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Approval Statement
We certify that the final electronic form of this material is in accordance with the regulations set forth by the health authority for the country of this document, and is a fair and truthful presentation of the facts about the product and the applicable Gilead standards.

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Remdesivir – Important Information

Remdesivir is not currently registered for use in New Zealand and is being provided to you under Section 29 of the Medicines Act 1981 for the treatment of patients with coronavirus disease 2019 (COVID-19). Gilead Sciences is the manufacturer of remdesivir, but in New Zealand Pharmacy Retailing NZ Ltd is the supplier and they should be consulted with regard to meeting your obligations under Section 29 of the Act.

Therapeutic Indications

Remdesivir is not currently registered for use in New Zealand. Usage of remdesivir should be solely in accordance with guidance provided by the NZ Department of Health and/or PHARMAC.

Formulations

Remdesivir 100mg **powder for injection**. A vial contains 100mg of remdesivir. After reconstitution, each vial contains 5mg/mL of remdesivir solution.

Dosage and Method of Administration

Use of remdesivir is confined to healthcare facilities in which patients can be monitored closely. Remdesivir is for single use in one patient only. Therecommended dosage of remdesivir in patients 12 years of age and older and weighing at least 40 kg is:

- Day 1 - a single loading dose of remdesivir 200 mg given by intravenous infusion
- Day 2 onwards - 100 mg given once-daily by intravenous infusion

The total duration of treatment should be at least 5 days and not more than 10 days.

For patients requiring invasive mechanical ventilation and/or ECMO, the suggested dose is a single loading dose of remdesivir 200 mg on Day 1, followedby once-daily maintenance doses of remdesivir 100 mg for 9 days.

For patients not requiring invasive mechanical ventilation and/or ECMO, the suggested dose is a single loading dose of remdesivir 200 mg on Day 1, followed by once-daily maintenance doses of remdesivir 100 mg for 4 days. If a patient does not demonstrate clinical improvement, treatment may beextended for up to 5 additional days (up to 10 days total).

Remdesivir is to be administered via intravenous infusion in a total volume of up to 250 mL 0.9% saline over 30 to 120 minutes.

Elderly:

No dose adjustment is required in patients over the age of 65 years.

Renal impairment:

The pharmacokinetics of remdesivir have not been evaluated in patients with renal impairment. Patients with eGFR greater than or equal to 30 mL perminute have received remdesivir for treatment of COVID-19 with no dose adjustment of remdesivir.

All patients must have an eGFR determined before dosing of remdesivir and while receiving remdesivir as clinically appropriate. Because the excipient sulfobutylether-β-cyclodextrin (SBECD) is renally cleared and accumulates in patients with decreased renal function, administration of drugs formulatedwith SBECD (such as remdesivir) is not recommended in patients with eGFR less than 30 mL per minute unless the potential benefit outweighs the potential risk.

In animal studies on rats and monkeys, severe renal toxicity was observed. The mechanism of this renal toxicity is not fully understood. A relevance forhumans cannot be excluded.

Hepatic impairment:

The pharmacokinetics of remdesivir have not been evaluated in patients with hepatic impairment. It is not known if dosage adjustment is appropriate inpatients with hepatic impairment.

Paediatric population:

The safety and efficacy of remdesivir in children under the age of 12 years and weighing <40 kg have not yet been established. No data are available.

Pregnancy category B2:

No adequate and well-controlled studies of remdesivir use in pregnant women have been conducted. Remdesivir should be used during pregnancy only ifthe potential benefit justifies the potential risk for the mother and the foetus. Women of child-bearing potential must use effective contraception during treatment.

Contraindications

Hypersensitivity to the active substance(s), sulfobutyl betadex sodium, hydrochloric acid, or sodium hydroxide.

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Adverse Effects

The most common adverse reaction in healthy volunteers is increased transaminases (14%). The most common adverse reaction in patients with COVID-19 is nausea (4%). Other common (≥1/100 to <1/10) adverse reactions include headache and rash.

Special Warnings and Precautions for Use

Hypersensitivity including infusion-related and anaphylactic reactions

Hypersensitivity reactions including infusion-related and anaphylactic reactions have been observed during and following administration of remdesivir. Signs and symptoms may include hypotension, hypertension, tachycardia, bradycardia, hypoxia, fever, dyspnea, wheezing, angioedema, rash, nausea, vomiting, diaphoresis, and shivering. Slower infusion rates, with a maximum infusion time of up to 120 minutes, can be considered to potentially prevent these signs and symptoms. If signs and symptoms of a clinically significant hypersensitivity reaction occur, immediately discontinue administration of remdesivir and initiate appropriate treatment.

