COVID-19: Prevention

A Crawley BSP, M LeBras PharmD, L Regier BSP Feb 2024

Vaccine Pearls: may ↓"long COVID" by ~1/3 ;[51] if immunocompromised, extra dose required for initial series; still recommended post-COVID-19 infection (hybrid immunity more robust[NACI]); mix-and-match brands OK & may ↑ response.[52]

Table 1. COVID-19 Vaccines NACI

Primary Series

1st-line: SPIKEVAX XBB1.5 or COMIRNATY XBB1.5

- **≥5 years** NACI strong recommendation (should offer)
- **≥6 mos to 4 yrs** NACI discretionary recommendation (may offer)
- **≥6 months to 4 years & high risk of severe illness** e.g. lung dx, ≥1 comorbidity, neurologic disorder NACI strong recommendation (should offer)

Booster Doses

1st-line: SPIKEVAX XBB1.5 or COMIRNATY XBB1.5

- **Fall 2023, ≥6mos**: offer new booster to ALL individuals previously vaccinated if ≥6mos since last dose/COVID (consider ≥3mos). Esp if: ≥65yr, LTC, pregnancy, Indigenous, comorbidities e.g. diabetes, immunocompromised, lung disease, CKD, CVD.[NACI strong (should offer)]
- **Spring 2024**: offer 2nd dose of XBB1.5 to those at high risk *i.e. ≥65yr, LTC, ≥6mos & immunocompromised.[NACI discretionary (may offer)]

*No further doses required if primary series includes XBB1.5 vaccine dose once series is complete. Exception high risk **.[NACI]*

Table 2. Original Monovalent Vaccine Efficacy Estimates in Adults

	Infection risk if exposed to COVID-19	**Hospitalization** risk if ~first infection	**Mortality** risk if ~first infection
Unvaccinated adults	**~100%?** (if infection-naïve)	**Wide range of risk (see Table 3)** **1%** to **30%+** [30,47]	**0.1%** to **30%+** [30,47]
Adults vaccinated w/ initial series	↓ risk by 20-33% [36,42]	↓ risk by 65% [38]	↓ risk by 79% [37]
Adults vaccinated + 1 booster	↓ risk by 54-69% [36]	↓ risk by 85% [38]	↓ risk by 94% [37]
Adults vaccinated + 2 boosters	↓ risk by 75-83%? [39]	↓ risk by 95%? [39]	↓ risk by **99%?** [39]

Notes: Vaccine efficacy wanes over time; in general, a booster "renews" a patient nearly back to a previous level of protection. CDN: 12-15x↑ ICU admission & mortality among unvaccinated vs fully vaccinated with booster dose.[123]

