Remdesivir (GS-5734)

A Review of Pertinent Drug Information for SARS-CoV-2

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Remdesivir (GS-5734)

Mechanism of Action: Interference with viral RNA-dependent RNA polymerase; premature termination of viral RNA transcription

Status: Investigational, COVID-19 Phase III trials ongoing

Formulation: Intravenous only

Dosing: 200 mg IV loading dose, then 100 mg IV daily for 5-10 days
Pediatric Dosing: 5 mg/kg IV loading dose (max 200 mg), then 2.5 mg/kg IV daily (max 100 mg)

Manufacturer: Gilead Sciences

*Optimal duration currently under investigation
Remdesivir Structure Activity Relationship

Monophosphoramidate 1’Cyano C-adenosine Nucleoside Analog

Society of Infectious Diseases Pharmacists

Siegel; ACS 2017.
Monophosphoramidate 1’Cyano C-adenosine Nucleoside Analog

Remdesivir Structure Activity Relationship

Siegel; ACS 2017.
Remdesivir Structure Activity Relationship

C-Adenosine Analog  Monophosphate Form  Remdesivir
Remdesivir Structure Activity Relationship

C-Adenosine Analog
Rate limiting phosphorylation

Monophosphate Form

Remdesivir

Siegel; ACS 2017.
Remdesivir Structure Activity Relationship

C-Adenosine Analog
Rate limiting phosphorylation

Monophosphate Form
Charge reduces permeability

Remdesivir

Siegel; ACS 2017.
C-Adenosine Analog
Rate limiting phosphorylation

Monophosphate Form
Charge reduces permeability

Remdesivir
Neutral charge, bypasses rate limiting step

Remdesivir Structure Activity Relationship

Siegel; ACS 2017.
Remdesivir Structure Activity Relationship

Monophosphoramidate 1’Cyano C-adenosine Nucleoside Analog
Monophosphoramidate $1'\text{Cyano}$ C-adenosine Nucleoside Analog
C-Adenosine Analog
Poor selectivity, highly cytotoxic

Remdesivir

Remdesivir Structure Activity Relationship

Siegel; ACS 2017.
Remdesivir Structure Activity Relationship

C-Adenosine Analog
Poor selectivity, highly cytotoxic

Remdesivir
1’Cyano modification confers selectivity

Siegel; ACS 2017.
Distribution: Unbound 12.1%; Widely distributed
- Bladder, kidneys, liver, prostate gland, salivary gland (mandibular), pancreas
- Seminal vesicle, epididymis, testes
- Poorly crosses blood-brain barrier

Metabolism: Phosphoramidate prodrug activated by esterases; CYP3A4 substrate

Elimination: Renal 63%, biliary 27.8%

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Remdesivir (GS-5734)</th>
<th>Nucleoside Metabolite (GS-441524)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C_{max}</td>
<td>2.6 µg/mL</td>
<td>0.14-0.15 µg/mL</td>
</tr>
<tr>
<td>T_{max}</td>
<td>-</td>
<td>2.75-4 hr</td>
</tr>
<tr>
<td>Half-life</td>
<td>0.84-1.04 hr</td>
<td>20.4-25.3 hr</td>
</tr>
</tbody>
</table>

Safety

• Multiple-dose, 5-14 days
  • Any TEAE - 56-72%; All Grade 1-2
  • ALT/AST increase
    • Onset 5-25 days; resolution 3-47 days
• Phlebitis
• Constipation
• Dyspepsia
• Extremity pain
• Headache
• Nausea

• Ebola RCT
  • Single patient experienced hypotension and cardiac arrest after RDV initiation; cannot be distinguished from fulminant Ebola
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Sulfobutylether-beta Cyclodextrin (SBECO)

Remdesivir 150 mg solution - 9 g
Remdesivir 150 mg lyophilized powder - 4.5 g
Voriconazole 400 mg - 6.4 g
Safety

- Multiple-dose, 5-14 days
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Sulfobutylether-beta Cyclodextrin (SBECED)

- Remdesivir 150 mg solution - 9 g
- Remdesivir 150 mg lyophylized powder - 4.5 g
- Voriconazole 400 mg - 6.4 g