Transaminase elevations:

Transaminase elevations have been observed in remdesivir clinical development program, including in healthy volunteers and patients with COVID-19. Hepatic laboratory testing should be performed in all patients prior to starting remdesivir and should be monitored while receiving remdesivir as clinically appropriate. No clinical studies with remdesivir have been conducted in patients with hepatic impairment. Remdesivir should only be used in patients with hepatic impairment if the potential benefit outweighs the potential risk.

- Remdesivir should not be initiated in patients with Alanine Aminotransferase (ALT) ≥5 times the upper limit of normal (ULN) at baseline
- Remdesivir should be discontinued in patients who develop:
    - ALT ≥5 times the ULN during treatment with remdesivir. Remdesivir may be restarted when ALT is <5 times the ULN **OR**
    - ALT elevation accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR

Risk of reduced antiviral activity when coadministered with chloroquine or hydroxychloroquine

Coadministration of remdesivir and chloroquine phosphate or hydroxychloroquine sulphate is **not** recommended based on in vitro data demonstrating an antagonistic effect of chloroquine on the intracellular metabolic activation and antiviral activity of remdesivir.

Interactions with Other Medicines and Other Forms of Interactions

Drug-drug interaction trials of remdesivir and other concomitant medications have not been conducted. The overall potential for interactions is currently unknown; patients should remain under close observation during the days of remdesivir administration. **Due to antagonism observed in vitro, concomitant use of remdesivir with chloroquine phosphate or hydroxychloroquine sulphate is not recommended.**

Effects of other medicinal products on remdesivir

In vitro, remdesivir is a substrate for esterases in plasma and tissue, drug metabolizing enzymes CYP2C8, CYP2D6, and CYP3A4, and is a substrate for Organic Anion Transporting Polypeptides 1B1 (OATP1B1) and P glycoprotein (P gp) transporters.

The potential of interaction of remdesivir with inhibitors/inducers of the hydrolytic pathway (esterase) or CYP2C8, 2D6 or 3A4 has not been studied. The risk of clinically relevant interaction is unknown. Strong inhibitors may result in increased remdesivir exposure. The use of strong inducers (e.g. rifampicin) may decrease plasma concentrations of remdesivir and is not recommended.

Dexamethasone is reported to be a moderate inducer of CYP3A and P-gp. Induction is dose-dependent and occurs after multiple doses. **Dexamethasone is unlikely to have a clinically significant effect on remdesivir as remdesivir has a moderate-high hepatic extraction ratio, and is used for a short duration in the treatment of COVID-19.**

Effects of remdesivir on other medicinal products

In vitro, remdesivir is an inhibitor of CYP3A4, OATP1B1 and OATP1B3. The clinical relevance of these in vitro drug interactions has not been established. Remdesivir may transiently increase plasma concentrations of medicinal products that are substrates of CYP3A or OATP 1B1/1B3. No data is available, however it can be suggested that medicinal products that are substrates of CYP3A4 or substrates of OATP 1B1/1B3 should be administered at least 2 hours after remdesivir. Remdesivir induced CYP1A2 and potentially CYP3A in vitro. Co-administration of remdesivir with CYP1A2 or CYP3A4 substrates with narrow therapeutic index may lead to loss of their efficacy.

Dexamethasone is a substrate of CYP3A4 and although remdesivir inhibits CYP3A4, due to remdesivir's rapid clearance after intravenous administration, remdesivir is unlikely to have a significant effect on dexamethasone exposure.

For an independent, online drug interaction resource for medicines used to treat COVID-19, please visit https://www.covid19-druginteractions.org/

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Remdesivir – 100mg Powder for Injection

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DESCRIPTION

Available as a sterile, preservative-free, white to off-white to yellow lyophilized powder that is to be reconstituted with 19 mL of Sterile Water for Injection and further diluted into 0.9% sodium chloride infusion bag prior to administration by intravenous infusion. Following reconstitution, each vial contains 100 mg/20 mL (5 mg/mL) of remdesivir concentrated solution.

STORAGE

Store remdesivir powder for injection, 100 mg, vials at **below 30°C** until required for use. The lyophilized powder must be reconstituted and diluted prior to use. Do not use after expiration date.