Intervention	Initial Dosing (Primary Series)	Booster Dosing
Vaccines		
Pfizer-BioNTech mRNA vaccines ❄ **COMIRNATY Omicron XBB.1.5** HC Sept'23 grey cap, ≥12 years: six 0.3mL doses/vial; **do not dilute**. blue cap, 5 to 11 years: six 0.3mL doses/vial; **do not dilute**. maroon cap, 6 mos to 4 years: ten 0.2mL doses/vial; **dilution required**. PL	≥12 years: 30mcg IM (0.3mL of grey cap vial) 5-11 years: 10mcg IM (0.3mL of **blue** cap vial) ≥6 mos to 4 yrs: 3mcg IM (0.2mL of **maroon** cap vial) **XBB.1.5 Initial ≥5yrs**: 1 dose. If immunocompromised, give 2nd dose 4-8 wks after later. **XBB.1.5 Initial 6mos to <5yrs**: 3 doses. 2 doses given 3-**8** wks apart, then 3rd dose given ≥8 wks after 2nd dose. If immunocompromised, give 4th dose 4-8 wks later (not preferred, **SPIKEVAX** preferred see below).[NACI] **Series initiated with non-XBB.1.4 vaccine** i.e. original monovalent, bivalent but not completed: Complete series with XBB.1.5 vaccine. Do not have to restart. e.g. ≥**5yrs**: 2 doses total, if immunocompromised 3 doses total.	Not required if primary series includes XBB.1.5 at this time. *If increased risk of severe illness e.g. ≥65yr, LTC, etc may receive 2nd XBB.1.5 dose spring 2024 NACI discretionary recommendation **Booster ≥12yrs**: 30mcg IM (0.3mL of grey cap vial) **Booster 5-11yrs**: 10mcg IM (0.3mL of **blue** cap vial) **Booster 6 mos to 4 yrs**: 3mcg IM (0.2mL of **maroon** cap vial)
Moderna mRNA vaccines ❄ **SPIKEVAX XBB.1.5** HC Sept'23 royal blue cap: **do not dilute; swirl vial**. ≥12 years: five 0.5mL doses/vial. 6 mos to 11 years: ten 0.25mL doses/vial. PL	≥12 years: 50mcg IM (0.5mL of **royal blue** cap vial) 5-11 years: 25mcg IM (0.25mL of **royal blue** cap vial) ≥6 mos to 4 yrs: 25mcg IM (0.25mL of **royal blue** cap vial) **XBB.1.5. Initial ≥5yrs**: 1 dose. If immunocompromised, give 2nd dose 4-8 wks later. **XBB.1.5 Initial 6mos to <5yrs**: 2 doses given **8** wks apart. If immunocompromised, give a 3rd dose 4-8 wks later (preferred over **COMIRNATY**).[NACI] **Series initiated with non-XBB.1.4 vaccine** i.e. original monovalent, bivalent but not completed: Complete series with XBB.1.5 vaccine. Do not have to restart. e.g. ≥**5yrs**: 2 doses total, if immunocompromised 3 doses total.	Not required if primary series includes XBB.1.5 at this time. *If increased risk of severe illness e.g. ≥65yr, LTC, etc may receive 2nd XBB.1.5 dose spring 2024 NACI discretionary recommendation **Booster ≥12yrs**: 50mcg IM (0.5mL of **royal blue** cap vial) **Booster 5-11y:** 25mcg IM (0.25mL of **royal blue** cap vial) **Booster 6 mos to 4 yrs**: 25mcg IM (0.25mL of **royal blue** cap vial)
Novavax recombinant spike protein **NUVAXOVID XBB.1.5** ❄ US Oct'23/ CDN Dec'23 one vial containing five 0.5mL doses PL	≥12 yrs: 5mcg IM (0.5mL) **Initial**: 2 doses given 3-**8** weeks apart. Consider 3rd dose if immunocompromised.[NACI 54, CDC]	Not preferred. Reserve if **CI** others.[NACI] **Booster ≥12y**: 0.5mL IM Health Canada
Medicago recombinant spike protein **COVIFENZ** ❄ developed in CDN 🇨🇦, plant-based. two vials; after mixing = ten 0.5mL doses	18-64 yrs: 3.75mcg IM (0.5mL) **Initial**: 2 doses given 3-**8** weeks apart. Consider 3rd dose if immunocompromised.[NACI 54]	Off-label for use as booster dose.
mAB		
Tixagevimab-Cilgavimab **EVUSHELD** ❄ dark grey cap 150mg tixagevimab vial white cap 150mg cilgavimab vial PL	**UNCERTAINTIES**: Sask: routine use **not** recommended. **Emerging antiviral resistance limits use**.[HC] **On-label dosing** 150mg/150mg if immunocompromised or vaccination not recommended.[32] **Off-label:** ≥12yrs & ≥40kg: 300mg tixagevimab IM + 300mg cilgavimab IM.[expert opinion for Omicron] ➔ Give **separate injections** into each gluteal muscle	Repeat dosing unstudied. FDA: repeat q6mos in those who require ongoing protection.[Expert]
Masking and Physical Distancing	**Effective**.[59] Surgical masks ↓ transmission by <50% in community setting,[72] and physical distancing ↓ transmission by 80% (2.6% vs 12.8%, **NNT≈10**) compared to no intervention.[44] N95 masks more effective than disposable masks.[43,44] Physical distancing 2m more effective than 1m.[44] Eye protection (e.g. face shield, goggles) also associated with ↓ infection risk.[44]	

Adverse Effects AE / Contraindications CI / Drug Interactions DI Monitoring M

- **AE**: injection site reactions (>50%, and more common with second dose);[21] fever 20%, headache 50%, fatigue 50%, chills 20%, myalgia 50%, arthralgia 20%. ↑AE in younger patients.[57] Most AE resolve within 2 days. Typically do **not** pre-dose with antipyretics as ?may limit immune response. **Uncertain**: asthenia (**COMIRNATY**), facial nerve paralysis (**COMIRNATY**), ischemic stroke ≥65y (**COMIRNATY BIVALENT**)[Preliminary data], chronic spontaneous urticaria (**SPIKEVAX**).[84]
- Report vaccine adverse events here. **Link**: Tips to Avoid Shoulder Injury (Waterloo).

