Important Safety Information on PAXLOVID (nirmatrelvir and ritonavir) Dosing and Dispensing in Renal Impairment, Risk of Serious Adverse Reactions Due to Drug Interactions, and English-Only Labels

2022/01/17

Audience
Healthcare professionals including physicians, pharmacists, nurse practitioners, nurses and public health officials.

Key messages

- **On January 17, 2022, PAXLOVID (nirmatrelvir and ritonavir) was authorized by Health Canada.**
- **PAXLOVID is indicated for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in adults with positive results of direct severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.**
- **In order to provide rapid access to PAXLOVID, Pfizer will distribute product cartons and blisters with the US Emergency Use label, in English-only, for a period of time.**
- **Healthcare professionals are advised that:**
    - **PAXLOVID is not recommended in patients with severe renal impairment. Patients with moderate renal impairment require a dose reduction. Healthcare professionals who dispense PAXLOVID should remove two nirmatrelvir tablets (one morning tablet and one evening tablet) from the daily blister cards for patients with moderate renal impairment.**
    - **PAXLOVID may interact with various medications, which could result in serious or life-threatening adverse reactions, or a loss of therapeutic effect.**
    - **Important Canadian-specific information is absent from the PAXLOVID carton and blister labels.**
    - **The Canadian Product Monograph (CPM) should be referenced for complete product information. The CPM is available in French and English on Health Canada's Drug Product Database, at pfizer.ca, on the federal government's COVID-19 vaccines and treatments portal, and by scanning the QR code on the English-only carton label to visit www.covid19oralrx.com.**
    - **The Information for healthcare professionals section of this communication provides more detailed guidance.**

What is the issue?

PAXLOVID (nirmatrelvir and ritonavir) was authorized by Health Canada on January 17, 2022. PAXLOVID is not recommended in patients with severe renal impairment and requires a dosage reduction in patients with moderate renal impairment. PAXLOVID may also interact with various medications, which could result in serious or life-threatening adverse reactions, or a loss of therapeutic effect and possible development of viral resistance. In order to provide rapid access to PAXLOVID, Pfizer will distribute product cartons and blisters labelled in English-only for a period of time. As a result, important Canadian-specific information is absent from these labels.

Products affected

PAXLOVID (150 mg nirmatrelvir; 100 mg ritonavir) co-packaged tablets for oral use. Drug Identification Number (DIN): 02524031

Background information

PAXLOVID is indicated for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in adults with positive results of direct severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.

PAXLOVID is not authorized for:

- the initiation of treatment in patients requiring hospitalization due to severe or critical COVID-19;
- pre-exposure or post-exposure prophylaxis for prevention of COVID-19;
- use for longer than 5 consecutive days.

To provide earlier access to PAXLOVID in the context of the global pandemic, Pfizer is providing cartons and blisters with the US Emergency Use label. This label is presented in English-only and is missing some important Canadian-specific information normally found on Health Canada approved labels (see the Information for healthcare professionals section and images in Appendix A).

Each carton of PAXLOVID contains 30 tablets divided in 5 daily-dose blister cards. Each daily blister card contains 4 nirmatrelvir tablets (150 mg each) and 2 ritonavir tablets (100 mg each), which are separated into morning and evening doses.

Information for consumers

PAXLOVID is used in adults with mild-to-moderate COVID-19 and who are at high risk for getting severe COVID-19, which can result in hospitalization or death.

PAXLOVID is not recommended in patients with severe kidney disease. Patients with moderate kidney disease should talk to their healthcare professional, as they will require a reduced dose.