PREPARATION

1. Remove the required number of single-dose vial(s) from storage.
2. For each vial, aseptically reconstitute remdesivir lyophilized powder by addition of 19 mL of Sterile Water for Injection using a suitably sized syringe and needle per vial. Discard the vial if a vacuum does not pull the Sterile Water for Injection into the vial.
3. Immediately shake the vial for 30 seconds.
4. Allow the contents of the vial to settle for 2 to 3 minutes. A clear solution should result. If the contents of the vial are not completely dissolved, shake the vial again for 30 seconds and allow the contents to settle for 2 to 3 minutes. Repeat this procedure as necessary until the contents of the vial are completely dissolved.
5. Following reconstitution, each vial contains 100 mg/20 mL (5 mg/mL) of remdesivir solution. Inspect the vial to ensure the container closure is free from defects and the solution is free of particulate matter.
6. After reconstitution, the total storage time before administration should not exceed 4 hours at room temperature or 24 hours at refrigerated temperature (2°C to 8°C). Dilute immediately after reconstitution.

DILUTION

7. Withdraw and discard the required volume of 0.9% sodium chloride from the infusion bag using an appropriately sized syringe and needle per the table below. Care should be taken during admixture to prevent inadvertent microbial contamination.
8. Withdraw the required volume of reconstituted remdesivir powder for injection using an appropriately sized syringe per the table below. Discard any unused portion remaining in the remdesivir vial.
9. Transfer the required volume of reconstituted remdesivir powder for injection to the selected infusion bag.
10. Gently invert the bag 20 times to mix the solution in the bag. Do not shake.

Remdesivir dose	0.9% saline infusion bag volume to be used	Volume of saline to be withdrawn and discarded from 0.9% saline infusion bag	Required volume of remdesivir injection solution
200 mg (2 vials)	250 mL	40 mL	40 mL (2 x 20 mL)
	100 mL		
100 mg (1 vial)	250 mL	20 mL	20 mL
	100 mL		

Note: 100 mL should be reserved for patients with severe fluid restriction, e.g. with ARDS or renal failure.

Storage: The prepared diluted solution is stable for 4 hours at room temperature (20°C to 25°C) or 24 hours in the refrigerator at 2°C to 8°C.

ADMINISTRATION

Administer the diluted solution via intravenous infusion over 30 to 120 minutes. After infusion is complete, flush with at least 30 mL of 0.9% saline.

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Remdesivir – Frequently Asked Questions

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What is allowed under Medicines Act 1981?

The Medicines Act 1981 permits an authorised prescriber to prescribe, administer or arrange for the administration of medicines for the treatment of a patient in his or her care. The medicine and its use may or may not be approved.

What are my responsibilities as the treating medical practictioner?

Gilead is supplying remdesivir on an as-is basis to support the unmet need and is provided on the condition that all treatment decisions will be under the responsibility of the treating medical practictioner. The medical practitioner is solely responsible and liable for the decision to prescribe to a relevant patient and the usual ethics approvals consistent with customary professional medical practices and applicable laws and regulations.

Is remdesivir compatible with other IV medications? What other diluents can be used?

The prepared diluted solution should not be administered simultaneously with any other medication. The compatibility of remdesivir injection with IV solutions and medications other than 0.9% saline is not known. Remdesivir powder for injection must be reconstituted with Sterile Water for Injection and diluted in 0.9% saline.

What should be done with any unused remdesivir?

Maintain adequate records showing receipt, use, and disposition of remdesivir for its intended purpose. Do not reuse or save unused remdesivir injection solution, or diluted solution for infusion for future use. This product contains no preservative. For unused intact vials, maintain adequate records showing disposition of remdesivir; do not discard unused intact vials.

What do I do if there is a product recall?

Healthcare providers and/or their designee are responsible for traceability, compliance with known storage requirements and to cooperate with Gilead if there is a product quality complaint or a product recall.

Can I disclose or publish data about remdesivir?

Gilead is the owner of all intellectual property rights in remdesivir and related clinical information provided by Gilead. All non-public remdesivir clinical information provided to healthcare practitioners pursuant to the emergency exemption is provided by Gilead on a confidential basis. Healthcare practitioners receiving remdesivir must maintain confidentiality and may only use and disclose Gilead's confidential information strictly for the purpose of treating patients. Any public statement or publication about remdesivir requires Gilead's advance written approval.

Can I resell or export remdesivir?

Gilead supplied remdesivir to support unmet patient need in New Zealand and stock must not be resold, promoted or advertised within New Zealand or outside of New Zealand.

How do I report adverse events for patients on remdesivir?

Healthcare providers and/or their designee are responsible for mandatory reporting of adverse events, adverse reactions, and any specific situation reports occurring during remdesivir treatment.

