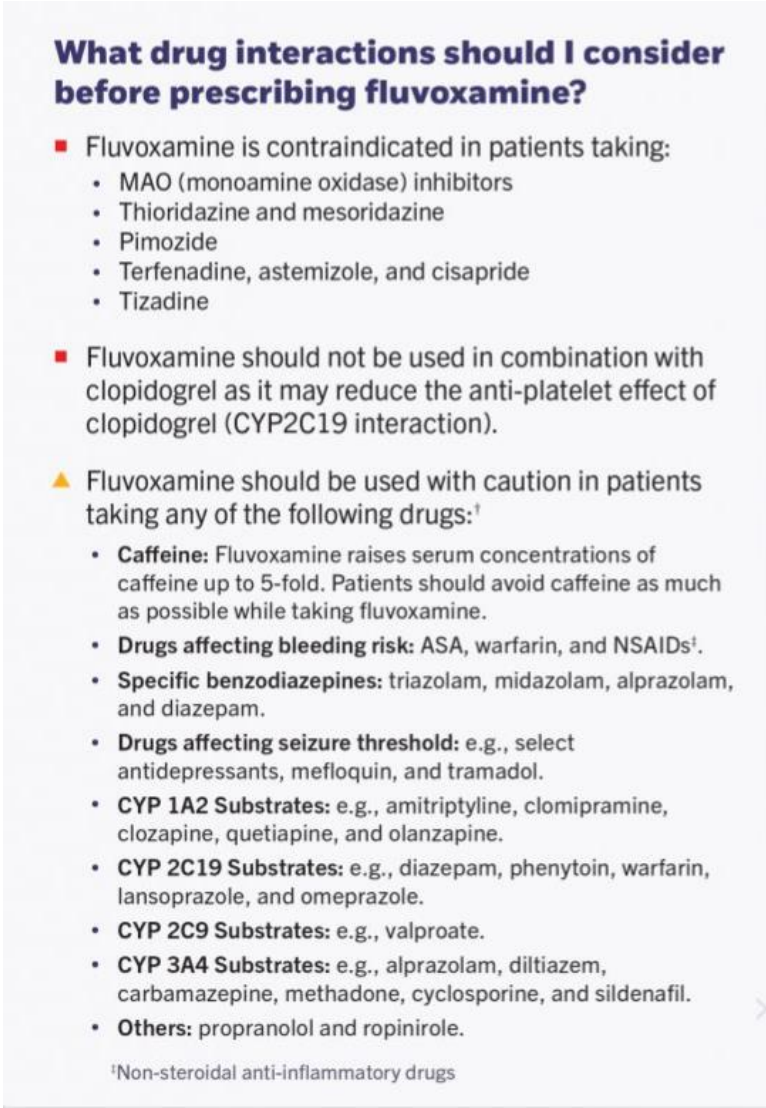
DRUG INTERACTIONS

- May drug interactions, including with caffeine!

- Recommend Pharmacist Consult

Resources:

- [Fluvoxamine: What Prescribers and Pharmacists Need to Know - Ontario COVID-19 Science Advisory Table (covid19-sciencetable.ca)]



What drug interactions should I consider before prescribing fluvoxamine?

- Fluvoxamine is contraindicated in patients taking:
  - MAO (monoamine oxidase) inhibitors
  - Thioridazine and mesoridazine
  - Pimozide
  - Terfenadine, astemizole, and cisapride
  - Tizadine
- Fluvoxamine should not be used in combination with clopidogrel as it may reduce the anti-platelet effect of clopidogrel (CYP2C19 interaction).
- Fluvoxamine should be used with caution in patients taking any of the following drugs:[†]
  - **Caffeine:** Fluvoxamine raises serum concentrations of caffeine up to 5-fold. Patients should avoid caffeine as much as possible while taking fluvoxamine.
  - **Drugs affecting bleeding risk:** ASA, warfarin, and NSAIDs[‡].
  - **Specific benzodiazepines:** triazolam, midazolam, alprazolam, and diazepam.
  - **Drugs affecting seizure threshold:** e.g., select antidepressants, mefloquin, and tramadol.
  - **CYP 1A2 Substrates:** e.g., amitriptyline, clomipramine, clozapine, quetiapine, and olanzapine.
  - **CYP 2C19 Substrates:** e.g., diazepam, phenytoin, warfarin, lansoprazole, and omeprazole.
  - **CYP 2C9 Substrates:** e.g., valproate.
  - **CYP 3A4 Substrates:** e.g., alprazolam, diltiazem, carbamazepine, methadone, cyclosporine, and sildenafil.
  - **Others:** propranolol and ropinirole.

