Remdesivir (Lexi-Drugs)

Special Alerts

▼ Remdesivir COVID-19 Emergency Use Authorization Expanded August 2020

FDA expanded the May 2020 emergency use authorization for remdesivir to include all hospitalized adult and pediatric patients with suspected or laboratory-confirmed COVID-19, irrespective of disease severity. The emergency use authorization allows for remdesivir to be distributed in the United States and administered intravenously (IV) by health care providers, as appropriate, to treat adults and children requiring hospitalization for suspected or laboratory-confirmed COVID-19, and for whom use of an IV agent is clinically appropriate.

Fact sheet for health care providers: https://www.fda.gov/media/137566/download

Fact sheet for patients and parents/caregivers: https://www.fda.gov/media/137565/download

Further information may be found at:

FDA: https://www.fda.gov/news-events/press-announcements/covid-19-update-fda-broadens-emergency-use-authorization-veklury-remdesivir-include-all-hospitalized

▼ Remdesivir: Concomitant Use With Chloroquine or HydroxychloroquineJune 2020

The FDA is warning health care providers that co-administration of remdesivir and chloroquine phosphate or hydroxychloroquine sulfate is not recommended as it may result in reduced antiviral activity of remdesivir. Health care providers should review the most up-to-date fact sheet when prescribing remdesivir.

Further information may be found at https://www.fda.gov/safety/medical-product-safety-information/remdesivir-gilead-sciences-fda-warns-newly-discovered-potential-drug-interaction-may-reduce.

Fact sheet for health care providers: https://www.fda.gov/media/137566/download

Fact sheet for patients and parents/caregivers: https://www.fda.gov/media/137565/download

▼ COVID-19 Important UpdatesMarch 2020

At this time, while there are a number of medicines being investigated for treatment and/or prevention of COVID-19, optimal therapy has not been established. We continue to monitor developments and synthesize content based on expert clinical experience and published literature and guidelines from major health organizations. Our UpToDate and Lexicomp infectious disease / critical care teams are continuously reviewing and updating our content for clinicians during this crisis.

Further information may be found at:

FDA: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-continues-facilitate-development-treatments

CDC: https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html

NIH National Library of Medicine: Clinicaltrials.gov<u>https://clinicaltrials.gov/ct2/results?cond=Covid-19&term=&cntry=&state=&city=&dist=</u>

Pronunciation

Vm

Р

(rem DE si vir)

Brand Names: Canada

Veklury

Pharmacologic Category

Antiviral Agent

Dosing: Adult

Note: Remdesivir is currently under investigation for use in the treatment of coronavirus disease 2019 (COVID-19) (see <u>ClinicalTrials.gov</u>). Limited drug-drug interaction data are available. Minimize any unnecessary comedication whenever possible given lack of information about interaction risk.

Coronavirus disease 2019 (COVID-19), severe (hospitalized patients): IV: 200 mg as a single dose on day 1, followed by 100 mg once daily (Beigel 2020). Recommended total duration in patients **not** requiring mechanical ventilation/extracorporeal membrane oxygenation (ECMO) is 5 days or until hospital discharge, whichever is first (FDA 2020a; Goldman 2020; NIH 2020); may extend for up to 5 additional days in patients who do not demonstrate clinical improvement. Patients requiring invasive mechanical ventilation/ECMO should receive a total of 10 days of treatment (FDA 2020a). **Note:** Severe disease is defined as SpO₂ ≤94% on ambient air, requiring supplemental oxygen, mechanical ventilation, or ECMO. Because supplies may be limited, National Institutes of Health guidelines recommend prioritizing remdesivir use based on oxygen requirements and mode of oxygen delivery; refer to https://www.covid19treatmentguidelines.nih.gov for more information (NIH 2020).

Dosage adjustment for concomitant therapy: Significant drug interactions exist, requiring dose/frequency adjustment or avoidance. Consult drug interactions database for more information.

* See <u>Dosage and Administration in AHFS Essentials</u> for additional information.