Please submit using the **provided reporting form** in the event that any of the following occurs in relation to remdesivir:

- Adverse Events, Adverse Reactions, Serious Adverse Events, Serious Adverse Reactions, Special Situation Reports (these include, but are not limited to, off-label use, overdose, misuse, abuse, or medication errors)

Please submit via email to Gilead Sciences Pharmacovigilance within 1 working day of becoming aware of such reports: au.nz.safety@gilead.com

Gilead may request additional information related to the use of remdesivir. Gilead will retain all safety information provided under this agreement for as long as required to meet regulatory obligations related to remdesivir.

Healthcare professionals are urged to report suspected ADRs directly to the Centre for Adverse Reactions Monitoring (CARM) within the New Zealand Pharmacovigilance Centre (NZPhvC) using the following options:

- Online reporting or using electronic forms at https://nzphvc.otago.ac.nz/report/
- The electronic adverse reaction reporting tool available in Practice Management Software programmes
- Freepost Yellow Cards available from the address below, and also found in the MIMS New Ethicals and inside the back cover of the Prescriber Update.
- CARM is available to discuss ADRs by telephone and also accepts reports by email or fax. Outside office hours a telephone-answering machine will take messages
- An iPhone/iPad iOS application is also available for download via the NZPhvC website https://nzphvc.otago.ac.nz/app

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Where can I obtain additional information about remdesivir?

Please contact the Medical Affairs Department at Gilead Sciences Australia & New Zealand:

- Dr Paul Slade – Senior Director, Medical Affairs Mobile: +61 452 241 653 Email: paul.slade@gilead.com
- Medical Information Phone: 0800 443 933 Email: au.nz.medinfo@gilead.com

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Report as soon as possible to AU.NZ.Safety@Gilead.com

STUDY NUMBER	COUNTRY	REPORTER NO. (if applicable)	PATIENT NO. (if applicable)

☐ **INITIAL REPORT DATE:** ☐ **FOLLOW-UP #1 DATE:** **# 2 DATE:** **# 3 DATE:**

1. PATIENT INFORMATION

Birth Year: _____ (YYYY) **Sex:** ☐ Male ☐ Female **Race:** ☐ Caucasian ☐ Of African descent ☐ Asian ☐ Hispanic ☐ Other – Specify: _____

Weight: _____ ☐ lb ☐ kg **Height:** _____ ☐ in ☐ cm

2. ADVERSE EVENT

Event Term	Start Date (DD/MMM/YYYY) / Stop Date (DD/MMM/YYYY)	Outcome	Seriousness Criteria (Check all of the following that apply for this event)	Event Related to (check all that apply)	Alternative Causality (check all that apply)
		☐ Continuing ☐ Resolved ☐ Resolved w/sequelae ☐ Fatal ☐ Unknown	☐ Death ☐ Life-Threatening *(Immediate Risk Of Death)* ☐ Required Hospitalization/ Prolonged Hospitalization ☐ Significant Disability/Incapacity ☐ Congenital Anomaly/Birth Defect ☐ Medically Significant ☐ None of the Above	**Suspect Drug(s)** ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No	☐ Study Disease-related ☐ Pre-existing Condition ☐ Concomitant Medication: _____ ☐ Intercurrent Illness: _____ ☐ Other: _____ ☐ Study Procedure
Event Term	**Start Date** (DD/MMM/YYYY) / **Stop Date** (DD/MMM/YYYY)	**Outcome**	**Seriousness Criteria** (Check all of the following that apply for this event)	**Event Related to** (check all that apply)	**Alternative Causality** (check all that apply)
		☐ Continuing ☐ Resolved ☐ Resolved w/sequelae ☐ Fatal ☐ Unknown	☐ Death ☐ Life-Threatening *(Immediate Risk Of Death)* ☐ Required Hospitalization/ Prolonged Hospitalization ☐ Significant Disability/Incapacity ☐ Congenital Anomaly/Birth Defect ☐ Medically Significant ☐ None of the Above	**Suspect Drug(s)** ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No	☐ Study Disease-related ☐ Pre-existing Condition ☐ Concomitant Medication: _____ ☐ Intercurrent Illness: _____ ☐ Other: _____ ☐ Study Procedure
Event Term	**Start Date** (DD/MMM/YYYY) / **Stop Date** (DD/MMM/YYYY)	**Outcome**	**Seriousness Criteria** (Check all of the following that apply for this event)	**Event Related to** (check all that apply)	**Alternative Causality** (check all that apply)
		☐ Continuing ☐ Resolved ☐ Resolved w/sequelae ☐ Fatal ☐ Unknown	☐ Death ☐ Life-Threatening *(Immediate Risk Of Death)* ☐ Required Hospitalization/ Prolonged Hospitalization ☐ Significant Disability/Incapacity ☐ Congenital Anomaly/Birth Defect ☐ Medically Significant ☐ None of the Above	**Suspect Drug(s)** ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No	☐ Study Disease-related ☐ Pre-existing Condition ☐ Concomitant Medication: _____ ☐ Intercurrent Illness: _____ ☐ Other: _____ ☐ Study Procedure

