COVID-19 (SARS-CoV-2)
Drug Information

Last updated: March 19, 2020 – all information subject to change.

I. EXPERIMENTAL Antiviral Therapy

Disclaimer: Any treatment of COVID-19 using experimental medications or off-label indications of approved drugs should ideally be done in the context of a clinical trial or Health Canada Special Access Program. Currently the WHO does not recommend any specific anti-COVID-19 treatment. Consult ID for consideration of any directed COVID-19 therapy and inclusion of patients in ongoing clinical protocols. Content of this document is for information only.

For details on dosing and adverse events monitoring, click on drug name for details in table.

Hydroxychloroquine

- As of March 19, 2020, supply is limited in Canada.
- Better tolerated than chloroquine.

Chloroquine – currently on long term shortage in Canada.

Lopinavir/Ritonavir (Kaletra®)

- This open-labelled randomized trial did not find benefit of lopinavir/ritonavir over standard care https://www.nejm.org/doi/full/10.1056/NEJMoa2001282
- **MAJOR drug-drug interactions**. Must be reviewed by a pharmacist before initiating lopinavir/ritonavir.

http://www.covid19-druginteractions.org/

https://hivclinic.ca/wp-content/plugins/php/app.php

Remdesivir

- Investigational nucleotide analog with broad-spectrum antiviral activity
- Access options:
    - Enroll in one of the clinical trials https://rdvcu.gilead.com/, or
    - Health Canada Special Access Program as a patient-specific application via the Gilead portal https://www.canada.ca/en/health-canada/services/drugs-health-products/special-access/drugs/remdesivir.html
- Prior to initiation, check one or both of the following databases for **drug-drug interactions**:
    - University of Liverpool COVID interactions http://www.covid19druginteractions.org/

- UHN Immunodeficiency clinic drug interactions checker https://hivclinic.ca/wp-content/plugins/php/app.php

Tocilizumab

- Interleukin-6 (IL6) antibody approved for treatment of cytokine release syndrome associated with cellular therapy (CAR-T)
- COVID-19 dose to be determined; access not yet established.

Corticosteroid

- Do not routinely give systemic corticosteroid for treatment of viral pneumonias outside of clinical trials. https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected

II. Administration of Experimental COVID19 Therapies in Cases of Swallowing Difficulties

http://www.covid19-druginteractions.org/ "Administration in cases of swallowing difficulties"

https://hivclinic.ca/drug-information/additional-info/ "Information on crushing and liquid antiretroviral drug formulations"

III. Special Populations

- Solid organ transplant, stem cell transplant, and haematology-oncology
  - **Lopinavir/ritonavir: Use with caution due to MAJOR drug-drug interactions between lopinavir/ritonavir and many immunosuppressants, antimicrobials and cancer treatment**. Must be reviewed by a pharmacist before initiating lopinavir/ritonavir. **Therapeutic drug monitoring required,** with dose adjustment for many medications, including but not limited to calcineurine inhibitors.
    AVOID concomitant voriconazole due to high risk of voriconazole toxicity.

IV. Non-Antimicrobial Clinical Topics

- **Do ACE inhibitor and angiotensin receptor blocker worsen outcome? Current evidence does not support purported harmful effects in context of COVID pandemic:**

Clarifying statements on the effect of ACEI and ARB:

Hypertension Canada https://hypertension.ca/wp-content/uploads/2020/03/2020-30-15-Hypertension-Canada-Statement-on-COVID-19-ACEi-ARB.pdf
European Society of Cardiology https://www.escardio.org/Councils/Council-on-Hypertension-(CHT)/News/position-statement-of-the-esc-council-on-hypertension-on-ace-inhibitors-and-ang

International society of hypertension https://www.escardio.org/Councils/Council-on-Hypertension-(CHT)/News/position-statement-of-the-esc-council-on-hypertension-on-ace-inhibitors-and-ang

- **Does ibuprofen worsen outcome in COVID?**

Thus far, evidence supporting this claim is lacking. European Medicines Agency Statement: https://www.ema.europa.eu/en/documents/press-release/ema-gives-advice-use-non-steroidal-anti-inflammatories-covid-19_en.pdf

