UBC CPD

COVID-19 Therapeutics

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BC COVID-19 Therapeutics Committee

Currently Available Therapies

- Nirmatrelvir/ritonavir (Paxlovid)
 - Take-home oral direct-acting antiviral (protease inhibitor)
 - 5-day course given within 5-7 days of symptom onset
 - Various drug-drug interactions and contraindications
- Sotrovimab (Xevudy)
 - IV monoclonal antibody against SARS-COV-2 spike protein
 - Prone to loss of efficacy with emerging variants of concern, including BA.2
- Remdesivir (Veklury)
 - 3-day IV direct-acting antiviral for those unable to take nirmatrelvir/ritonavir
- Evidence is similar for all drugs
 - RCT-level data, Delta wave, unvaccinated participants with a risk-factor
 - Reduces progression of mild-moderate COVID to requiring hospitalization (6% to 1%)



Who to Treat?

- BCCDC Analysis
- In Omicron
- Adjusted for incidental COVID
- Recommend if ≥ 5%; Suggest if 3-4%

		CEV 1				CEV 2	
	0 doses	2 doses	3 doses		0 doses	2 doses	3 doses
70+				70+			
60-69				60-69			
50-59				50-59			
18-49				18-49			
						CEV 3	
CEV = Clinically Extremely				0 doses	2 doses	3 doses	
1	ulnerable = Severe			70+			
immunocompromise			60-69				
in	2 = Moderate immunocompromise			50-59			
3 = high-risk conditions			18-49				

Risk of hospitalization from COVID-19 in BC, excluding those admitted for other reasons # of at-risk conditions Age group 0 doses 1 dose 2 doses 3 doses 0 at risk conditions 18-29 30-39 40-49 50-59 60-69 70-79 80+ 1-2 at risk conditions 18-29 30-39 40-49 50-59 60-69 70-79 80+ 3+ at risk conditions 18-29 30-39 40-49 50-59 60-69 70-79 80+ Legend of Risk of Hospitalzation from Omicron in BC Highest Risk (≥ 10%) Increased Risk (5-9%) Slightly Increased Risk (3-4%) No Increased Risk (1-2%) Below Average Risk (<1%)

ELIGIBILITY CRITERIA

Confirmed COVID-19 AND

Symptomatic for five days or less (symptom onset day is considered day zero) AND

Are at increased risk for disease progression (see Table below – check ONE box)

Age	Number of Vaccine Doses/Previous Infection						
	0, AND No previous infection	1 to 2, OR Previous infection alone	3 OR Previous infection + any vaccination				
Any adult	Individuals identified as clinically extremely vulnerable (CEV) Group 1, Group 2 and Group 3 (See Toolkit #2 – CEV Definitions)						
18-49	\geq 3 chronic conditions/co-morbidities, OR Indigenous Not at increased risk otherwise	Not at increased risk	Not at increased risk				
50-69	Any individual	≥ 3 chronic conditions/co-morbidities, OR Indigenous Not at increased risk otherwise	Not at increased risk				
70+	Any individual	$ \geq 1 \text{ chronic conditions/co-morbidities, OR} $ $ Indigenous $ $ Not at increased risk otherwise $	$ \geq 3 \text{ chronic conditions/co-morbidities, OR} $ $ Indigenous $ $ Not at increased risk otherwise $				

No exclusion criteria (refer to back of prescription for details)

Drug-drug interactions assessed using best possible medication history (select one below):

No serious drug-drug interactions identified

Interactions identified and **management plan implemented** (please describe below):

Step-by-Step Assessment – ToolKit 1

• Available on the BCCDC Website (search: BCCDC COVID Therapeutics)

In this Tool you will find:

- 1. <u>Who can prescribe</u> and centralized prescribing through <u>HealthLink</u> BC (811)
- 2. Expanded eligibility criteria including the patient self-screener
- 3. How to determine risk of hospitalization
- 4. <u>Recommendations</u> for treatment based on risk and, if treatment is being pursued:
- 5. Confirming COVID-19 Testing
- 6. <u>Assessing vaccine</u> or previous infection status
- 7. Establishing symptoms and progression
- 8. Calculating treatment window
- 9. Assessing contraindications
- 10. Assessing and managing drug-drug interactions (including how to access the pharmacy support line)
- 11. Peer-peer physician support including for pregnant women, pediatrics and ID
- 12. PAXLOVID Prescription link and pharmacies that carry PAXLOVID
- 13. <u>Referring for sotrovimab</u> to the Health Authorities
- 14. Patient counselling and resources