Various medications may interact with PAXLOVID. Taking PAXLOVID with these medicines may cause serious or life-threatening side effects or affect how PAXLOVID works. Patients should tell their healthcare professional about all the medicines they are taking, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

Information for healthcare professionals
Healthcare professionals are advised that:

- **PAXLOVID is not recommended in patients with severe renal impairment. Patients with moderate renal impairment require a dose reduction.** Each daily blister card contains two more nirmatrelvir tablets than are needed for dosing in patients with moderate renal impairment. It is recommended that all prescriptions specify the dose and the number of tablets for each active ingredient as follows:

eGFR*	PAXLOVID Dose
≥60 mL/min (normal renal function or mild renal impairment)	300 mg nirmatrelvir (two tablets of 150 mg each) with 100 mg ritonavir (one tablet of 100 mg), taken together twice daily for 5 days.
≥30 to <60 mL/min (moderate renal impairment)	150 mg nirmatrelvir (one tablet of 150 mg) with 100 mg ritonavir (one tablet of 100 mg), taken together twice daily for 5 days.
<30 mL/min (severe renal impairment)	PAXLOVID is not recommended.

*eGFR=estimated glomerular filtration rate based on the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) formula

  When dispensing PAXLOVID, healthcare professionals should ensure that patients with moderate renal impairment receive additional support and instructions given the risk of dosing errors. This includes removing two nirmatrelvir tablets from daily blister cards (i.e., one of the 150 mg nirmatrelvir tablets from the morning dose and one of the 150 mg nirmatrelvir tablets from the evening dose) prior to dispensing, notifying patients that blister cards have been altered at the pharmacy and counselling patients about renal dosing instructions.

- **PAXLOVID may interact with various medications that could result in serious adverse reactions, including a loss of therapeutic effect.** PAXLOVID, a CYP3A inhibitor, may increase the plasma concentrations of concomitant medications metabolized by CYP3A. The use of concomitant medications that inhibit or induce CYP3A may increase or decrease concentrations of PAXLOVID, respectively. These interactions may lead to serious (and sometimes life-threatening) adverse reactions from greater exposure to concomitant medications or PAXLOVID. These interactions may also lead to a loss of therapeutic effect of PAXLOVID and possible development of viral resistance. Refer to the CPM for more information on potential drug interactions.

- **The following important Canadian-specific information is absent from PAXLOVID carton and blister labels:**
  - Drug Identification Number (DIN)
  - drug class
  - “Pr” (prescription) symbol
  - name and address of the Canadian importer and distributor

    - to keep out of the reach and sight of children
    - all corresponding text in French

- The carton and blister labels include the statement "*For use under Emergency Use Authorization."* The US Food and Drug Administration (FDA) specific information should be disregarded as this is not relevant to the Canadian authorization.
- The CPM should be referenced for complete product information. The CPM is available in French and English on Health Canada's Drug Product Database, at pfizer.ca, on the federal government's COVID-19 vaccines and treatments portal, and by scanning the QR code on the English-only carton label to visit www.covid19oralrx.com.

For any medical questions, contact **Pfizer Canada ULC Medical Information** at www.pfizermedicalinformation.ca or 1-800-463-6001. For any other general inquiries, contact **Pfizer Canada ULC Customer Service** at 1-888-888-9221 or CANADAPAXLOVIDCS@Pfizer.com.

Action taken by Health Canada
On January 17, 2022, PAXLOVID was authorized by Health Canada.

Health Canada is permitting the use of an English-only label that reflects the US label for emergency use for a period of time. Health Canada has imposed terms and conditions requiring Pfizer Canada ULC to provide supplies with Canadian-specific labels as soon as possible.

Health Canada has worked with Pfizer Canada ULC to prepare this alert for PAXLOVID. Health Canada is communicating this important safety information to healthcare professionals and Canadians via the Recalls and Safety Alerts Database on the Healthy Canadians Web Site. This communication update will be further distributed through the MedEffect™ e-Notice email notification system, as well as through social media channels, including LinkedIn and Twitter.

Report health or safety concerns
Managing marketed health product-related side effects depends on healthcare professionals and consumers reporting them. Any serious or unexpected side effects in patients receiving PAXLOVID should be reported to Pfizer Canada ULC or Health Canada.

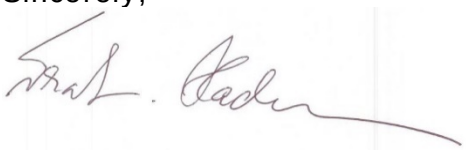
Pfizer Canada ULC
17300 Trans-Canada Highway
Kirkland, QC
H9J 2M5
www.pfizersafetyreporting.com
Telephone: 1-866-723-7111
Fax: 1-855-242-5652

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax.