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment: Adult

The renal dosing recommendations are based upon the best available evidence and clinical expertise. Senior Editorial Team: Bruce Mueller, PharmD, FCCP, FASN, FNKF; Jason Roberts, PhD, BPharm (Hons), B App Sc, FSHP, FISAC; Michael Heung, MD, MS.

Note: The remdesivir formulation contains the excipient sulfobutylether-beta-cyclodextrin (SBECD), which accumulates in patients with kidney dysfunction, although the clinical significance of this accumulation is not certain (Luke 2010; Hoover 2018). SBECD is dialyzable (46% removed by an ~4-hour dialysis session) (Luke 2012).

eGFR ≥30 mL/minute: No dosage adjustment necessary (FDA 2020a).

eGFR <30 mL/minute: Use not recommended unless potential benefit outweighs potential risk (FDA 2020a). No safety or pharmacokinetic data are available for patients with kidney impairment or who are receiving renal replacement therapies (Barlow 2020).

Dosing: Hepatic Impairment: Adult

Baseline hepatic impairment: There are no dosage adjustments provided (has not been studied); not recommended to be used in patients with baseline ALT ≥5 times the ULN (FDA 2020a).

Hepatoxicity during therapy:

ALT ≥5 times the ULN: Discontinue remdesivir; may resume when ALT is <5 times the ULN (FDA 2020a).

ALT elevation AND signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR: Discontinue remdesivir (FDA 2020a).

Dosing: Pediatric

Coronavirus disease 2019 (COVID-19), severe (hospitalized patients); treatment:

Note: Remdesivir is currently under investigation for use in the treatment of COVID-19 (see ClinicalTrials.gov). While efficacy has been demonstrated in adults (Beigel 2020), data are not yet available in pediatric patients. Pediatric patients with severe disease are being considered for compassionate use access. The FDA has issued an Emergency Use Authorization for use in pediatric and adult patients hospitalized with severe disease (SpO2 ≤94% on room air or requiring oxygen, mechanical ventilation, or extracorporeal membrane oxygenation [ECMO]) (FDA 2020a). Because supplies may be limited, National Institutes of Health guidelines recommend prioritizing remdesivir use based on supplemental oxygen requirements and mode of oxygen delivery; refer to https://www.covid19treatmentguidelines.nih.gov for more information (NIH 2020). Limited drug-drug interaction data are available. Minimize any unnecessary comedication whenever possible given lack of information about interaction risk.

Infants, Children, and Adolescents (Chiotos 2020; FDA 2020a):

≥3.5 kg to <40 kg: Lyophilized powder: IV: Loading dose: 5 mg/kg/dose on day 1, followed by 2.5 mg/kg/dose once daily.

≥40 kg: Injection solution, lyophilized powder: IV: Loading dose: 200 mg on day 1, followed by 100 mg once daily.

Duration: In patients not requiring mechanical ventilation or ECMO, recommended treatment duration is 5 days or until hospital discharge, whichever is first (FDA 2020a; Goldman 2020; NIH 2020). If patient does not improve clinically, may extend duration to a total of 10 days. A 10-day treatment duration is recommended for patients who require mechanical ventilation or ECMO (FDA 2020a).

Dosage adjustment for concomitant therapy: Significant drug interactions exist, requiring dose/frequency adjustment or avoidance. Consult drug interactions database for more information.

Dosing: Renal Impairment: Pediatric

Note: The remdesivir formulation contains the excipient sulfobutylether-beta-cyclodextrin (SBECD), which accumulates in patients with kidney dysfunction, although the clinical significance of this accumulation is not certain (Hoover 2018; Luke 2010). SBECD is dialyzable (46% removed by an ~4-hour dialysis session) (Luke 2012).

