Remdesivir (All Populations Monograph)

Indications/Dosage

Off-Label, Recommended

- coronavirus disease 2019 (COVID-19) †
- severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection †

† Off-label indication

This drug may also have activity against the following microorganisms:

severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

NOTE: Some organisms may not have been adequately studied during clinical trials; therefore, exclusion from this list does not necessarily negate the drug's activity against the organism.

INVESTIGATIONAL USE: For the treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection †, the virus that causes coronavirus disease 2019 (COVID-19) †

Intravenous dosage

- Adults
  
  200 mg IV on day 1 then 100 mg IV once daily for 4 to 9 days is being evaluated in multi-center randomized trials. [65128] [65129] [65130] [65131] [65132] [65133]

- Infants, Children, and Adolescents
  
  Efficacy in pediatric patients and optimal dosing are not established. A dosing regimen of 5 mg/kg/dose IV once daily (Max: 200 mg) on day 1, followed by 2.5 mg/kg/dose IV once daily (Max: 100 mg) was used in 41 pediatric patients (including 2 neonates) who received remdesivir in a phase 3 Ebola study. [65123] [65164] [65166] Optimal duration of therapy for COVID-19 is unknown; a 5- to 10- day course is being studied in adult patients. [65123] [65131]
Maximum Dosage Limits

- **Adults**
  
  Safety and efficacy have not been established; however, investigational doses of 200 mg IV on day 1, followed by 100 mg IV once daily have been used.

- **Geriatric**
  
  Safety and efficacy have not been established; however, investigational doses of 200 mg IV on day 1, followed by 100 mg IV once daily have been used.

- **Adolescents**
  
  Safety and efficacy have not been established; however, investigational doses of 5 mg/kg/dose (Max: 200 mg) IV on day 1, followed by 2.5 mg/kg/dose IV once daily (Max: 100 mg) have been used.

- **Children**
  
  Safety and efficacy have not been established; however, investigational doses of 5 mg/kg/dose (Max: 200 mg) IV on day 1, followed by 2.5 mg/kg/dose IV once daily (Max: 100 mg) have been used.

- **Infants**
  
  Safety and efficacy have not been established; however, investigational doses of 5 mg/kg/dose IV on day 1, followed by 2.5 mg/kg/dose IV once daily have been used.

- **Neonates**
  
  Safety and efficacy have not been established.

Patients with Hepatic Impairment Dosing

Specific guidelines for dosage adjustments in hepatic impairment are not available.

Patients with Renal Impairment Dosing

Specific guidelines for dosage adjustments in renal impairment are not available.

† Off-label indication

Revision Date: 03/24/2020 05:13:43 PM

References
Remdesivir is an investigational antiviral medication with a broad spectrum of in vitro activity against RNA viruses belonging to Filoviridae, Paramyxoviridae, Pneumoviridae, and Orthocoronavirinae families. Although not FDA approved, the drug has been made available through the Expanded Access or Compassionate Use programs for the treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19). Requests for the drug must be submitted to the drug manufacturer (Gilead Science, Inc.) by the treating physician [65134][65156][65161]
Classifications

Revision Date: 03/25/2020 02:09:09 PM

References


Mechanism of Action

Remdesivir is a monophosphoramidate prodrug of remdesivir-triphosphate (RDV-TP), an adenosine analog that acts as an inhibitor of RNA-dependent RNA polymerases (RdRps). Remdesivir-TP competes with adenosine-triphosphate for incorporation into nascent viral RNA chains. Once incorporated into the viral RNA at position i, RDV-TP terminates RNA synthesis at position i+3. Because RDV-TP does not cause immediate chain termination (i.e., 3 additional nucleotides are incorporated after RDV-TP), the drug appears to evade proofreading by viral exoribonuclease (an enzyme thought to excise nucleotide analog inhibitors). Remdesivir has a broad spectrum of in vitro antiviral activity against RNA viruses, including viruses belonging to Filoviridae, Paramyxoviridae, Pneumoviridae, and Orthocoronavirinae families. [65120][65133][65134][65135][65136][65137][65156][65161]

Revision Date: 03/25/2020 11:13:15 AM

References


65135 – Agostini ML, Andres EL, Sims AC, et al. Coronavirus susceptibility to the antiviral remdesivir (GS-5734) is mediated by the viral polymerase and the proofreading exoribonuclease. mBIO 2018;9:e00221-18.
Pharmacokinetics

Remdesivir is administered intravenously.

Pharmacokinetic data in humans are not available; however, the distribution and metabolism of remdesivir have been examined in nonhuman primates. Following administration of a 10 mg/kg intravenous dose to rhesus monkeys, the parent drug demonstrated a short plasma half-life (0.39 hours), which was followed by transient concentrations of an intracellular intermediate alanine metabolite and more persistent concentrations of a nucleoside monophosphate (Nuc). Remdesivir rapidly distributed into peripheral blood mononuclear cells (PBMCs), where it was converted to remdesivir-triphosphate (RDV-TP), the pharmacologically active metabolite. In PBMCs, RDV-TP had a half-life of 14 hours and maintained concentrations required for greater than 50% virus inhibition for 24 hours. To evaluate the distribution of remdesivir, cynomolgus monkeys were administered a single 10 mg/kg intravenous dose of $[^{14}C]$remdesivir. Within 4 hours of administration, the drug was found to distribute into the testes, epididymis, eyes, and brain. Compared with the other tissues, concentrations in the brain were relatively low; however, they remained detectable above the drug plasma level for 168 hours post-dose. These data suggest once-daily dosing provides prolonged intracellular RDV-TP concentrations in potential sanctuary sites.[65161]

References


Pregnancy/Breast-feeding

Pregnancy

There are no data regarding the use of remdesivir during pregnancy to determine the drug-associated risk for major birth defects, miscarriages, or adverse maternal or fetal outcomes. Administer during pregnancy only if the potential benefits to the mother justify the potential risks to the fetus.
Breast-Feeding

There are no data regarding the use of remdesivir during breast-feeding. It is unknown whether or not the drug is excreted into human breast milk. Consider the benefits of breast-feeding, the risk of potential infant drug exposure, and the risk of an untreated or inadequately treated condition. If a breast-feeding infant experiences an adverse effect related to a maternally administered drug, health care providers are encouraged to report the adverse effect to the FDA.

Revision Date: 03/26/2020 09:56:01 AM

US Drug Names

Global Drug names

Copyright © 2017 Elsevier Inc. All rights reserved.