For other health product inquiries related to this communication, contact Health Canada at: Therapeutic Products Directorate, Bureau of Gastroenterology, Infection and Viral Diseases
E-mail: bgivd_enquiries@hc-sc.gc.ca

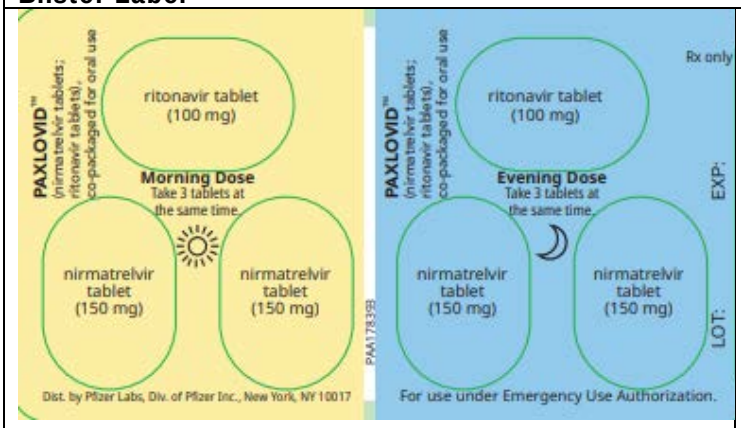
Sincerely,



Original signed by
Vratislav Hadrava M.D., Ph.D.
Vice President & Medical Director
Pfizer Canada ULC

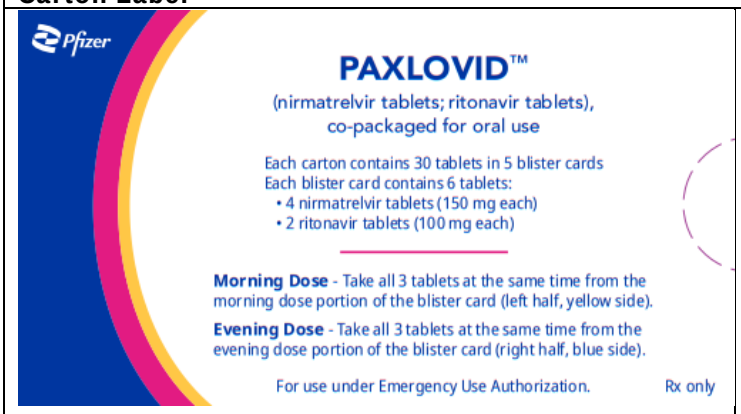
Appendix A: PAXLOVID English-only blister and carton labels

Blister Label



PAXLOVID™
(nirmatrelvir tablets; ritonavir tablet) co-packaged for oral use
Morning Dose
Take 3 tablets at the same time.
ritonavir tablet (100 mg)
nirmatrelvir tablet (150 mg)
nirmatrelvir tablet (150 mg)
Evening Dose
Take 3 tablets at the same time.
ritonavir tablet (100 mg)
nirmatrelvir tablet (150 mg)
nirmatrelvir tablet (150 mg)
Rx only
Dist. by Pfizer Labs, Div. of Pfizer Inc., New York, NY 10017
For use under Emergency Use Authorization

Carton Label



PAXLOVID™
(nirmatrelvir tablets; ritonavir tablets), co-packaged for oral use
Each carton contains 30 tablets in 5 blister cards
Each blister card contains 6 tablets:
• 4 nirmatrelvir tablets (150 mg each)
• 2 ritonavir tablets (100 mg each)
Morning Dose - Take all 3 tablets at the same time from the morning dose portion of the blister card (left half, yellow side).
Evening Dose - Take all 3 tablets at the same time from the evening dose portion of the blister card (right half, blue side).
For use under Emergency Use Authorization.
Rx only

Store at room temperature 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F).
DOSAGE AND USE
See accompanying FDA authorized Fact Sheet. You can also see FDA authorized Fact Sheet by scanning QR code or go to https://www.pfi.sr/c19oralrx.

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