Infants, Children, and Adolescents weighing ≥3.5 kg (FDA 2020a): **Note:** Calculate eGFR using the Schwartz equation for infants (using 0.45 as constant [k]), Bedside Schwartz equation for children and adolescents <18 years, and Cockcroft-Gault equation for adolescents ≥18 years as recommended by the manufacturer (FDA 2020a).

eGFR ≥30 mL/minute: No dosage adjustment recommended.

eGFR <30 mL/minute: Avoid use unless potential benefit outweighs potential risk (FDA 2020a). There are no safety or pharmacokinetic data available for patients with kidney impairment or who are receiving renal replacement therapies (Barlow 2020; FDA 2020a).

Dosing: Hepatic Impairment: Pediatric

Infants ≥3.5 kg, Children, and Adolescents (FDA 2020a):

Baseline hepatic impairment: The need for dosage adjustments in hepatic impairment is unknown (pharmacokinetics have not been studied); not recommended to be used in patients with baseline ALT ≥5 times the ULN.

Hepatotoxicity during therapy:

ALT >5 times the ULN: Discontinue remdesivir; may resume when ALT is <5 times the ULN.

ALT elevation AND signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR: Discontinue remdesivir.

Use: Off-Label: Adult

▼ Coronavirus disease 2019 (COVID-19)Level of Evidence [B]

A single case report describes clinical improvement after receipt of remdesivir in a patient infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) whose clinical status was worsening prior to receiving the drug; however, no conclusions about the safety and efficacy of remdesivir in this case can be made RefHolshue 2020. Preliminary analysis of a randomized, double-blind, placebo-controlled trial in hospitalized adult patients with coronavirus disease 2019 (COVID-19) demonstrated a faster time to recovery in the remdesivir group (median: 11 days versus 15 days in the placebo group) RefBeigel 2020.

Level of Evidence Definitions

Level of Evidence Scale

- **A** Consistent evidence from well-performed randomized, controlled trials or overwhelming evidence of some other form (eg, results of the introduction of penicillin treatment) to support the off-label use. Further research is unlikely to change confidence in the estimate of benefit.
- **B** Evidence from randomized, controlled trials with important limitations (inconsistent results, methodological flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on confidence in the estimate of benefit and risk and may change the estimate.
- **C** Evidence from observational studies (eg, retrospective case series/reports providing significant impact on patient care), unsystematic clinical experience, or from potentially flawed randomized, controlled trials (eg, when limited options exist for condition). Any estimate of effect is uncertain.
- **G** Use has been substantiated by inclusion in at least one evidence-based or consensus-based clinical practice guideline.

Administration: IV

Administer as an IV infusion over 30 to 120 minutes. Flush line with at least 30 mL NS after remdesivir infusion is complete (FDA 2020a).

Administration: Pediatric

Parenteral: IV: Administer as an IV infusion over 30 to 120 minutes. It is recommended to flush line with at least 30 mL NS after remdesivir infusion is complete (FDA 2020a); <30 mL may be used as long as the flush volume exceeds the priming volume of the tubing (Gilead written communication 2020b). Do not administer simultaneously with any other medication or IV solutions other than NS (FDA 2020a).

Storage/Stability

Injection solution concentrate (5 mg/mL): Store intact vials refrigerated at 2°C to 8°C (36°F to 46°F). Prior to dilution, allow vial to warm to room temperature; intact vials can be stored up to 12 hours at room temperature prior to dilution. Once diluted for infusion, may store at 20°C to 25°C (68°F to 77°F) for \leq 4 hours or refrigerated at 2°C to 8°C (36°F to 46°F) for 24 hours (FDA 2020a).

Lyophilized powder: Store intact vials at $<30^{\circ}$ C ($<86^{\circ}$ F). After reconstitution, vials can be stored at 20° C to 25° C (68° F to 77° F) for ≤ 4 hours prior to administration or refrigerated at 2° C to 8° C (36° F to 46° F) for 24 hours. Dilute within the same day as administration; once diluted for infusion, may store at 20° C to 25° C (68° F to 77° F) for ≤ 4 hours or refrigerated at 2° C to 8° C (36° F to 46° F) for 24° Hours (FDA 2020a).