Table 1. Serious Adverse Events with COVID-19 Vaccines.[22-26]

Cumulative serious AE rate ≈ **0.01%**, which is << COVID-19 hospitalization risk.[58]

	Myocarditis (± pericarditis)	**VITT** (clot with ↓ platelets)	**GBS** (nerve damage)
COMIRNATY*	< 1 in 10,000 (in males age 12-30yr) < 1 in 100,000 (all other patients)	**not detected**	**not detected**
SPIKEVAX*		**not detected**	**not detected**
NUVAXOVID	lack of data	lack of data	lack of data
COVIFENZ	lack of data	lack of data	lack of data

***mRNA XBB.1.5**: NACI no longer recommends one product over another among 12 to 29 years as risk of myocarditis is thought to be lower than previous original vaccines due to 1-dose schedule and longer interval (≥6mos) in most and lower dosage of Moderna vaccine available now.

For more details on the risk of myocarditis, VITT, and GBS, see **Online Extras Table 5**.

- **CI for all vaccines**: anaphylaxis to a component or previous COVID-19 vaccine of the same platform. **Precautions**: history of immediate allergic reaction to any other vaccine or injection; if one COVID-19 vaccine is **CI**, other platforms are precautioned. History of myocarditis (mRNA vaccines). **Kids**: history of MIS-C. **Additional warnings for adenoviral vector vaccines**: **Contraindicated** if history of VITT or CLS; **Caution** if history of thromboembolic disease.
- Usually OK to still give vaccine if mild acute illness (e.g. cough & cold).
- Planning/Pregnancy/Lactation: Recommended;[NACI] no difference in spontaneous abortion or congenital abnormalities risk.[131]
- **DI**: None. May give a COVID-19 vaccine **at any time** in relation to other vaccines.
- **M**: Observe for 15 mins after vaccine; 30 mins if precautions/anaphylaxis history.

No longer preferred (Fall 2023) and/or available: **Pfizer-BioNTech COMIRNATY Original / Omicron BA.4/BA.5 BIVALENT, COMIRNATY** BNT162b2, **Moderna SPIKEVAX Original/Omicron BA.4/5 BIVALENT, SPIKEVAX Original/Omicron BA.1 BIVALENT, SPIKEVAX** mRNA-1273, **VAXZEVRIA AstraZeneca, JCOVDEN Janssen (J&J), NUVAXOVID Novavax**

Unclear benefit for hospitalization or mortality endpoints with prophylactic use. ↓ incidence of symptomatic COVID-19 by 83% (0.3% tix-cil vs 1.8% placebo, **NNT≈67** over ~6 mos) for high-risk COVID-19-**negative**. See RxFiles **PROVENT** Trial Summary.

- **AE**: Injection site reactions, ?cardiac events e.g. MI **NNH≈263**/6mos.[PROVENT]
- **CI**: **Caution**: CVD e.g. CAD, MI, HF, stroke, etc. **DI**: wait ≥14d post COVID-19 vaccine.

A Crawley BSP, M LeBras PharmD, L Regier BSP Dec 2023

Clinical Pearls

- COVID-19 therapies are not a substitute for vaccination. If mRNA vaccine-hesitant, consider non-mRNA.
- COVID-19 therapies typically target pts at highest risk for severe COVID-19 complications. Most data for **unvaccinated** pts; expert opinion/observational data suggests role in **vaccinated but high-risk** pts too.[33-35]
- Nirmatrelvir/ritonavir **PAXLOVID** has numerous critically important drug interactions. Consult ≥2 sources. Complete a full medication history (including herbal and OTC products) prior to prescribing.
- If contraindication to nirmatrelvir/ritonavir **PAXLOVID**, refer patients for remdesivir if ≤7 days of sx onset.

