June 2022

pad Refills

Your dose of drug information in between details

The Why, Who, What, Where and How of nirmatrelvir/ritonavir (Paxlovid™)

1. **Why Paxlovid (nirmatrelvir/ritonavir)?** Paxlovid is approved by Health Canada for the treatment of mild to moderate COVID-19 in adults at high risk for progression to severe COVID-19. This approval is based on the results of the 2022 EPIC-HR trial which included 2,246 participants (mean age 46, SARS-CoV-2 variant 98% Delta) meeting these criteria:
   - age ≥18 plus a pre-specified risk factor for progression to severe disease OR age ≥60 regardless of medication conditions
   - without prior confirmed SARS-CoV-2 infection or vaccination.

   There was a 5.6% absolute risk reduction in the primary outcome of COVID-19 related hospitalization or death from any cause through 28 days (reduced from 6.4% of participants in the placebo group to 0.78% in the Paxlovid group).[1]

2. **Who is currently eligible for Paxlovid in B.C.?** COVID-19 positive patients (either via rapid antigen or polymerase chain reaction test) AND who have been symptomatic for 5 days or less AND who are high-risk individuals as defined in the COVID Therapeutics Committee (CTC) Practice Tool #1.[2] COVID-19 positive patients must contact prescribers or complete a self-assessment online to determine eligibility.[3] Contraindications include hypersensitivity to either nirmatrelvir or ritonavir, liver disease (defined as Child-Pugh Score class 3 or cirrhosis), eGFR of less than 30 mL/min and several drug interactions (see Practice Tool #3)[4] that are not modifiable and may result in serious toxicity or potential loss of virologic response.

3. **What is Paxlovid?** Paxlovid contains nirmatrelvir and ritonavir. Nirmatrelvir is a SARS-CoV-2 protease inhibitor that prevents viral replication. Ritonavir is an inhibitor of cytochrome P450 3A4 (CYP3A4)-mediated metabolism and is co-administered to prolong the duration of action of nirmatrelvir, enabling twice a day dosing. CYP3A4 is a common metabolic pathway for many medications and the inhibitory effects of ritonavir last 2-3 days after it is discontinued. Therefore, it is essential to assess each patient for possible drug interactions by consulting at least two drug interaction resources such as CTC Practice Tool #3 and Liverpool Interaction Checker[5] for management strategies. For support on assessing drug interactions in the following specific patient populations, you can call the BC Cancer Agency, or St Paul's HIV Ambulatory Pharmacy.[6] Consider patient factors that may be important to managing drug interactions such as indication, safety of withholding medications and complexity of dose adjustment.

4. **Where can you find and send a prescription for Paxlovid?** Prescribers can use the fillable PDF prescription[7] and fax it to community pharmacies. A list of community pharmacies that dispense Paxlovid can be found here.[8]

5. **How can we educate patients?** Paxlovid tablets are taken twice daily and dosage needs to be adjusted for renal function. Counsel patients on the most common adverse events: taste disturbance, diarrhea, vomiting, headache, myalgia and hypertension.[9] Inform patients to contact their doctor or pharmacist if they experience any adverse events. Clinicians should report any serious adverse events to Health Canada.[10]

[1]EPIC HR N Engl J Med 2022 (PMID:35172054); [2]BC COVID-19 Therapeutics Committee Practice Tool #1; [3]BC COVID-19 Self Assessment; [4]BC COVID-19 Therapeutics Committee Practice Tool #3; [5]University of Liverpool Drug Interaction Checker; [6]Dispensing Paxlovid and Monitoring Adverse Drug Events: A Guide for B.C. Community Pharmacists-Province of British Columbia: Appendix C; [7]British Columbia Paxlovid 5-day Treatment Pack Prescription; [8]British Columbia Pharmacy Association: Paxlovid for Community Pharmacies; [9]BC COVID-19 Therapeutics Committee Practice Tool #4; [10]Health Canada Adverse Reaction Reporting.

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