[‡]Non-steroidal anti-inflammatory drugs

Fluvoxamine

Common Side Effects:

- Nausea
- Constipation
- Diarrhea
- Dry Mouth
- Insomnia
- Agitation
- Somnolence
- Nervousness
- Headache
- Dizziness

Rare but Serious Side Effects

- QT prolongation: Avoid in patients with history of congenital long QT or other QT prolonging medications
- Serotonin Syndrome: More likely if maximum dose exceeded or used with other serotonergic drugs

Evusheld (Tixagevimab/Cilgavimab)

Mechanism

- Combination of 2 long-acting monoclonal antibodies that bind to distinct epitopes of SARS-CoV-2 spike protein
- Blocks interaction with host cellular receptor to prevent viral entry
- Intended to convey passive immunity

Benefits:

- PROVENT: reduced risk of developing symptomatic COVID-19 by 83% at 6 months, with NNT of 68 in unvaccinated patients at elevated risk

Target Population

- Patients weighing *at least 40kg* with no *current COVID-19 infection or exposure* who have *select immunocompromising conditions* including: Solid organ transplant, stem cell transplant, CAR-T cell therapy, other hematologic cancer patients on active treatment

Evusheld (Tixagevimab/Cilgavimab)

Evusheld will be provided through select clinics that care for eligible populations i.e. cancer centres and transplant sites

Dexamethasone

Mechanism

- Multi-modality anti-inflammatory, steroids theoretically mitigate the COVID-19 systemic inflammatory response

Benefits

- RECOVERY: Reduction in mortality of 18% (NNT of 35) and 26% reduction in progression to mechanical ventilation (NNT of 35) in patients on supplemental oxygen
- In patients not on oxygen, dexamethasone tended to increase risk of death by 19%

Target Population

- Patients with *confirmed COVID-19* who are *moderately or critically ill* (on supplemental oxygen, high flow oxygen, NIV, IMV or ECMO)

Dexamethasone

How to Prescribe:

- Dexamethasone 6mg IV/PO for 10 days or until discharge

Side Effects and Monitoring

- Hyperglycemia – monitor blood sugar as appropriate
- Secondary infection, psychiatric effects
- Avascular Necrosis

Rule Out Latent Infection

- HBsAg
- TBST in appropriate patients
- Patients from Strongyloides Endemic Areas:
  - Systemic steroids can lead to hyper-infection in patients with strongyloides infection
  - Strongyloides Serology – PHOL offered 1 day turnaround to hospitals if specify indication as COVID
  - Can consider empiric Ivermectin UNLESS from area endemic for Loa Loa (West and Central Africa) – consider ID consult

Tocilizumab

Mechanism

- Monoclonal antibody target IL-6 receptors, an important inflammatory mediator

Benefits

- Meta-analysis of 9 RCTs examining a total of 5923 patients showed tocilizumab reduces mortality by 10% and progression to IMV by 12%

Target Population

- Patients with *confirmed COVID-19* who are *moderately ill (on low flow oxygen),* have an *elevated CRP >75* and have *disease progression despite 24-48 hours of systemic steroids* and are *within 14 days of diagnosis or admission*
- (Patients with *confirmed COVID-19* who are *critically ill* (on high flow oxygen, NIV, IMV or ECMO) and *within 14 days of admission/diagnosis*)

Tocilizumab

Due to complexities in administration, currently there is no program for Tocilizumab administration in LTC facilities or as an outpatient.

Patients who would qualify for tocilizumab should be considered for transfer to hospital if within goals of care.

Poll

Would you feel comfortable prescribing/administering treatments for mild COVID-19 your facility?

A. Paxlovid only
B. Remdesivir only
C. Comfortable with Paxlovid or Remdesivir
D. Would feel comfortable only if Infectious Disease/Hospitalist Consult
E. Would not feel comfortable treating mild disease at my facility

Poll

Would you feel comfortable prescribing/administering treatments for mild COVID-19 your facility?

A. Fluvoxamine only
B. Budesonide only
C. Comfortable with Fluvoxamine or Budesonide
D. Would feel comfortable only if Infectious Disease/Hospitalist Consult
E. Would not feel comfortable treating mild disease at my facility

Poll

Would you feel comfortable prescribing/administering Dexamethasone or Remdesivir for moderate COVID-19 your facility?

A. Dexamethasone only
B. Remdesivir only
C. Both Dexamethasone and Remdesivir
D. Would feel comfortable only if Infectious Disease/Hospitalist Consult
E. Would not feel comfortable treating moderate disease at my facility

Thank you

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