SA Health

Remdesivir Drug Monograph

Version 3.0

Approval date: 12/04/22

Government of South Australia
SA Health

1. Remdesivir drug monograph

Remdesivir[1,4,13] **ID approval and patient consent (verbal or written) required** **For the most recent updates on the use of remdesivir in patients with COVID-19 infections visit the Remdesivir drug guideline available via the NSW Therapeutic Advisory Group**	
Drug Class	○ Antiviral, a nucleotide analogue prodrug that binds to the viral RNA-dependent RNA polymerase and inhibits viral replication through premature termination of RNA transcription.
Indications	• Second line treatment (when nirmatrelvir plus ritonavir is not suitable) of mild COVID-19 for non-pregnant adult patients who do not require supplemental oxygen and are within 7 days of symptom onset **AND** are immunosuppressed irrespective of vaccination status **OR** • are not vaccinated and age ≥ 65 years (≥ 50 years if Aboriginal and/or Torres Strait Islander) and two or more risk factors for progressing to severe illness • Treatment of breastfeeding or pregnant women in their second or third trimester within 7 days of symptom onset and do not require supplemental oxygen AND: • are Immunosuppressed irrespective of vaccine status **OR** • who have reduced immunity to COVID-19 e.g. not vaccinated or do not have an up-to-date vaccine status **AND** who have one or more risk factors for progressing to severe or critical illness.
Contra-indications	• Known hypersensitivity to any ingredient of remdesivir product or remdesivir metabolites. • Mechanical ventilation for >48 hours at the time of commencement • Renal impairment[1]: eGFR < 30mL/min/1.73m^2 (contact ID to discuss risk vs benefit) • Formulated with the excipient sulfobutyl betadex sodium (SBECD) which accumulates in renal impairment • For patients on dialysis please seek specialist advice as SBECD is cleared to varying degrees depending on the type of dialysis • Hepatic impairment: ALT ≥ 5 times the upper normal limit (ULN) at baseline • Patients with evidence of multiorgan failure, including coagulopathy (significant thrombocytopenia), hepatic failure, renal failure or significant cardiomyopathy are not eligible to access remdesivir from the National Medicines Stockpile

[1] NOTE: Dose adjustments are based on eGFR (CKD-EPI). For patients with extremes of body size, multiply the eGFR by the patient's body surface area (in m^2) and divide by 1.73 m^2

Precautions	• Factors where the benefit of remdesivir is uncertain & requires careful consideration before use:
	  ○ Presence of an intercurrent illness likely to lead to the patient's death within one year;
	  ○ Advanced age with limitations on activities of daily living;
	  ○ Need for more than a 5 day treatment course (not available via NMS)

Drug Interactions	• Drug-drug interaction trials of remdesivir and other concomitant medications have not been conducted in humans. Remdesivir is a substrate for several drug metabolising enzymes however clinical relevance of these interactions has not been established • Use with hydroxychloroquine or chloroquine is not recommended as it may result in reduced antiviral activity of remdesivir • For detailed information regarding drug interactions with remdesivir please check the University of Liverpool COVID-19 resource page

Preparation	• There are 2 preparations available in Australia via the NMS
	  ○ Powder for Injection
	  ▪ 100 mg sterile, preservative-free, white to off-white to yellow lyophilised powder vial.
	  ▪ Requires storage below 30°C.
	  ▪ Contains sulfobutyl betadex sodium (SBECD 3 g), hydrochloric acid & sodium hydroxide.
	  ○ Concentrated solution vial
	  ▪ 100 mg/20 mL concentrate solution (clear colourless to yellow) vial; sterile preservative-free.
	  ▪ Requires refrigerated storage at 2–8°C.
	  ▪ Stable for up to 12 hours at room temperature (20–25°C) prior to dilution.
	  ▪ Contains sulfobutyl betadex sodium (SBECD 6 g), hydrochloric acid & sodium hydroxide.
	  ▪ Concentrated solution not recommended in children < 12 years of age or adolescents weighing <40kg

Dose	• **Mild illness:** 200mg via intravenous infusion on day 1, then 100mg IV daily for a further 2 days (total 3 days treatment) • **Moderate to critical illness:** 200mg via intravenous infusion on day 1, then 100mg IV daily for a further 4 days (total 5 days treatment only per NMS)
Administration	• There are different formulations of remdesivir available via the National Medicines Stockpile and administration instructions may vary. • For administration details please refer either to the Australian Injectables Drugs Handbook and the NSW Therapeutic Advisory Group page on remdesivir.