Supportive Care for Acute COVID-19 Outpatients

- Analgesics/antipyretics (e.g. acetaminophen); antitussives (e.g. dextromethorphan). Patient tool.
- Close monitoring for new/worsening dyspnea; progression from dyspnea to hospitalization can be rapid. Lying in prone position (rather than supine) may help. Patients in SK may call 811.
- Quarantine from family and/or wear mask; handwash; disinfect.
- Drink fluids regularly to avoid dehydration; rest to promote recovery.

Table 3. Risk Factors for Severe COVID-19.[29]

Age (esp. ≥65yrs & **≥75yrs**), obesity, diabetes, immunocompromised, CKD, asthma, COPD, CVD, cancer, HIV, Indigenous, neurologic conditions, cystic fibrosis, smoking, liver dx, pregnancy, sickle cell disease, tuberculosis.
See Risk Calculator from BC CTC.

Drug	Indications / Role in Therapy	Dosing	Cost	Adverse Effects AE / Contraindications CI / Drug Interactions DI / Comments
Nirmatrelvir-Ritonavir **PAXLOVID** 150mg nirmatrelvir tabs and 100mg ritonavir tabs (in blister cards) PL WHO'23: option for pregancy / lactation See **EPIC-HR** Trial Summary.	✓ 1st line for high-risk outpatients (≥18yrs) with mild-to-moderate COVID-19. Give within 5 days and if no contraindications/overriding DIs. **Link**: Eligibility criteria in Sask. ❶ immunocompromised ❷ under or unvaccinated ❸ ≥70y with risk factors **Link**: Sask prescriber assessment form. Off-label: ≥12y, high-risk, mild COVID.[AMMI, FDA] Off-label: ?↓ long COVID observational data.[89]	**eGFR ≥ 60mL/min**: 300mg nirmatrelvir (two pink tabs) + 100mg ritonavir (one white tab) **po q12h x 5 days** **eGFR 30-59mL/min**: 150mg nirmatrelvir (one pink tab) + 100mg ritonavir (one white tab) **po q12h x 5 days** **eGFR < 30mL/min ± dialysis (off-label)**: Evolving data. SK: CI based on prescribing guidelines.[71]	Federally acquired medication	↓ hospitalization/death by 89% (0.8% nirmatrelvir/r vs 6.3% placebo, **NNT≈18**) when given to high-risk patients within 5 days of symptom onset.[EPIC-HR, Cochrane'22] Minimal benefits in low-risk patients.[EPIC-SR, 35,] Most benefit in older adults ≥65 years.[63] • AE: **Bad taste** (common); nausea/vomiting/diarrhea; headache; myalgia; ↑BP. SAE are rare. Rebound infection after 5d tx (~5%, no different than placebo[80]); do not re-treat. • CI: severe liver dx (Child-Pugh C); some antiepileptics e.g. phenytoin • DI: CYP3A4 substrate & strong inhibitor. **MANY**: atorvastatin, rosuvastatin, apixaban, amlodipine, tamsulosin, clopidogrel, ticagrelor, colchicine, clozapine. Nirmatrelvir/r should not be dose adjusted to manage DIs. **Useful checkers**: Liverpool, medSask, BC CTC. Assess harm of disrupting current drug tx relative to expected nirmatrelvir/r benefit!
Remdesivir **VEKLURY** 100mg vial PL See **PINETREE** Trial Summary.	✓ high-risk outpatients (≥18yrs) if CI or DI to nirmatrelvir/r.[1] ✓ hospitalized patients (≥12yrs & ≥40kg) with pneumonia & requiring O_2. Off-label: use >3.5kg.[AMMI]	**Outpatients**: 200mg IV day 1, then 100mg IV days 2 & 3. **eGFR <30mL**: may use standard dose,[SHA] others suggest dose-adjustment.[61] **Inpatients**: 200mg IV day 1, then 100mg IV day 2 & onwards for total duration of **5**-10d.	Federally acquired medication	↓ hospitalization by 87% (0.7% remdesivir vs 5.3% placebo, **NNT≈22**) when given to high-risk outpatients within 7 days of symptom onset.[PINETREE] No proven (outpatient) ↓ in mortality. • AE: **Nausea**, headache, ↑LFTs, rash, ↓BP, ↓HR, anaphylaxis. Serious adverse effects rare. • CI: ALT > 5x ULN. • Dialysis: give dose after dialysis[SHA] or during [BC CDC] on dialysis days. • DI: Strong 3A4 inducers (e.g. CBZ, rifampin) ↓ levels. Hydroxychloroquine may ↓efficacy.