Preparation for Administration: Adult

Injection solution concentrate (5 mg/mL): Allow injection solution vial to warm to room temperature prior to dilution. Further dilute in 250 mL NS; withdraw and discard the required volume of NS from the infusion bag (40 mL for a 200 mg dose; 20 mL for a 100 mg dose) prior to addition of remdesivir. Transfer required volume of remdesivir to the infusion bag and gently invert 20 times to mix the solution (FDA 2020a).

Lyophilized powder: Reconstitute vial with 19 mL SWFI; shake for 30 seconds. Allow vial contents to settle for 2 to 3 minutes; if not completely dissolved, repeat process as necessary until vial contents are

completely dissolved. Reconstituted vial contains 100 mg per 20 mL (5 mg/mL). Further dilute in 100 or 250 mL NS; withdraw and discard the required volume of NS from the infusion bag (40 mL for a 200 mg dose; 20 mL for a 100 mg dose) prior to addition of remdesivir. Transfer required volume of remdesivir to the infusion bag and gently invert 20 times to mix the solution (FDA 2020a).

Preparation for Administration: Pediatric

Parenteral: IV: Preparation should occur on the day of administration. See Emergency Use Authorization Fact Sheet for Health Care Providers for detailed preparation instructions.

Lyophilized powder: Reconstitute 100 mg vial with 19 mL SWFI; discard vial if a vacuum does not pull diluent into the vial. Immediately shake for 30 seconds. Allow vial contents to settle for 2 to 3 minutes; if not completely dissolved, repeat process as necessary until vial contents are completely dissolved. Resulting concentration of the reconstituted vial is 5 mg/mL; further dilution is necessary prior to administration.

Patients 3.5 to <40 kg: Further dilute dose in NS to a final concentration of 1.25 mg/mL; a syringe (for volumes <50 mL) or an infusion bag may be used for preparation of the dose. If using infusion bags, withdraw and discard a volume of NS equal to the volume of the reconstituted remdesivir dose from the bag prior to addition of remdesivir; following transfer of remdesivir to NS, gently invert 20 times to mix the solution (FDA 2020a).

Patients ≥40 kg: Further dilute dose in NS to a final total volume of 100 or 250 mL. If using infusion bags, withdraw and discard a volume of NS equal to the volume of remdesivir (ie, 40 mL for a 200 mg dose; 20 mL for a 100 mg dose) prior to addition of remdesivir; following transfer of remdesivir to NS, gently invert 20 times to mix the solution (FDA 2020a).

Injection solution concentrate (5 mg/mL): Patients ≥40 kg only: Allow vial(s) to warm to room temperature prior to dilution. Further dilute in NS to a total final volume of 250 mL; withdraw and discard a volume of NS equal to the volume of remdesivir (ie, 40 mL for a 200 mg dose; 20 mL for a 100 mg dose) from infusion bag prior to addition of remdesivir; transfer remdesivir to NS and gently invert 20 times to mix the solution (FDA 2020a).

Compatibility

See Trissel's IV Compatibility Database

Open Trissel's IV Compatibility

Medication Patient Education with HCAHPS Considerations

What is this drug used for?

• It is used in certain people to treat COVID-19.

Other side effects of this drug: Talk with your doctor right away if you have any of these signs of:

• Liver problems like dark urine, fatigue, lack of appetite, nausea, abdominal pain, light-colored stools, vomiting, or yellow skin or eyes

- Infusion site reactions like upset stomach, throwing up, sweating a lot, shivering, severe dizziness, or passing out
- Signs of a significant reaction like wheezing; chest tightness; fever; itching; bad cough; blue skin color; seizures; or swelling of face, lips, tongue, or throat.

Remdesivir FDA fact sheets – <u>Health care provider</u>; <u>Patient</u>

Note: This is not a comprehensive list of all side effects. Talk to your doctor if you have questions.

