AHS Paxlovid™ Outpatient Prescribing Clinical Resource

Background

Currently available AHS approved outpatient treatments available for unvaccinated, mild-moderate COVID-19 patients have equivalent outcome benefits but are limited in supply, have complex patient and drug characteristics, and access/availability intricacies requiring prioritization of medications to certain patient groups.

	Administration	Access/Availability	Patient Characteristics	Monitoring	Literature / evidence
Sotrovimab 500mg	one time IV therapy no renal dosing adjustment	Centralized patient identifier and prescriber (MAP^) Dispensing & Administration via MIHCP[++] or targeted infusion clinics	1. UNDER vaccinated[#] + high risk[**] for severe disease/outcomes 2. Immunocompromised regardless vaccination status[$] 3. Living in LTC, DSL4, 4D settings LIMITED TO KNOWN BA1 OMICRON VARIANT	by centralized prescriber Limited drug interactions	COMET-ICE RR 0.20 hospitalization or death ARR 4.6% NNT 22
Paxlovid™ (nirmatrelvir 150mg / ritonavir 100mg)	oral therapy - 2 x nirmatrelvir + 1 x ritonavir BID x 5 days renal dosing adjustment	Decentralized access through primary care Patient self-administration	1. UNDER vaccinated[#] + high risk[**] for severe disease/outcomes 2. Immunocompromised regardless vaccination status (not taking absolutely contraindicated drug or Solid organ transplant at any time and allogenic stem cell transplants within first 3 months) 3. Living in LTC, DSL4, 4D settings	Multiday by prescriber/ pharmacist (for drug interaction management) Many drug interactions	EPIC HR RR 0.15 hospitalization or death ARR 5.8% NNT 18
Remdesivir	200mg IV day 1, 100mg IV days 2 & 3 No renal dosing adjustment	Centralized patient identifier and prescriber (MAP) Administration via MIHCP, targeted infusion clinics or some health facilities	1. UNDER vaccinated[#] + high risk[**] for severe disease/outcomes 2. Immunocompromised regardless vaccination status[$] 3. Living in LTC, DSL4, 4D settings	Multiday by centralized prescriber Limited drug interactions	PINETREE HR 0.13 hospitalization or death ARR 4.6% NNT 22

[1]High risk patient criteria:

a) Age 55 and over, regardless of comorbidities OR Age 45 and over for First Nations peoples, OR
b) Age 18 and over with at least one of the following comorbidities:
   i. Diabetes requiring medication
   ii. Obesity (BMI > 30 kg/m^2)
   iii. Chronic kidney disease (eGFR < 60 mL/min/1.73 m^2)
   iv. Congestive heart failure (New York Heart Association class II, III, or IV)
   v. Chronic obstructive pulmonary disease
   vi. Moderate-to-severe asthma OR
c) Pregnancy

[$]Definition of immunocompromised:

a) Transplant patients (solid organ or stem cell)
b) Oncology patients who have received a dose of any IV or oral chemotherapy or other immunosuppressive treatment since December 2020
c) Patients with inflammatory conditions (e.g. rheumatoid arthritis, lupus, inflammatory bowel disease) receiving a dose of any systemic immunosuppressant since December 2020

**Pregnancy – while some product monographs do not recommend Paxlovid™in pregnancy, AHS has not included it as an absolute contraindication (see below) as:

1. Ritonavir is routinely given in pregnant patients for anti-retroviral therapy and no difference in the rate of overall birth defects for ritonavir compared with the background birth defect rate (see fact sheet)
2. COVID-19 in pregnancy is associated with adverse maternal and fetal outcomes, including preeclampsia, eclampsia, preterm birth, premature rupture of membranes, venous thromboembolic disease, and fetal death.
3. No significant development effects in animal studies for nirmatrelvir doses resulting in 3-8 times higher exposure than the authorized human dose of Paxlovid™ (see fact sheet)

[++]MIH=Mobile Integrated Healthcare Community Paramedics

^=Monoclonal Antibody Program

[#]UNDER vaccinated= 0 to 1 dose of 2 dose vaccine

Alberta Health Services
Healthy Albertans. Healthy Communities. Together.
Prepared by: AHS Pharmacy Services
Last revised: February 2022
Version: 2.0