World Health Organization: https://twitter.com/WHO/status/1240409217997189128

V. Online Resources on COVID

SHS-UHN ASP website https://www.antimicrobialstewardship.com/covid-19
Lancet https://www.thelancet.com/coronavirus
JAMA https://jamanetwork.com/journals/jama/pages/coronavirus-alert#clinical-information
NEJM: https://www.nejm.org/coronavirus
CSHP COVID19 PSN – **Open-access** https://qid.io/COVID19PSN/home
University of Liverpool: http://www.covid19-druginteractions.org/
EMCrit Project https://emcrit.org/ibcc/COVID19/
ID Stewardship https://www.idstewardship.com/coronavirus-covid-19-resources-pharmacists/

VI. Overview of Experimental Agents

Drug	Dose (s)	Dosage form	Key Adverse Effects/ Monitoring	Comments
HYDROXYCHLOROQUINE (Prodrug of chloroquine) As of March 19, 2020, supply is limited in Canada.	**Various regimens** **400mg PO q12h day1, then 200mg PO q12h days 2 to 5** Dose optimization PK/PD study for SARS-CoV-2 https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa237/5801998 ** No dose adjustment for kidney or liver disease Take with food if GI intolerance Separate from antacids by ≥ 4 hours	Oral tablet 200 mg	**Most common:** Dizziness, headache, anorexia, nausea, vomiting, bloating, glucose abnormalities Most serious toxicities associated with long term use **Serious:** Retinopathy (dosage , LFT abnormalities, QT prolongation, hemolysis in G6PD deficient patients Package insert suggests G6PD testing prior to initiation but post-marketing studies suggest risk is low. **Pregnancy**: Associated with fetal ocular toxicity in animal studies but used safely during pregnancy for malaria **Breastfeeding:** Excreted into breast milk in low levels	**Proposed mechanisms:** 1. Interferes with glycosylation of cellular ACE2 receptor (COVID-19 uses ACE2 receptors to bind to target cells) 2. Impairs acidification of endosomes which is required for virus/cell fusion 3. Immunomodulatory effects https://www.nature.com/articles/s41422-020-0282-0
LOPINAVIR/RITONAVIR	400/100 mg PO q12h	Oral tablet 200/50 mg Caution on commercially available suspension: incompatible with polyurethane NG/NJ tubes due to propylene glycol & alcohol content; consider dissolving in a syringe at bedside	**Common:** Nausea, vomiting, diarrhea **Serious:** LFT elevations, pancreatitis, QT prolongation *****Major substrate and inhibitor of CYP450 enzymes – check drug interactions** http://www.covid19-druginteractions.org/ **Pregnancy:** Short-term use in HIV does not suggest major safety concerns. No evidence of teratogenicity in animals.	

Drug	Dose (s)	Dosage form	Key Adverse Effects/ Monitoring	Comments
		Exposure reduced ~ 50% with compounded suspension	**Breastfeeding:** Excreted into breast milk in low levels	
REMDESIVIR	200mg IV x 1 day 1, then 100mg IV q24h	IV only Vehicle contains SBECD which may accumulate in renal impairment	Elevated LFTs, hypotension during infusion Check drug interactions http://www.covid19-druginteractions.org/ Contraindicated in pregnancy and breastfeeding	Access through RCT or Special Access Compassionate Use: Gilead Global Portal https://rdvcu.gilead.com/ Note: inclusion/exclusion criteria change frequently – check website above Mechanism: Nucleotide analogue works by inhibiting RNA-dependent RNA polymerase inhibitor
TOCILIZUMAB	Dosing for COVID to be determined	IV only	Monitor closely for allergic reactions Drug-induced hepatotoxicity and GI perforation reported May increase risk of serious bacterial, mycobacterial, fungal, viral infections **Pregnancy:** Animal studies have shown increased risk of abortion and embryofetal death when administered during organogenesis but no teratogenicity. Low birth weight and neonatal asphyxia reported in women exposed during pregnancy **Breastfeeding:** Unknown if tocilizumab is excreted in breast milk	RCTs underway Mechanism: Recombinant humanized monoclonal antibody against IL-6. Approved for use in rheumatic disorders and for cytokine release syndrome following CAR-T therapy only.