Does **NOT** meet NIOSH/ASHP criteria for hazardous compound

Consult updated pharmacy instructions from Gilead for additional information

### In vitro Activity

<table>
<thead>
<tr>
<th>Filoviridae</th>
<th>Paramyxoviridae</th>
<th>Pneumoviridae</th>
<th>Orthocoronaviridae</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ebola</strong></td>
<td>Measles</td>
<td>Respiratory Syncytial Virus</td>
<td>HCoV-NL63</td>
</tr>
<tr>
<td><strong>Marburg</strong></td>
<td>Mumps</td>
<td>Human Metapneumovirus</td>
<td>HCoV-OC43</td>
</tr>
<tr>
<td></td>
<td>Nipah</td>
<td></td>
<td>HCoV-229E</td>
</tr>
<tr>
<td></td>
<td>Hendra</td>
<td></td>
<td>HCoV-HKU1</td>
</tr>
</tbody>
</table>

HCoV = Human Coronavirus; MERS = Middle East Respiratory Syndrome; SARS = Severe Acute Respiratory Syndrome

*Brown; Antivir Res 2019.*
*Lo; Sci Rep 2017.*
*Sheahan; Sci Transl Med 2017.*
### In vitro Activity

<table>
<thead>
<tr>
<th>Virus</th>
<th>EC50 (cells)</th>
<th>CC50 (cells)</th>
<th>Selectivity Index</th>
</tr>
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<tr>
<td>SARS-CoV-2</td>
<td>0.77 µM (Vero E6)</td>
<td>&gt;100 µM (Vero E6)</td>
<td>&gt;130</td>
</tr>
<tr>
<td>SARS-CoV-1</td>
<td>0.069 µM (HAE)</td>
<td>&gt;10 µM (HAE)</td>
<td>&gt;144</td>
</tr>
<tr>
<td>MERS</td>
<td>0.074 µM (HAE)</td>
<td>&gt;10 µM (HAE)</td>
<td>&gt;135</td>
</tr>
<tr>
<td>Ebola</td>
<td>0.086 µM (MCr)</td>
<td>6.1 (Hep-2)</td>
<td>N/A</td>
</tr>
</tbody>
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EC50 = 50% effective concentration; CC50 = 50% cytotoxic concentration; Selectivity Index = CC50/EC50; Vero E6 = African monkey kidney cells; HAE = human airway epithelial cells; MCr = macrophages; Hep-2 = human epithelial type 2 cells.

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*SARS-CoV-2 EC$_{50}$*

Ribavirin 109.5 µM
Penciclovir 95.96 µM
Favipiravir 61.9 µM
Hydroxychloroquine 0.77 µM
Chloroquine 1.13-5.47 µM

Sheahan; Sci Transl Med 2017.
Agostini; Am Soc Micro 2018.
Yao; CID 2020.
Coronaviruses and Proofreading

- Ribavirin
- Penciclovir
- Favipiravir
- Remdesivir

Removed by proofreading
Maintains activity; high fitness cost

Agostini; mBio 2018.
Jordan; AAC 2018.
**In vivo Animal Prophylaxis**

<table>
<thead>
<tr>
<th>Virus</th>
<th>Virologic</th>
<th>Clinical/Pathologic</th>
<th>Survival</th>
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<tr>
<td>SARS-CoV-1</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
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<tr>
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*MERS-infected mice showed improved survival; rhesus macaques euthanized day 6 post-infection unable to determine survival impact of remdesivir*
### In vivo Animal Treatment

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<th>Survival</th>
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</thead>
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<tr>
<td>SARS-CoV1</td>
<td>✓</td>
<td>✓</td>
<td>✓ (Day 1) &lt;br&gt;✗ (Day 2)</td>
</tr>
<tr>
<td>MERS</td>
<td>✓</td>
<td>✓</td>
<td>✓*</td>
</tr>
<tr>
<td>Ebola</td>
<td>✓</td>
<td>✓</td>
<td>---</td>
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</tbody>
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*MERS-infected mice did not show improved survival; rhesus macaques euthanized day 6 post-infection unable to determine survival impact of remdesivir; Macaques in Ebola model were euthanized if deemed clinically moribund*
“A drug that inhibits viral replication may be of little use once virus replication has reached its peak…”
Randomized, Controlled Ebola Trial

- Standard of Care +
  - ZMapp (Control)
    - Triple monoclonal antibody
  - Remdesivir (RDV)
    - 200 mg load
    - 100 mg daily x9-13d
  - REGN-EB3
    - Triple monoclonal antibody
  - MAb114
    - Single Ebola survivor monoclonal

1:1:1:1
Stratified on cycle-threshold (i.e. viral load)
1^o Outcome: 28 day mortality
• Similar duration of symptoms (~5.5 days)/viral load
  • Per day OR 1.12 (1.00-1.24)
• Baseline characteristics generally well matched
  • Higher SCr/LFTs in ZMapp/RDV (sicker?)
• ZMapp and RDV arms halted; mortality signal

Randomized, Controlled Ebola Trial

Mulangu; NEJM 2019.
Randomized, Controlled Ebola Trial

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  - Per day OR 1.12 (1.00-1.24)
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  - ZMapp and RDV arms halted; mortality signal

Started too late? (latest start day 3)
Flaw in animal model?
Standard of care/resources?