Sotrovimab **XEVUDY** 500mg vial PL See **COMET-ICE** Trial Summary.	**Utilization on hold in Sask due to uncertain efficacy vs Omicron.[WHO'22]** ✓ mild-to-moderate outpatient COVID-19 in high-risk patients age ≥12yrs & ≥40kg.	500mg IV once over 60 minutes May slow rate of infusion if reaction occurs.	Federally acquired medication	↓ hospitalization by 85% (1% sotrovimab vs 7% placebo, **NNT≈17**) when given to high-risk patients within 7 days of symptom onset.[COMET-ICE] **Guidelines suggest may not be effective against Omicron BA.2 variant.**[1, WHO] • AE: Infusion reactions, diarrhea, anaphylaxis (treat with epinephrine). Serious AE rare. • CI: Hypersensitivity to any components. DI: None known.
Tixagevimab-Cilgavimab **EVUSHELD** ❄ 150mg tixagevimab vial and 150mg cilgavimab vial PL	✓ for high-risk outpatients (≥12yrs & ≥40kg) with mild-to-moderate COVID-19. See RxFiles **TACKLE** Trial Summary.	≥18yrs: 300mg tixagevimab IM (dark grey vial cap) + 300mg cilgavimab IM (white vial cap) **Requires separate injections** (3mL each drug).	Federally acquired medication	↓ hospitalization by 57% (4.1% tix-cil vs 9.5% placebo, *interim result*) when given to unvaccinated (& mainly high risk) patients within 7 days of symptom onset.[TACKLE] Possible role in acute treatment, **but emerging antiviral resistance limits role**.[HC] For AE, CI, & DI for tixagevimab-cilgavimab, see previous page.
Molnupiravir **LAGEVRIO** 200mg capsule PL	**Currently not authorized** in Canada. Studied in mild-to-moderate outpatient COVID-19 in high-risk pts age ≥18yrs.	800mg (4 caps) q12h po x 5 days	Unavailable in Canada	↓ hospitalization/death (**NNT≈33**) when given to high-risk pts ≤5d sx onset.[MOVe-OUT] Later RCT and systematic review found NS.[128 PANORAMIC, 122] Inferior to sotrovimab.[OpenSAFELY] • AE: Diarrhea, nausea, dizziness, ?impaired bone/cartilage growth. • CI: Use contraception (♂ & ♀) during tx. DI: None known.
Inhaled Budesonide **PULMICORT TURBUHALER** 100, 200, 400mcg inhaler PL	**Uncertain benefit.** Off-label & **not recommended**.[IDSA (conditional)] Studied in high-risk, mostly unvaxxed adults ≥50yrs. Continue ICS in asthma.	800mcg inhaled BID x 7-14 days (until symptoms resolve)	$130 (1 inhaler)	Faster COVID-19 symptom resolution (12 days budesonide vs 15 days usual care) when given to high-risk outpatients within 14 days; mixed data for hospitalizations.[PRINCIPLE,17] • AE: Sore throat, dysphonia, cough, thrush. Rinse mouth after use. • DI: ↑levels by CYP3A4 inhibitors (e.g. ritonavir, ketoconazole).
Fluvoxamine **LUVOX, g** 50, 100mg tabs PL	**Uncertain benefit.** Off-label & **not recommended**.[IDSA, WHO] Studied in high-risk, unvaxxed pts ≥18yr.	100mg BID po x 10 days See Fact Sheet from Waterloo	$20 (1 course)	↓ hospitalization by ~30% (11% fluvox vs 16% placebo) when given to unvaxx, high-risk outpts within 7d of sxs, but methodology issues.[TOGETHER] No benefit 50mg BID.[COVID-OUT, ACTIV-6] • AE: Nausea, constipation, sedation. DI: Many. See RxFiles Antidepressants.
Colchicine, g 0.6mg tab PL	**Uncertain benefit.** Off-label & **not recommended**.[IDSA (strong)] Studied in high-risk, unvaccinated outpatients age ≥40yrs. No benefit for inpatients.[60]	0.5-0.6mg BID po x 3 days, then daily x 27 days	$20 (1 course)	↓ hospitalization/death by 25% (4.5% colchicine vs 5.9% Pl, **NNT≈71**) when given to high-risk outpts ≤1d of positive COVID-19 test.[COLCORONA] Subsequent study found no difference.[ACT] • AE: Diarrhea 14% **NNH≈15**,[18] nausea, rash. **Serious**: ?pulmonary embolism 0.5%, neutropenia. • CI: Blood dyscrasias, transplant pts, CrCl<30mL/min. DI: P-gp & CYP3A4 inhibitors.
Hydroxychloroquine	✗ Ineffective. (Initial evidence mixed; subsequent meta-analysis showed inefficacy.[11])			Ineffective in preventing infection & ↑harms;[11] no clinical benefit in hospitalized patients.[12]
Ivermectin	✗ Ineffective. (Initial positive RCT data fabricated;[48] subsequent showed inefficacy.[13, COVID-OUT, ACTIV])			Failed to prevent COVD-19 hospitalization when given within 7 days of symptom onset.[13]