Prioritization principles

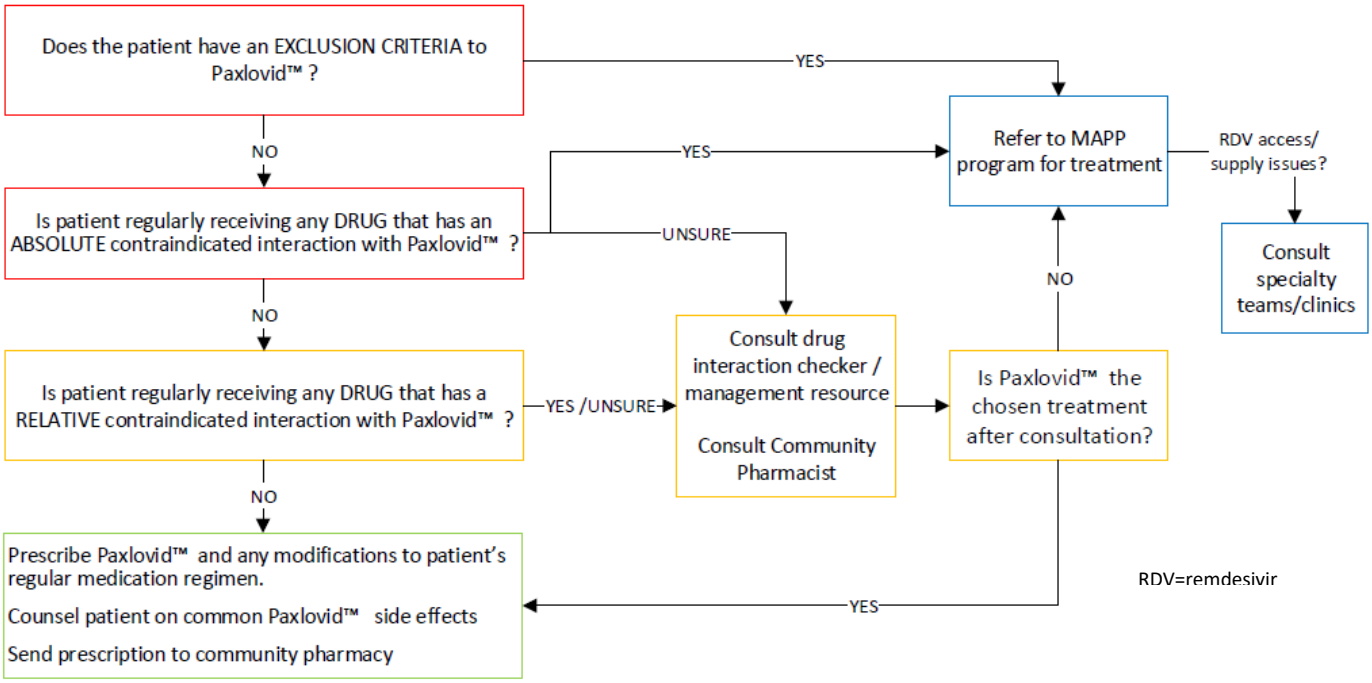
- Treatment should be offered to individuals with COVID-19 that are at high risk of progressing to severe disease
- Risk to patient safety and interruption of stabilized narrow therapeutic index drug therapy due to drug interactions should be minimized
- Ability to assess patients for therapy appropriateness to meet anticipated high demand for oral COVID therapy should be efficient and easy while minimizing lack of access to an indicated therapy
- Ease of therapy administration
- Patient preference should be considered but not the sole factor for determining therapy choice

Recommendation

- Availability will determine agent chosen if stocks limited
- Paxlovid™ offered preferentially unless patient meets exclusion criteria or is receiving unmanageable absolutely contraindicated drug. If patient meets exclusion criteria or is receiving absolutely contraindicated drug, other treatment may be considered.
- Where the patient has a relative contraindication to Paxlovid™, drug should be assessed to determine risk vs benefit of receiving Paxlovid™.

The following are EXCLUSION CRITERIA to Paxlovid™ therapy: Hypersensitivity to components of Paxlovid, pulmonary hypertension, TB, some transplants (Solid organ transplant on unmanageable absolutely contraindicated drug at any time and allogenic stem cell transplants within first 3 months) or eGFR <30 mL/min/1.73m^2

AHS Paxlovid™ Outpatient Prescribing Process



- **Providers should exercise clinical judgment** when assessing the risks and benefits of Paxlovid™ and determine the most appropriate strategy for managing drug-drug interactions between Paxlovid™ and concomitant medications. There is limited clinical information available for Paxlovid™, which is a new combination medication.

Drug Interactions to Paxlovid™

Ritonavir-boosted nirmatrelvir (Paxlovid™) has significant and complex drug-drug interactions, mainly due to ritonavir, a strong cytochrome P450 (CYP) 3A inhibitor. The dose of Paxlovid™ should not be adjusted to avoid or mitigate a drug-drug interaction with a concomitant medication. Interactions may not apply to patients receiving these medication on an as needed basis. Many drug interaction checkers exist but variations in information, recommendations or categorization of risk / severity may occur. Thus, multiple resources may need to be consulted. Some AHS recommended resources include:

- PracticeTool3_DrugInteractionsContraindications.pdf (bccdc.ca)
- Nirmatrelvir/Ritonavir (Paxlovid): What Prescribers and Pharmacists Need to Know - Ontario COVID-19 Science Advisory Table (covid19-sciencetable.ca)
- Statement on Paxlovid™ Drug-Drug Interactions | COVID-19 Treatment Guidelines (nih.gov) [sourced 19/01/2022]
- DDI Booklet 2019_English.pdf (hivclinic.ca)
- FACT SHEET FOR HEALTHCARE PROVIDERS: EMERGENCY USE AUTHORIZATION FOR PAXLOVID™ (fda.gov)
- LexiComp® Drug Interaction database

Some considerations that clinicians may need to assess in trying to manage drug-drug interactions include:

- Duration of therapies
- Dosing frequency of interacting drug(s)
- Half-life of interacting drug(s)
- Therapeutic window of interacting drug(s)
- Ability to do therapeutic drug monitoring and lab work
- Indication of concurrent medication(s)
- Recent vs distant event/procedure
- Number of interacting medications
- Magnitude of effect of the interaction
- Severity of outcome of interaction vs COVID outcome

Some options to manage interactions include:

- Decrease dose of concurrent medication(s)
- Hold concurrent medication(s) for 7 days or longer
- Continue concurrent medication at same dose with more frequent patient monitoring
- Use an alternative