Mulangu; NEJM 2019.
Compassionate Use Case Series

61 Patients

53 Patients

8 Excluded:
- 7 No post-baseline data
- 1 Erroneous start date

- 10 days: $n = 40; 75\%$
- 5-9 days: $n = 10; 19\%$
- < 5 days: $n = 3; 6\%$

Median follow-up 18 days (IQR 13-23)

Grein; NEJM 2020.
Compassionate Use Case Series

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<th>Characteristic</th>
<th>Patients (n = 53)</th>
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<tbody>
<tr>
<td>Median age (IQR) – yr</td>
<td>64 (48-71)</td>
</tr>
<tr>
<td>Male sex – no. (%)</td>
<td>40 (75)</td>
</tr>
<tr>
<td>Invasive ventilation – no. (%)</td>
<td>34 (64)</td>
</tr>
<tr>
<td>ECMO – no. (%)</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Median Sx before RDV (IQR) – days</td>
<td>12 (9-15)</td>
</tr>
<tr>
<td>Coexisting conditions* – no. (%)</td>
<td>36 (68)</td>
</tr>
</tbody>
</table>

*Specific conditions – n (%): hypertension 13 (25), diabetes 9 (17), hyperlipidemia 6 (11), asthma 6 (11); ECMO = extracorporeal membrane oxygenation; Sx = symptoms; RDV = remdesivir

Grein; NEJM 2020.
Compassionate Use Case Series

No pre-specified endpoints

1 - Discharged
2 – Ambient air
3 – Low-flow
4 – High-flow/NIPPV
5 – MV/ECMO
6 – Death

MV = mechanical ventilation; NIPPV = non-invasive positive pressure ventilation
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- **Improvement/Discharge**
  - N= 36/53 (67.9%)

- **Worsening**
  - N= 8/53 (15.1%)

- **Mortality**
  - N= 7/53 (13%)
  - Mean age 74.5 (range 68-79)
Compassionate Use Case Series

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Improvement/Discharge
N= 36/53 (67.9%)

Worsening
N= 8/53 (15.1%)

Mortality
N= 7/53 (13%)
Mean age 74.5 (range 68-79)

28-day/discharge/death data unavailable
N= 17/53 (32.1%)
8 MV, 1 ECMO at last time-point
**Compassionate Use Case Series**

<table>
<thead>
<tr>
<th>Adverse Events*</th>
<th>Patients – n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any adverse event</td>
<td>32 (60)</td>
</tr>
<tr>
<td><strong>ALT/AST increase</strong></td>
<td><strong>12 (23)</strong></td>
</tr>
<tr>
<td>Renal impairment/AKI</td>
<td>7 (14)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5 (9)</td>
</tr>
<tr>
<td>Rash</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Hypernatremia</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Multi-organ dysfunction syndrome</td>
<td>3 (6)</td>
</tr>
</tbody>
</table>

*Adverse events listed with >5% patients

Four patients discontinued for the following:
1. Worsening renal function
2. Multi-organ dysfunction
3. Transaminitis/rash
4. Transaminitis

“No new safety signals were detected in this compassionate use cohort of short-term remdesivir therapy.”
Take home points:

• Difficult to interpret without control group
  • Natural course vs. remdesivir effects
  • Historical comparisons of limited value
  • No pre-specified endpoints
  • Median start day 12 of illness; no quantitative PCR to evaluate viral load progression

• High risk of bias
  • Selection – patients screened for compassionate use
  • Sampling – unclear if consecutive patients, not all compassionate use patients included
  • Reporting – 8 patients excluded for erroneous/lack of data, high proportion without endpoints

• Safety profile consistent with previous data
  • Toxicity vs. underlying disease
Severe RCT in China