Monitoring	• As experience with remdesivir at these doses and for this duration is limited patients should have appropriate clinical and laboratory monitoring including:
	  ○ Baseline and day 1 and 3 creatinine, electrolytes, urea, LFTs and complete blood exam
	  ▪ Discontinue remdesivir if:
	  • eGFR < 30mL/min/m^2 (contact ID to discuss risk vs benefit)
	  • ALT ≥ 5 times ULN during treatment with remdesivir (remdesivir may be restarted when ALT is < 5 times ULN) OR
	  • ALT elevation accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR.
	  ○ Perform baseline and DAILY coagulation profile testing, including prothrombin time
	  ○ Heart rate

	○ Observe for infusion-related reactions. If present, immediately discontinue
Adverse Effects	• As experience with remdesivir at these doses and for this duration is limited patients it is important to document and report all suspected adverse effects. To date the following adverse effects have been observed: ○ Very common (>10%): graded elevations in ALT, AST and bilirubin ○ Common (>1%): prolonged prothrombin time, gastrointestinal symptoms (e.g. nausea, vomiting, diarrhoea), headache, rash ○ Rare (<0.1%): hypersensitivity reactions (anaphylactic reactions are rare but are a medical emergency; stop the infusion and begin treatment immediately) • Infusion-related reactions may include hypotension, nausea, vomiting, diaphoresis, shivering • Post-marketing adverse effects reported include bradycardia (including severe bradycardia and sinus bradycardia), cardiac failure and hypotension • Suspected or confirmed adverse reactions should be reported via Safety Learning System and also via the Therapeutic Goods Administrations adverse effects online form: TGA adverse event reporting
Patient information and consent forms	• Remdesivir patient information leaflets are available via the NSW Therapeutic Advisory Group • Example patient consent forms can be found here

2. Definitions/acronyms/abbreviations

BMI	Body Mass Index
COPD	Chronic obstructive pulmonary disease
eGFR	estimated Glomerular Filtration Rate
GI	Gastrointestinal
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human Immunodeficiency Virus
ID	Infectious Diseases
IV	Intravenous
LFTs	Liver function tests
NMS	National Medical Stockpile
NYHA	New York Heart Association

2 Resources

- National COVID-19 Clinical Evidence Taskforce (The Australian Living Guidelines)
- COVID-19 Resources: NSW Therapeutic Advisory Group
- COVID–19 (SARS–COV–2) – Management Guide (CALHN–PRC05409)
- Anaphylaxis: Management Guidelines (CALHN-OWI04038)
- COVID-19: Disease-modifying therapy recommendations for hospitalised adults (CALHN-GDE05778)
- CALHN COVID–19 internet page
- World Health Organisation. Therapeutics and COVID-19: Living Guideline

- Australian Technical Advisory Group on Immunisation (ATAGI)
- Clinical Excellence Commission: Medication Safety Updates
- COVID-19 Treatment: Nirmatrelvir-Ritonavir (Paxlovid®) (IH-CIS05842)
- COVID-19 Resources: Medicines Use in the treatment of COVID-19 – Consent Forms

3 References

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5 Document Ownership

Clinical Guideline owner: CALHN Infectious Diseases via Office of the Chief Pharmacist

Title: COVID-19: Medication Management of Mild Illness in the Outpatient Setting Clinical Guideline

ISBN: 978-1-76083-509-5

Objective reference number:

Review date: April 2025

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6 Document History

Version	Date approved	Approved by	Amendment notes
3.0	12/04/22	CALHN Drug and Therapeutics Committee South Australian Medicines Advisory Committee	Monograph updated to align with updated COVID-19: Medication management of Mild Illness in the Outpatient Setting Guideline v3.0
2.0	18/02/22	CALHN Drug and Therapeutics Committee COVID-19 Medicines Advisory Group	Add molnupiravir and nirmatrelvir plus ritonavir. Added link on sotrovimab monograph for breastfeeding advice.
1.0	19/01/22	South Australian Medicines Advisory Committee	New guideline to provide a pathway for the medication management of mild COVID-19 illness in the outpatient setting.