Ninavir™

Remdesivir lyophilized powder for IV infusion

PRESENTATION

Ninavir™ 100 IV Infusion: Each vial contains Remdesivir INN 100 mg as lyophilized powder.

DESCRIPTION

Remdesivir is a prodrug of a modified adenine nucleoside analog. Remdesivir undergoes efficient metabolic conversion in cells and tissues to active nucleoside triphosphate metabolite that inhibits viral RNA polymerases. Remdesivir is highly selective for viral polymerases and is therefore expected to have a low propensity to cause human toxicity. Remdesivir has wide therapeutic index in a human airway epithelial cell model. It also displays a high genetic barrier to resistance in different viruses and has a long intracellular half-life.

AUTHORIZED USE

Emergency use of Remdesivir for the treatment of suspected or laboratory confirmed Corona Virus Disease 2019 (Covid-19). Severe disease is defined as patients with an oxygen saturation (SpO2) ≤94% on room air or requiring supplemental oxygen or requiring mechanical ventilation or requiring extracorporeal membrane oxygenation (ECMO). Specifically, Remdesivir is only authorized for hospitalized adult and pediatric patients for whom use of an intravenous agent is clinically appropriate.

DOSAGE AND ADMINISTRATION

General Information

• Adult and pediatric patients (>28 days old) must have an eGFR determined and full-term neonates (≥7 days to ≤28 days old) must have serum creatinine determined before dosing of Remdesivir.

• Hepatic laboratory testing should be performed in all patients prior to starting Remdesivir and daily while receiving Remdesivir.

• Remdesivir should be administered via intravenous (IV) infusion only. Do not administer as an intramuscular (IM) injection.

Adult Patients

• The recommended dosage in adults requiring invasive mechanical ventilation and/or ECMO is a single loading dose of Remdesivir 200 mg on Day 1 followed by once-daily maintenance doses of Remdesivir 100 mg for 9 days.

• The recommended dosage in adults not requiring invasive mechanical ventilation and/or ECMO is a single 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 be extended for up to 5 additional days (i.e., up to a total of 10 days).

• 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.

Pediatric Patients

The recommended pediatric dose for pediatric patients weighing between 3.5 kg and <40 kg should be calculated using the mg/kg dose according to the patient's weight.

• For pediatric patients with body weight between 3.5 kg and <40 kg, use Remdesivir for injection, 100 mg, lyophilized powder only. Administer a body weight-based dosing regimen of one loading dose of Remdesivir 5 mg/kg IV (infused over 30 to 120 min) on Day 1 followed by Remdesivir 2.5 mg/kg IV (infused over 30 to 120 min) once daily for 9 days (for pediatric patients requiring invasive mechanical ventilation and/or ECMO, days 2 through 10) or for 4 days (for pediatric patients not requiring invasive mechanical ventilation and/or ECMO, days 2 through 5). If a patient does not demonstrate clinical improvement, treatment may be extended for up to 5 additional days (i.e., up to a total of 10 days).

• For pediatric patients with body weight ≥40 kg requiring invasive mechanical ventilation and/or ECMO, the adult dosage regimen of one loading dose of Remdesivir 200 mg IV (infused over 30 to 120 minutes) on Day 1 followed by Remdesivir 100 mg IV (infused over 30 to 120 minutes) once daily for 9 days will be administered.

• For pediatric patients with body weight ≥40 kg not requiring invasive mechanical ventilation and/or ECMO, the adult dosage regimen of one loading dose of Remdesivir 200 mg IV (infused over 30 to 120 minutes) on Day 1 followed by Remdesivir 100 mg IV (infused over 30 to 120 minutes) once daily for 4 days (days 2 through 5) will be administered. If a patient does not demonstrate clinical improvement, treatment may be extended for up to 5 additional days (i.e., up to a total of 10 days).

Reconstitution Instructions

• 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.

• Immediately shake the vial for 30 seconds.

• 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.