Consumer Information Use and Disclaimer: This information should not be used to decide whether or not to take this medicine or any other medicine. Only the healthcare provider has the knowledge and training to decide which medicines are right for a specific patient. This information does not endorse any medicine as safe, effective, or approved for treating any patient or health condition. This is only a brief summary of general information about this medicine. It does NOT include all information about the possible uses, directions, warnings, precautions, interactions, adverse effects, or risks that may apply to this medicine. This information is not specific medical advice and does not replace information you receive from the healthcare provider. You must talk with the healthcare provider for complete information about the risks and benefits of using this medicine.

Prescribing and Access Restrictions

Remdesivir is not commercially available; it is available as part of several ongoing clinical trials or from the manufacturer Gilead for treatment of coronavirus disease 2019 (COVID-19). Individual compassionate use requests are limited to pregnant women or pediatric patients <18 years of age with confirmed COVID-19 and severe disease; for compassionate use requests for these patients, visit: https://rdvcu.gilead.com. For adult, nonpregnant patients, drug can be obtained through the existing expanded access protocol (FDA 2020b). Additionally, the FDA has issued an Emergency Use Authorization (EUA) for adults and pediatric patients hospitalized with severe COVID-19. Under this EUA, remdesivir will be supplied to state health departments, who will distribute the allocated doses to hospitals within their state (HHS 2020a). As part of the EUA, fact sheets pertaining to emergency use of remdesivir are required to be available for health care providers and patients/caregivers, and certain mandatory requirements for remdesivir administration under the EUA must be met as outlined in the FDA emergency use authorization letter; the fact sheets and emergency use authorization letter may be accessed at https://www.gilead.com/remdesivir. Additionally, health care providers must track and report all medication errors and serious adverse events potentially associated with remdesivir use by either submitting a MedWatch form (https://www.fda.gov/medwatch/report.htm) or FDA Form 3500 (health professional) by fax (1-800-FDA-0178); a copy of all MedWatch forms should also be provided to Gilead (safety_fc@gilead.com).

Contraindications

Hypersensitivity to remdesivir or any component of the formulation (FDA 2020a).

Warnings/Precautions

Concerns related to adverse effects:

- Hepatic effects: Transaminase elevations have been observed in healthy volunteers and patients with coronavirus disease 2019 (COVID-19). Perform hepatic laboratory testing at baseline and daily during remdesivir administration; do not initiate remdesivir in patients with ALT ≥5 times the ULN at baseline. Discontinue remdesivir in patients who develop ALT ≥5 times the ULN (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 (FDA 2020a).
- Infusion reactions: Infusion-related reactions, including diaphoresis, hypotension, nausea, shivering, and vomiting, have been observed during and/or have been temporally associated with remdesivir administration. Discontinue administration and institute appropriate treatment if a clinically significant infusion reaction occurs (FDA 2020a).

Disease-related concerns:

• Renal impairment: Use is not recommended in patients with eGFR <30 mL/minute, unless the potential benefit outweighs the potential risk (FDA 2020a).

Dosage form specific issues:

- Injection: Contains the excipient cyclodextrin (sulfobutylether-beta-cyclodextrin), which may accumulate in patients with kidney impairment (NIH 2020).
- * See Cautions in AHFS Essentials for additional information.

Warnings: Additional Pediatric Considerations

Sulfobutylether-β-cyclodextrin sodium salt (SBECD) is an excipient in remdesivir; SBECD is renally cleared and accumulates in patients with decreased renal function. The lyophilized powder formulation contains 3 g of SBECD per 100 mg remdesivir, while the injection solution 5 mg/mL contains 6 g of SBECD per 100 mg remdesivir. Based on the lower SBECD content and resulting lower tonicity in the lyophilized powder as compared to the solution concentrate, the manufacturer recommends use of only the lyophilized powder in pediatric patients weighing <40 kg (FDA 2020a).

Pregnancy Considerations

Remdesivir is under study for the treatment of coronavirus disease 2019 (COVID-19). A limited number of pregnant women have received remdesivir through the compassionate use program. Use should not be withheld if otherwise needed (NIH 2020).