255 Patients

18 Excluded
14 Ineligible
4 Withdrew

236 Patients

Target Enrollment
n=453
Terminated Early

Placebo n = 78
Remdesivir n = 158

No dose: n = 3; 1.8%
< 5 days: n = 5; 3.2%
PP: n = 150; 94.9%

PP = Per protocol
# Severe RCT in China

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients (n = 236)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (IQR) – yr</td>
<td>65 (56-71)</td>
</tr>
<tr>
<td>Male sex – no. (%)</td>
<td>140 (59.3)</td>
</tr>
<tr>
<td>Low-flow O₂ – no. (%)</td>
<td>129 (82) 65 (83)</td>
</tr>
<tr>
<td>HFNC/MV/ECMO – no. (%)</td>
<td>28 (18) 10 (13)</td>
</tr>
<tr>
<td>NEWS-2 – (IQR)</td>
<td>5 (3-7) 4 (3-6)</td>
</tr>
<tr>
<td>Median Sx (IQR) – days</td>
<td>10 (9-12)</td>
</tr>
<tr>
<td>Coexisting conditions* – no. (%)</td>
<td>167 (70.7)</td>
</tr>
<tr>
<td>Corticosteroids – no. (%)</td>
<td>91 (38.6)</td>
</tr>
</tbody>
</table>

HFNC = high-flow nasal cannula; MV = mechanical ventilation; Sx = symptoms, NEWS-2 = National Early Warning Score-2

*Most common = HTN (43.4%), diabetes (23.7%), coronary heart disease (7.2%)

Concomitant antivirals permitted – LPV/r (17.8%), IFN-a2b (18.7%)
Severe RCT in China

Improvement = 2-pt Reduction

1 - Discharged
2 - Ambient air
3 - Low-flow
4 - High-flow/NIPPV
5 - MV/ECMO
6 - Death

MV = mechanical ventilation; NIPPV = non-invasive positive pressure ventilation

Time to Improvement

21 d (IQR 13-28) vs. 23 d (15-28)
HR 1.23 (95%CI 0.87-1.75)

Cumulative improvement rate

Remdesivir
Control

Hazard ratio 1.23 (95% CI 0.87-1.75); log-rank p=0.24

Wang; Lancet 2020.
Severe RCT in China

Improvement = 2-pt Reduction

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Time to Improvement
21 d (IQR 13-28) vs. 23 d (15-28)
HR 1.23 (95%CI 0.87-1.75)

Improvement – Early (<10 day)
18 d (IQR 12-28) vs. 23 d (15-28)
HR 1.52 (95%CI 0.95-2.43)

28-Day Mortality
14% vs. 13%
Difference 1.1% (95%CI -8.1 to 10.3)
Severe RCT in China

**Figure S4.** Kaplan Meier of time-to-clinical deterioration (defined as one category increase or death) in the intention-to-treat population.

**Deterioration**

**Viral Load**

![Graphs showing deterioration and viral load over time](https://via.placeholder.com/150)
Placebo-controlled data

“Our study found that remdesivir was adequately tolerated and **no new safety concerns were identified.**”

**Severe RCT in China**

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>Remdesivir – n (%)</th>
<th>Placebo – n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Any</strong></td>
<td>102 (66)</td>
<td>50 (64)</td>
</tr>
<tr>
<td>AST elevation</td>
<td>7 (5)</td>
<td>9 (12)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>16 (10)</td>
<td>5 (6)</td>
</tr>
<tr>
<td>Rash</td>
<td>11 (7)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Constipation</td>
<td>21 (14)</td>
<td>12 (15)</td>
</tr>
<tr>
<td><strong>Serious</strong></td>
<td>28 (18)</td>
<td>20 (26)</td>
</tr>
<tr>
<td>Acute Kidney Injury</td>
<td>1 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>Requiring Discontinue</strong></td>
<td>18 (12)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>ALT elevation</td>
<td>2 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>ARDS/resp. failure</td>
<td>7 (5)</td>
<td>1 (1)</td>
</tr>
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</table>

Wang; Lancet 2020.
Severe RCT in China

Take home points:
• Control group!
  • Highest quality data to date
• Negative study
  • Remdesivir did not significantly reduce TTCI - Underpowered
  • Signal of larger reduction with early therapy (< 10-day) – interpret with caution
  • No difference in prevention of deterioration or mortality
• Safety
  • Well tolerated compared to control, low level of discontinuation