Drug-drug Interactions – Toolkit 3

DRUG-DRUG INTERACTIONS and MANAGEMENT

The following drugs interact with nirmatrelvir/ritonavir. Some and are CONTRAINDICATED (management strategies may be possible. Consult <u>https://www.covid19-druginteractions.org/checker</u> before attempting. Drugs that are listed to interact in the monograph but have limited clinical impact are also included.

Legend:

CI-X: Contraindicated due to serious toxicity. Stopping the drug does not mitigate the interaction due to prolonged half-life, duration of enzyme induction or is not clinically appropriate due to risk or severity of condition
 CI-M: Co-administration is contraindicated but management strategies possible (e.g., holding drug or switch)
 DDI-M: Significant interaction but management strategies possible by prescriber or with expert consultation, or monitor
 OK: Interaction listed in the monograph, but the interaction has low clinical relevance

TI: Therapeutic Index; T1/2: Half-life; AUC: Area Under Curve (cumulative drug exposure); ↑: Increase; ↓: Decrease

Drug	Drug In	g Interaction Type, Information and Management Strategy			
Abemaciclib	DDI-M	Oral anticancer agent. \uparrow 'ed abemaciclib levels. Dose \downarrow to 100mg BID w/ BCCA consultation			
Alfuzosin	CI-M	$\uparrow\uparrow$ hypotension. If appropriate, hold drug; restart 3 days after finishing treatment			
Almotriptan	DDI-M	$\uparrow\uparrow$ 'ed levels. For migraines, use 6.25mg max dose, up to 12.5mg/24h period			
Alprazolam	DDI-M	$\uparrow\uparrow$ 'ed AUC by 2-5X. If appropriate, hold drug or significantly \downarrow dose			
ANTIDIABETICS	DDI-M	No drug level changes but hypoglycemia has been observed. Pt should self-monitor Sx and BG			
Amiodarone	CI-M	$\uparrow\uparrow$ 'ed amiodarone levels. Prolonged T1/2 and narrow TI; could consider hold w/ consultation			
Amitriptyline	OK	Small \uparrow in amitriptyline levels. Likely sub-clinical. Caution those sensitive to ADRs			
Amlodipine	DDI-M	\uparrow 'ed AUC by 2X. If BP <130, \downarrow dose by 50% during treatment and restart 3 days after finishing			
Apalutamide	CI-X	Oral cancer agent. \uparrow 'ed levels leading to seizures. Also an enzyme inducer			
Apixaban	CI-M	\uparrow 'ed levels of apixaban leading to \uparrow bleeding. Can consider switch to dabigatran. *See notes			
Aripiprazole	DDI-M	\uparrow 'ed AUC by 2X. Can consider \downarrow dose by 50% with mental health specialist consultation			

Other Useful Resources

BCCDC Website

Read: <u>Health Care Provider Information on sotrovimab (Xevudy) and</u> <u>nirmatrelvir/ritonavir (Paxlovid)</u> - *updated March 23 2022*

Clinical Practice Guide: Recommendations and Evidence

Practice Tool #1: Step-by-Step Assessment for Clinicians

Practice Tool #2: Definitions of Clinically Extremely Vulnerable (CEV)

Practice Tool #3: Drug-Drug Interactions and Contraindications

Practice Tool #4: Pharmacist Counselling Checklist 🕂

Pharmacare Website



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Ministry of Health **HIGH PRIORITY** nirmatrelvir/ritonavir (Paxlovid®) 5-day Treatment Pack Prescription

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					1	
\$\$			City	Postal Code	e	
Number	Allergies		I	I		
of Symptom (Onset (YYYY / MM / DD)					
IBILITY CI	RITERIA					
Confir	med COVID-19 AND					
Sympt	tomatic for five days or less (symp	tom onset day is con	sidered day zero) AND			
	tomatic for five days or less (symp increased risk for disease progres					
Are at	· · · · · · · · · · · · · · · · · · ·	sion (see Table below		on		
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