Remdesivir

What is it?

- An antiviral that acts on SARS-CoV-2 and other RNA viruses by interrupting replication. Remdesivir is a nucleotide analogue prodrug that when converted to the active remdesivir triphosphate interacts with RNA polymerase to prevent the production of viral genetic material. Reduced viral replication may reduce burden of illness.

In July 2020 remdesivir was authorized for use by Health Canada under Notice of Compliance with Conditions: the manufacturer must provide ongoing information on the drug's efficacy and active monitoring of safety.

Health Canada Indications:	• Hospitalized adults and youth aged ≥ 12 years (≥40 kg) with severe COVID-19 with pneumonia requiring supplemental oxygen • Non-hospitalized adults with a positive COVID-19 test who are at high risk of progression to severe COVID-19

- **Evidence:** The World Health Organization-sponsored study SOLIDARITY[1] is the largest randomized controlled trial (RCT) to date investigating remdesivir for **adults hospitalized with COVID-19**. It was an open-label trial investigating multiple interventions across many centres across the world from March 2020 to January 2021. For the remdesivir comparison (n = 8275), patients were randomized to receive remdesivir 200 mg IV on day one then 100 mg IV daily on days 2 through 10 in addition to standard care, or standard care alone. Outcome data was subdivided according to patients' baseline oxygen requirements.

SOLIDARITY: key findings from remdesivir comparison

- **Reduced mortality in those on oxygen at baseline but not ventilated:**
  - Overall population: all-cause mortality 14.5% (602/4146) remdesivir recipients vs 15.6% (643/4129) standard care only; RR 0.91 (95% CI 0.82 - 1.02), p = 0.12.
    Mortality outcome subdivided by oxygen requirements at randomization:
    - Not on O2 (n = 1730): 2.9% (25/869) remdesivir vs 3.8% (33/861) standard care only; RR 0.76 (95% CI 0.46 – 1.28), p = 0.3
    - **On O2 but not ventilated (n = 5839): 14.6% (426/2918) remdesivir vs 16.3% (476/2921) standard care only; RR 0.87 (95% CI 0.76 - 0.99), p = 0.003**
    - Ventilated (n = 706): 42.1% (151/359) remdesivir vs 38.6% (134/347) standard care only; RR 1.13 (95% CI 0.89-1.42), p = 0.32
- **Reduced progression to ventilation for those on O2 at baseline (n = 5839):**
  - 17.0% (496/2918) remdesivir vs 18.9% (553/2921) standard care only; RR 0.87 (95% CI 0.76-0.99), no p-value reported

Earlier, smaller RCTs reported mixed efficacy results for remdesivir.[2-6]

The PINETREE RCT investigated a 3-day course of remdesivir for **ambulatory patients with early, symptomatic COVID-19** (positive PCR test within past 4 days and symptom onset within past 7 days) who were unvaccinated with high risk factors for disease progression. When compared to placebo, the remdesivir recipients had a lower rate of the composite of COVID-19-related hospitalizations and death by day 28 [0.7% vs 5.3% (HR 0.13, 95% CI 0.03-0.59)], p = 0.008.[7]

Infectious Diseases Society of America (IDSA): conditionally recommends remdesivir for patients hospitalized with severe COVID-19, i.e. those with $SpO_2 \leq 94\%$ on room air, with a preference for 5 days of treatment over 10 days. They recommend against use for patients on invasive mechanical ventilation or ECMO. For those with mild-to-moderate COVID-19 at high risk for progression to severe disease and within 7 days of symptom onset, three days of remdesivir is recommended over no remdesivir.[8]

World Health Organization (WHO): conditionally suggests treatment with remdesivir for three days for patients with non-severe COVID-19 at highest risk of hospitalization. The recommendation for use in severe or critical COVID-19 is under review.[9]

Practical Considerations **Once remdesivir is prepared into solution for IV infusion the product is stable for 4 hours only.**

Prepared by: COVID-19 Clinical Pharmacy Working Group
Last Update: Jan 2023. Contact: tasha.ramsey@nshealth.ca

References:

1. WHO Solidarity Trial Consortium. Remdesivir and three other drugs for hospitalised patients with COVID-19: final results of the WHO Solidarity randomised trial and updated meta-analyses. The Lancet. 2022 May 2.
2. Wang Y, Zhang D, Du G, Du R, Zhao J, Jin Y et al. Remdesivir in adults with severe COVID-19: a randomised double-blind, placebo-controlled, multicentre trial. Lancet 2020;395:1569-78.
3. ACTT-1 Study Group Members. Remdesivir for the Treatment of COVID-19 – Final Report. N Engl J Med. 2020;383(19):1813. Epub 2020 Oct 8. Available at https://pubmed.ncbi.nlm.nih.gov/32445440/
4. Beigel JH, Tomashek LE, Dodd, Mehta AK, Zingman BS, Kalil AC et al. Remdesivir for the treatment of Covid-19 – Final report. NEJM. 2020;383:1813-1826. DOI: 10.1056/NEJMoa2007764.
5. Spinner CD, Gottlieb RL, Criner GJ, Arribas López JR, Cattelan AM, Viladomiu AS et al. Effect of remdesivir vs standard care on clinical status at 11 days in patients with moderate COVID-19. JAMA. 2020;324(11):1048-1057.
6. Ali K, Azher T, Baqi M, Binnie A, et al. Remdesivir for the treatment of patients in hospital with COVID-19 in Canada: a randomized controlled trial. CMAJ. 2022 Jan 1. doi: 10.1503/cmaj.211698
7. Gottlieb RL, Vaca CE, Paredes R, et al. Early remdesivir to prevent progression to severe Covid-19 in outpatients. N Engl J Med. DOI: 10.1056/NEJMoa2116846
8. Bhimraj A, Morgan RL, Shumaker AH, et al. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19. Infectious Diseases Society of America 2021; Version 8.0.0. Available at https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/. Accessed 31 May 2022.
9. Siemieniuk RA, Bartoszko JJ, Ge L, Zeraatkar D, Izcovich A, Pardo-Hernandez H et al. Drug treatments for covid-19: living systematic review and network meta-analysis. BMJ. 2020;370 m2980. Accessed 18 Mar 2022.
10. World Health Organization. Therapeutics and COVID-19, Living Guideline. 3 March 2022. Available at: https://www.who.int/publications/i/item/therapeutics-and-covid-19-living-guideline. Accessed 18 Mar 2022.