The American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) have developed an algorithm to aid practitioners in assessing and managing pregnant women with suspected or confirmed COVID-19 (https://www.acog.org/topics/covid-19; https://www.smfm.org/covid19). Interim guidance is also available from the CDC for pregnant women who are diagnosed with COVID-19 (https://www.cdc.gov/coronavirus/2019-ncov/hcp/inpatient-obstetric-healthcare-guidance.html).

Data collection to monitor maternal and infant outcomes following exposure to COVID-19 during pregnancy is ongoing. Health care providers are encouraged to enroll females exposed to COVID-19 during pregnancy in the Organization of Teratology Information Specialists (OTIS) pregnancy registry

(877-311-8972; https://mothertobaby.org/join-study/) or the PRIORITY (Pregnancy CoRonavIrus Outcomes RegIsTrY) (415-754-3729, https://priority.ucsf.edu/).

Breast-Feeding Considerations

It is not known if remdesivir is present in breast milk.

According to the manufacturer, the decision to breastfeed during therapy should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and the benefits of treatment to the mother. Interim guidance is available from the Centers for Disease Control and Prevention for lactating women who are diagnosed with COVID-19 (https://www.cdc.gov/coronavirus/2019-ncov/hcp/inpatient-obstetric-healthcare-guidance.html). Information related to COVID-19 and breastfeeding is also available from the World Health Organization (https://www.who.int/docs/default-source/maternal-health/faqs-breastfeeding-and-covid-19.pdf?sfvrsn=d839e6c0_1).

Adverse Reactions

Remdesivir is currently under investigation for use in the treatment of coronavirus disease 2019 (COVID-19) (see <u>ClinicalTrials.gov</u>). Serious or unexpected adverse reactions not previously reported may occur; refer to emergency use authorization (EUA) for information regarding reporting serious adverse reactions (FDA 2020a).

1% to 10%:

Endocrine & metabolic: Hyperglycemia (1.8% [placebo 2.1%]) (Beigel 2020), increased serum glucose (2.2% [placebo 1.1%]) (Beigel 2020)

Hepatic: Increased serum alanine aminotransferase (1.5% [placebo 1.7%]) (Beigel 2020; FDA 2020a), increased serum aspartate aminotransferase (2.8% [placebo 3.8%]) (Beigel 2020; FDA 2020a)

Renal: Acute renal failure (2.8% [placebo 3.3%]) (Beigel 2020), decreased estimated GFR (eGFR) (3.7% [placebo 3.3%]) (Beigel 2020), increased serum creatinine (1.5% [placebo 0.8%]) (Beigel 2020)

Miscellaneous: Fever (5.0% [placebo 3.3%]) (Beigel 2020)

<1%: Renal: Decreased creatinine clearance (0.6% [placebo 1.0%]) (Beigel 2020)

Frequency not defined: Miscellaneous: Infusion related reaction (including hypotension, nausea, vomiting, diaphoresis, and shivering) (FDA 2020a)

* See <u>Cautions in AHFS Essentials</u> for additional information.

Metabolism/Transport Effects

Substrate of CYP2C8 (minor), CYP2D6 (minor), CYP3A4 (minor), OATP1B1/1B3 (SLCO1B1/1B3), P-glycoprotein/ABCB1 (minor); **Note:** Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential

Drug Interactions Open Interactions

Chloroquine: May diminish the therapeutic effect of Remdesivir. Risk X: Avoid combination

CYP3A4 Inducers (Strong): May decrease the serum concentration of Remdesivir. *Risk C: Monitor therapy*

Hydroxychloroquine: May diminish the therapeutic effect of Remdesivir. Risk X: Avoid combination

Monitoring Parameters

Baseline and daily during remdesivir administration: Hepatic function tests (ALT, AST, bilirubin, alkaline phosphatase); hematology; renal function tests (serum creatinine, CrCl) and serum chemistries; signs/symptoms of infusion reaction (FDA 2020a).

Advanced Practitioners Physical Assessment/Monitoring

Obtain liver function tests (avoid use if ALT ≥5 times the ULN), hematology, renal function tests (avoid use in severe impairment), and serum chemistries. Assess for signs and symptoms of infusion reaction.