• Following reconstitution, each vial contains 100 mg/20 mL (5 mg/mL) of Remdesivir solution.

• Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

• 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).

Dilution Instructions

• Care should be taken during admixture to prevent inadvertent microbial contamination. By using the table below, please determine the volume of 0.9% saline to withdraw from the infusion bottle. It is always recommended to administer IV medication immediately after preparation when possible.

Recommended Dilution Instructions—Remdesivir for Injection Lyophilized Powder in Adults and Pediatric Patients Weighing ≥40 kg

Remdesivir dose	0.9% saline infusion bottle volume to be used	Volume of saline to be withdrawn and discarded from 0.9% saline infusion	Required volume of reconstituted Remdesivir for injection
200 mg (2 vials)	250 mL	40 mL	2 X 20 mL
	100 mL	40 mL	2 X 20 mL
100 mg (1 vial)	250 mL	20 mL	20 mL
	100 mL	20 mL	20 mL

• Please withdraw the required volume of saline from the bottle using an appropriately sized syringe and needle. Discard the saline that was withdrawn from the bottle.
• Please withdraw the required volume of reconstituted Remdesivir for injection from the Remdesivir vial using an appropriately sized syringe per above table.
• Please discard any unused portion remaining in the Remdesivir vial.
• Please transfer the required volume of reconstituted Remdesivir for injection to the selected infusion bottle.
• Gently invert the bottle 20 times to mix the solution. Please do not shake.

Administration Instructions

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 saline is not known.

Please administer the diluted solution with the infusion rate described in the below table.

Recommended Rate of Infusion-Diluted Remdesivir for Injection Lyophilized Powder in Adults and Pediatric Patients Weighing ≥40 kg

Infusion bottle volume	Infusion time	Rate of infusion
250 mL	30 min	8.33 mL/min
	60 min	4.17 mL/min
	120 min	2.08 mL/min
100 mL	30 min	3.33 mL/min
	60 min	1.67 mL/min
	120 min	0.83 mL/min

CONTRAINDICATIONS

Remdesivir is contraindicated in patients with known hypersensitivity to any ingredient of Remdesivir.

SERIOUS SIDE EFFECTS

An adverse reaction associated with Remdesivir in clinical trials in healthy adult subjects was increased liver transaminases.

PRECAUTIONS AND WARNINGS

There are limited clinical data available for Remdesivir. Serious and unexpected adverse events may occur that have not been previously reported with Remdesivir use.

USE IN PREGNANCY AND LACTATION

No adequate and well-controlled studies of Remedesivir use in pregnant women have been conducted. Remdesivir should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus.

There is no information regarding the presence of Remdesivir in human milk, the effects on the breastfed infant, or the effects on milk production. Because of the potential for viral transmission to SARS-CoV-2-negative infants and adverse reactions from the drug in breastfeeding infants, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Remdesivir and any potential adverse effects on the breastfed child from Remdesivir or from the underlying maternal condition.

STORAGE AND HANDLING

Keep away from light and out of the reach of children. Please do not reuse or save unused Remdesivir lyophilized powder, injection solution, or diluted solution for infusion for future use. This product contains no preservative.

Lyophilized Powder

• Please store Remdesivir for injection, 100 mg, vials below 30°C until required for use. Do not use after expiration date.
• After reconstitution, vials can be stored up to 4 hours at room temperature (20°C to 25°C) prior to administration or 24 hours at refrigerated temperature (2°C to 8°C). Please dilute within the same day as administration.

Diluted Solution for Infusion

Please store diluted Remdesivir solution for infusion up to 4 hours at room temperature (20°C to 25°C) or 24 hours at refrigerated temperature (2°C to 8°C).

COMMERCIAL PACK

Ninavir™ 100 IV Infusion: Each pack contains one blister of 1 vial of lyophilized powder of Remdesivir INN 100 mg & 2 ampoules of 10 ml Water for Injection (WFI), 1 bottle of 250 ml normal saline with hanger, one 20 ml syringe and one infusion set.

Manufactured by
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