Vitamin D:[27,28] inconsistent benefit in hospitalized pts[64,66] & prevention.[69 CORONAVIT] **Zinc:** Uncertain benefit, 25mg elemental BID x 15d ↓ICU admission.[75] **Others (not routinely available in SK)**: casirivimab-imdevimab, bebtelovimab, high-titer convalescent plasma, bamlanivimab-etesevimab, regdanvimab, pegylated interferon lambda . Real-world **NNTs** will vary based on pt risk, current COVID-19 wave, variant, etc. Bacterial co-infection ~8.5%, reassess if ABX required.[76]

Post-COVID Condition "Long COVID": sx persist ≥12wks; variable course, ~20-50% sx >1yr; incidence 5-40% (?↑ delta); risk factors: >40yrs, severe illness (hospitalization/ICU), BMI ≥30, comorbidities, smoking, female.[139-142] **Treatment**: pacing; reassurance/validation; symptomatic tx; reassess polypharmacy; Off-label: ?vaccination - mixed results; ?metformin x 14d, ?**PAXLOVID** [ongoing].[143-147] **Prevention**: ?vaccination - 2 doses vs unvaxx OR 0.57; ?**PAXLOVID.**[147-149]

COVID-19 Online Extras

Abbreviations: CLS=capillary leak syndrome **GBS**=Guillain-Barré syndrome **mRNA**=messenger ribonucleic acid **mAB**=monoclonal antibody **MIS-C**=multisystem inflammatory syndrome in children **r**=ritonavir **VITT**=vaccine-induced immune thrombotic thrombocytopenia

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Table 4. Useful Links and Resources

Guidelines & Reviews

NIH COVID-19 Guidelines
IDSA COVID-19 Guidelines
WHO COVD-19 Guidelines
Saskatchewan COVID-19 Outpatient Treatment Guidelines
Medical Letter COVID-19 Treatments and COVID-19 Vaccines
Pharmacist Letter COVID-19 Treatments and COVID-19 Vaccines
UpToDate COVID-19 Review
British Columbia COVID-19 Treatments
Ontario Science Table Nirmatrelvir/Ritonavir (Paxlovid) Briefing

Clinical Tools

medSask Paxlovid Center: immunocompromising medications, prescriber assessment tool (prescription), paxlovid patient handout
SHA: Outpatient COVID-19 management, Post-COVID Condition / "Long COVID"
Drug Interactions checkers: Liverpool, medSask, BC CTC, Ontario Science Table, IDSA Drug Interaction Guidance
Sask Paxlovid Dispensing +/- Prescribing Pharmacies
medSask COVID-19 vaccine doses, eligibility, and intervals
Health Canada COVID Vaccines Components
Health Canada Approved COVID-19 Therapies in Canada
Canadian Pharmacists Association Patient Tools
- Top Tips to Prevent the Spread of Viruses
- Managing COVID-19 at Home

Centre for Effective Practice COVID-19 Resource Centre
Sask Health Vaccine Clinics in Saskatchewan [or call 1-833-727-5829]
Sask Health Vaccine Comparison Chart
Health Canada Where to Book a Vaccine Appointment
Waterloo: Tips to Avoid Shoulder Injury Related to Vaccine Administration
ACFP: COVID Tools for Practice
Low dead-volume syringes helps ↑ # of doses/vial.