Nursing Physical Assessment/Monitoring

Check ordered labs and report any abnormalities. Monitor for and educate patient to report any signs and symptoms of an infusion related reaction (nausea, vomiting, diaphoresis, shaking).

Product Availability

Investigational agent; not approved for use in the United States.

Dosage Forms: US

Excipient information presented when available (limited, particularly for generics); consult specific product labeling. [DSC] = Discontinued product

Solution, Intravenous [preservative free]:

Generic: 100 mg/20 mL (20 mL)

Solution Reconstituted, Intravenous:

Generic: 100 mg (1 ea [DSC]); 150 mg (1 ea)

Solution Reconstituted, Intravenous [preservative free]:

Generic: 100 mg (1 ea)

Dosage Forms: Canada

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution, Intravenous:

Veklury: 100 mg/20 mL (20 mL)

Solution Reconstituted, Intravenous:

Veklury: 100 mg (1 ea)

Generic Available (US)

Yes

Pricing: US

Solution (Remdesivir Intravenous)

100 mg/20 mL (per mL): \$31.20

Solution (reconstituted) (Remdesivir Intravenous)

100 mg (per each): \$624.00

150 mg (per each): \$0.01

Disclaimer: A representative AWP (Average Wholesale Price) price or price range is provided as reference price only. A range is provided when more than one manufacturer's AWP price is available and uses the low and high price reported by the manufacturers to determine the range. The pricing data should be used for benchmarking purposes only, and as such should not be used alone to set or adjudicate any prices for reimbursement or purchasing functions or considered to be an exact price for a single product and/or manufacturer. Medi-Span expressly disclaims all warranties of any kind or nature, whether express or implied, and assumes no liability with respect to accuracy of price or price range data published in its solutions. In no event shall Medi-Span be liable for special, indirect, incidental, or consequential damages arising from use of price or price range data. Pricing data is updated monthly.

Mechanism of Action

Remdesivir is an adenosine nucleotide prodrug that is metabolized to the pharmacologically active nucleoside triphosphate metabolite after being distributed into cells. Remdesivir triphosphate acts as an adenosine triphosphate analog and competes for incorporation into RNA chains by the SARS-CoV-2 RNAdependent RNA polymerase, resulting in delayed chain termination during viral RNA replication (FDA 2020a).

Pharmacodynamics/Kinetics

Excretion: Urine (74% [majority as metabolites]); feces (18%).

Pharmacodynamics/Kinetics: Additional Considerations

Pediatric: Pharmacokinetics have not been evaluated. Pharmacokinetic models predict that use of adult dosing in pediatric patients ≥40 kg and the recommended weight-based dosing regimen in pediatric patients <40 kg will result in remdesivir and metabolite exposure that is comparable to adult exposure (FDA 2020a).

Index Terms

Coronavirus; COVID-19; GS-5734; Veklury

References

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(2):e00221-18. doi:10.1128/mBio.00221-18[PubMed 29511076]

Barlow A, Landolf KM, Barlow B, et al. Review of emerging pharmacotherapy for the treatment of coronavirus disease 2019 [published online April 7, 2020]. *Pharmacotherapy*. doi:10.1002/phar.2398[PubMed 32259313]

Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of covid-19 - preliminary report [published online May 22, 2020]. *N Engl J Med*. doi:10.1056/NEJMoa2007764[PubMed 32445440]

Chiotos K, Hayes M, Kimberlin DW, et al. Multicenter initial guidance on use of antivirals for children with COVID-19/SARS-CoV-2 [published online April 22, 2020]. *J Pediatric Infect Dis Soc.*[PubMed 32318706]

Gilead Sciences update on the company's ongoing response to COVID-19. https://www.gilead.com/purpose/advancing-global-health/covid-19. Accessed March 2, 2020a.

Gilead Sciences. Pediatrics and remdesivir [written communication]. Foster City, CA: Gilead Sciences Inc; May 8, 2020a.