If Patient died, please provide:

Date of Death: _____ / _____ / _____ (DD/MMM/YYYY)

Autopsy performed? ☐ Yes *(Attach copy)* ☐ No

If Patient required hospital admission or prolongation of an existing hospitalization, please provide:

Admission Date : _____ / _____ / _____ (DD/MMM/YYYY)

Discharge Date : _____ / _____ / _____ (DD/MMM/YYYY)

GILEAD

3. Medical History

Relevant Medical History: ☐ None ☐ Yes, provide details:

Drug Allergies: ☐ None ☐ Yes, provide details:

Has the patient participated in any previous Gilead Study?
☐ No
☐ Yes, Study No. if applicable:

4. Event Description

Describe signs and symptoms, possible causes, progression, treatments, etc. Did the event abate after suspect drug was stopped; did the event recur after suspect drug was restarted?

5. Suspect Drug(s)

Drug	Dose	Route	Frequency	Start Date (DD/MMM/YYYY)	Stop Date (DD/MMM/YYYY)	Action Taken due to Event	Blinded? (If applicable)
						☐ None ☐ Dose Reduced ☐ Dose Interrupted ☐ Permanently Discontinued	☐ No ☐ Yes
Drug	**Dose**	**Route**	**Frequency**	**Start Date** (DD/MMM/YYYY)	**Stop Date** (DD/MMM/YYYY)	**Action Taken due to Event**	**Blinded?** (If applicable)
						☐ None ☐ Dose Reduced ☐ Dose Interrupted ☐ Permanently Discontinued	☐ No ☐ Yes
Drug	**Dose**	**Route**	**Frequency**	**Start Date** (DD/MMM/YYYY)	**Stop Date** (DD/MMM/YYYY)	**Action Taken due to Event**	**Blinded?** (If applicable)
						☐ None ☐ Dose Reduced ☐ Dose Interrupted ☐ Permanently Discontinued	☐ No ☐ Yes
Drug	**Dose**	**Route**	**Frequency**	**Start Date** (DD/MMM/YYYY)	**Stop Date** (DD/MMM/YYYY)	**Action Taken due to Event**	**Blinded?** (If applicable)
						☐ None ☐ Dose Reduced ☐ Dose Interrupted ☐ Permanently Discontinued	☐ No ☐ Yes
Drug	**Dose**	**Route**	**Frequency**	**Start Date** (DD/MMM/YYYY)	**Stop Date** (DD/MMM/YYYY)	**Action Taken due to Event**	**Blinded?** (If applicable)
						☐ None ☐ Dose Reduced ☐ Dose Interrupted ☐ Permanently Discontinued	☐ No ☐ Yes

• 6. Concomitant Medications

☐ Check if no concomitant medications were being taken ☐ Attached

Drug (Exclude those used to treat the event)	Start Date (DD/MMM/YYYY)	Stop Date (DD/MMM/YYYY)	Continuing	Indication
			☐	
			☐	

			☐	
			☐	
			☐	
			☐	
			☐	

7. RELEVANT LABORATORY DATA: ☐ Check if none ☐ Attached

Test	Normal range (Units)	Date (DD/MMM/YYYY)	Result	Date (DD/MMM/YYYY)	Result	Date (DD/MMM/YYYY)	Result

8. RELEVANT DIAGNOSTIC PROCEDURES: ☐ Check if none ☐ Attached

Procedure	Date (DD/MMM/YYYY)	Result

9. REPORTER INFORMATION AND SIGNATURE

Reporter Name: _____	Title: _____	
Address: _____	Telephone No. _____	_____ **Signature** of Reporter
	Facsimile No.: _____	_____ **Date** (DD/MMM/YYYY)
	E-Mail: _____	

Please be aware that information provided to Gilead relating to you, may be used to comply with applicable laws and regulations. Gilead processes your personal or sensitive data in accordance with applicable data protection laws and the Gilead Privacy Statement, available to you either on www.gilead.com/privacy or upon request.