Table 5. Adverse Events with COVID-19 Vaccines: Additional Information.

Myocarditis with mRNA vaccines

- Myocarditis risk is greater with a COVID-19 **infection** than a vaccine (1500 cases per million patients).[23]
- Most common in young adult males. For example, with a **second** mRNA dose:
  - ➔ up to 69 cases per million in males 12-17yrs.[22]
  - ➔ up to 4 cases per million in males >30yrs.[22]
  - ➔ up to 4 cases per million in males 5-11yrs.[49]
- Ask patients to monitor for new chest pain, shortness of breath, or palpitations. Median time to onset of symptoms is 2 days.[85]
- Myocarditis cases are usually mild, with onset <1 week after vaccine. The vast majority of cases resolve after supportive care in a hospital or outpatient setting. Most cases require NSAID and/or colchicine therapy; however, some require no treatment.[85]
- Myocarditis risk may be greater with **SPIKEVAX** than **COMIRNATY** (one analysis suggested a ~5x higher risk with **SPIKEVAX**),[26] greater with short (i.e. ≤30 days) interval between COVID-19 doses for those 16-17 yrs (≤30 days 21.3 per 100,000 vs >31-55 days ~5 per 100,000),[85] and ? greater with heterologous **COMIRNATY** and **SPIKEVAX** dosing.[138]

VITT (Vaccine-Induced Immune Thrombotic Thrombocytopenia) with adenoviral vector vaccines

- Most common in adult females (e.g. 3.8 cases per million doses of Janssen vaccine in general population vs up to 10.6 cases per million in females 30-49yrs).[24]
- Ask patients to monitor for signs and symptoms: e.g. new petechiae or bruising, shortness of breath, chest pain, lower extremity edema, abdominal pain, unabating severe headache, severe backache, new focal neurologic symptoms, seizures.
- Fatal in up to 20% of cases. Onset typically within 2 weeks of vaccine.
- Some evidence that mRNA vaccines are safe in patients who have previously experienced VITT.[62]

Guillain-Barré syndrome (GBS) with adenoviral vector vaccines

- In reports, median age of 56 years, 13 days after Janssen vaccination. Fatal in <1% of cases. Overall rate of 9.8 cases per million doses (4x background rate).[25] Others suggest up to 4 cases per million doses.[83]
- Ask patients to monitor for tingling in extremities; weakness; difficulty with facial movements, breathing, or swallowing.
- Causal relationship not yet established. Of note, other vaccines (e.g. for influenza) have previously been associated with GBS.[31]

Not available in Canada

Bebtelovimab PL 175mg vial	**Currently not authorized** in Canada. Studied in mild-to-moderate outpatient COVID-19 in low-risk pts age ≥12yrs.	175mg IV once over >30 seconds	Unavailable in Canada	**BLAZE-4** unpublished data: ↑ symptom resolution (6d with bebtelovimab vs 8d placebo), but no change in hospitalizations.[9] ?↓ activity vs omicron BQ.1 and BQ.1.1.[FDA] • **AE**: Infusion reactions, itch, rash. **DI**: None known.

Discontinued:

Janssen (J&J) adenoviral vector **D/C by company June 2023** PL **JCOVDEN** Ad.26.COV2.S one vial containing five 0.5mL doses ❄	≥18 yrs: 0.5mL IM **Initial**: 1 dose. If immunocompromised, give a 2nd dose 4 weeks later of an mRNA vaccine.	Not preferred. Reserve if **CI** others.[NACI] **≥18yrs, Booster dose**: 0.5mL IM -booster 1: give 2 mos post initial series.

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References for COVID-19 Chart

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