Gilead Sciences. Questions re: remdesivir [written communication]. Foster City, CA: Gilead Sciences Inc; May 19, 2020b.

Goldman JD, Lye DCB, Hui SH, et al. Remdesivir for 5 or 10 days in patients with severe covid-19 [published online May 27, 2020]. *N Engl J Med*. doi:10.1056/NEJMoa2015301

Holshue ML, DeBolt C, Lindquist S, et al; Washington State 2019-nCoV Case Investigation Team. First case of 2019 novel coronavirus in the United States [published online January 31, 2020]. *N Engl J Med*. doi:10.1056/NEJMoa2001191[PubMed 32004427]

Hoover RK, Alcorn H Jr, Lawrence L, et al. Clinical pharmacokinetics of sulfobutylether-β-cyclodextrin in patients with varying degrees of renal impairment. *J Clin Pharmacol*. 2018;58(6):814-822. doi:10.1002/jcph.1077[PubMed 29578585]

Luke DR, Tomaszewski K, Damle B, Schlamm HT. Review of the basic and clinical pharmacology of sulfobutylether-beta-cyclodextrin (SBECD). *J Pharm Sci.* 2010;99(8):3291-3301. doi:10.1002/jps.22109[PubMed 20213839]

Luke DR, Wood ND, Tomaszewski KE, Damle B. Pharmacokinetics of sulfobutylether-β-cyclodextrin (SBECD) in subjects on hemodialysis. *Nephrol Dial Transplant*. 2012;27(3):1207-1212. doi:10.1093/ndt/gfr472[PubMed 21868395]

National Institute of Allergy and Infectious Diseases (NIAID). NIH clinical trial shows remdesivir accelerates recovery from advanced COVID-19. https://www.niaid.nih.gov/news-events/nih-clinical-trial-shows-remdesivir-accelerates-recovery-advanced-covid-19National. Accessed May 1, 2020.

National Institutes of Health. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. https://www.covid19treatmentguidelines.nih.gov/. Updated July 17, 2020. Accessed July 27, 2020.

Sheahan TP, Sims AC, Graham RL, et al. Broad-spectrum antiviral GS-5734 inhibits both epidemic and zoonotic coronaviruses. *Sci Transl Med.* 2017;9(396):eaal3653. doi:10.1126/scitranslmed.aal3653[PubMed 28659436]

Sheahan TP, Sims AC, Leist SR, et al. Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. *Nat Commun*. 2020;11(1):222. doi:10.1038/s41467-019-13940-6[PubMed 31924756]

US Department of Health and Human Services (HHS). HHS announces shipments of donated remdesivir for hospitalized patients with COVID-19. https://www.hhs.gov/about/news/2020/05/09/hhs-ships-first-doses-of-donated-remdesivir-for-hospitalized-patients-with-covid-19.html. Accessed May 12, 2020a.

US Food and Drug Administration (FDA). Fact sheet for health care providers Emergency Use Authorization (EUA) of remdesivir (GS-5734™). https://www.fda.gov/media/137566/download. Accessed August 3, 2020a.

US Food and Drug Administration (FDA). Frequently asked questions on the Emergency Use Authorization for remdesivir for certain hospitalized COVID-19 patients. https://www.fda.gov/media/137574/download. Accessed May 6, 2020b.

Wang M, Cao R, Zhang L, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro [published online February 4, 2020]. *Cell Res*. doi:10.1038/s41422-020-0282-0[PubMed 32020029]

World Health Organization (WHO). WHO R&D Blueprint – Ad-hoc expert consultation on clinical trials for Ebola Therapeutics: Appendix 4. Summaries of evidence from selected experimental therapeutics, as of October 2018. https://www.who.int/ebola/drc-2018/summaries-of-evidence-experimental-therapeutics.pdf?ua=1. Published October 11, 2018. Accessed March 24, 2020.

Last Updated 9/3/20



© 2020 UpToDate, Inc. and its affiliates and/or licensors. All rights reserved.