Remivir™

Remdesivir Lyophilized Powder for IV Injection

DESCRIPTION

Remivir™ is a preparation of Remdesivir. It is an adenosine nucleotide prodrug that distributes into cells where it is metabolized to form the pharmacologically active nucleoside triphosphate metabolite. Metabolism of Remdesivir to Remdesivir triphosphate has been demonstrated in multiple cell types. Remdesivir triphosphate acts as an analog of adenosine triphosphate (ATP) and competes with the natural ATP substrate for incorporation into nascent RNA chains by the SARS-CoV-2 RNA-dependent RNA polymerase, which results in delayed chain termination during replication of the viral RNA. Remdesivir triphosphate is a weak inhibitor of mammalian DNA and RNA polymerases with low potential for mitochondrial toxicity.

AUTHORIZED USE

Emergency use of remdesivir for 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 bag/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 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 sterile saline from the bag/bottle using an appropriately sized syringe and needle. Discard the saline that was withdrawn from the bag/bottle.
• Please withdraw the required volume of reconstituted Remdesivir for injection from the Remdesivir vial using an appropriately sized syringe as 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 bag/bottle.
• Gently invert the bag/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 bag 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 Remdesivir.

SERIOUS SIDE EFFECTS

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

PRECAUTION AND WARNING

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 Remdesivir 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

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 at or below 25°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).

PHARMACEUTICAL PRECAUTION

Keep away from light and wet place. Store at or below 25°C temperature. Keep out of reach of children.

PACKAGING

Remivir™ 100 Lyophilized Powder for Injection: Box containing one vial of Remdesivir INN 100 mg Lyophilized powder for solution for infusion.

SK+F
Manufactured by
ESKAYEF PHARMACEUTICALS LTD.
TONGI, GAZIPUR, BANGLADESH
TM TRADEMARK
PM07302 V03