Wang; Lancet 2020.
### Available Results

<table>
<thead>
<tr>
<th>Variable</th>
<th>NEJM CU Series</th>
<th>Lancet Severe RCT</th>
<th>NIAID Adaptive &amp;</th>
<th>SIMPLE Severe &amp;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample, (n)</td>
<td>53</td>
<td>237</td>
<td>606 events</td>
<td>397</td>
</tr>
<tr>
<td>Severity</td>
<td>Hypoxia/Supp. O₂</td>
<td>Hypoxia/PNA/PF &lt; 300</td>
<td>Hypoxia/PNA/Supp. O₂</td>
<td>PNA/Hypoxia; Not MV</td>
</tr>
<tr>
<td>Duration of Sx, days (IQR)</td>
<td>12 (9-15)</td>
<td>10 (9-12)</td>
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<tr>
<td>Intervention</td>
<td>10-day</td>
<td>10-day PBO</td>
<td>10-day PBO</td>
<td>5-day</td>
</tr>
<tr>
<td>28 day-Mortality, (%)</td>
<td>13</td>
<td>14</td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td>TTCR (days)/Recovery (%)</td>
<td>67.9%</td>
<td>21 days</td>
<td>23 days</td>
<td>11 days*</td>
</tr>
<tr>
<td>AEs Discontinue Tx, n (%)</td>
<td>4 (7.5)</td>
<td>18 (12)</td>
<td>4 (5)</td>
<td>9 (5)</td>
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Sx = symptoms; TTCR = time to clinical recovery; AE = adverse effects; Tx = treatment

&Preliminary results

*p<0.001

**14-day mortality data

Grein; NEJM 2020.
Wang; Lancet 2020.

https://www.fda.gov/media/137566/download
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<td>4 (5)</td>
<td>9 (5) 20 (10)</td>
</tr>
</tbody>
</table>

Sx = symptoms; TTCR = time to clinical recovery; AE = adverse effects; Tx = treatment
&Preliminary results
*p<0.001
**14-day mortality data

Grein; NEJM 2020.
Wang; Lancet 2020.
https://www.fda.gov/media/137566/download
<table>
<thead>
<tr>
<th>Trial</th>
<th>Sponsor</th>
<th>Population</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adaptive</td>
<td>NIAID</td>
<td>SpO$_2$ &lt; 94%</td>
<td>RDV ± baracitinib; Adaptive</td>
</tr>
<tr>
<td>SIMPLE-Mod</td>
<td>Gilead</td>
<td>SpO$_2$ ≥ 94%</td>
<td>5 vs. 10 days RDV vs. SOC; Extension</td>
</tr>
<tr>
<td>SIMPLE-Severe</td>
<td>Gilead</td>
<td>SpO$_2$ &lt; 94%</td>
<td>5 vs. 10 days RDV; Extension &amp; MV arms</td>
</tr>
<tr>
<td>DisCoVeRy</td>
<td>Inserm</td>
<td>SpO$_2$ &lt; 94%</td>
<td>RDV vs. HCQ vs. IFN-ß vs. LPV/r vs. SOC</td>
</tr>
<tr>
<td>Solidarity</td>
<td>WHO</td>
<td>Hospitalized</td>
<td>RDV vs. HCQ vs. SOC</td>
</tr>
</tbody>
</table>

RDV = remdesivir; PCB = placebo; HCQ = hydroxychloroquine; LPV/r = lopinavir/ritonavir; IFN-ß = interferon beta; *Estimated completion; Current as of 4/15/2020, subject to change; Source: ClinicalTrials.gov
May 01, 2020

Gilead’s Investigational Antiviral Remdesivir Receives U.S. Food and Drug Administration Emergency Use Authorization for the Treatment of COVID-19

-- Authorization Enables Broader Use of Remdesivir to Treat Hospitalized Patients with Severe COVID-19 Disease in the United States --

Emergency Use Authorization

- Suspected or laboratory-confirmed COVID-19
  - Adults and pediatrics
- **Severe**: \( \text{SpO}_2 \leq 94\% \) on room air or requiring \( \text{O}_2 \) support
  - No MV/ECMO = 5 days (additional 5 days option)
  - MV/ECMO = 10 days
- Distribution controlled by U.S. Government
  - Consistency with EUA requirements
  - Gilead to supply to authorized distributors

Source: https://www.fda.gov/media/137566/download
Emergency Use Authorization

Healthcare Provider Fact Sheet:
• Must provide copy of “Fact Sheet for Patients or parent/caregivers”
• Discuss information
  • EUA ≠ FDA approved
  • Patient or parent/caregiver can refuse
  • Risks/benefits of remdesivir, availability of alternatives
• Report Serious Adverse Events
  • FDA Medwatch: [www.fda.gov/medwatch/report.htm](http://www.fda.gov/medwatch/report.htm)
  • Include “EUA Remdesivir use” in top line of event description
• Monograph included

Source: [https://www.fda.gov/media/137566/download](https://www.fda.gov/media/137566/download)
Gilead is transitioning the provision of emergency access to remdesivir from individual compassionate use requests to expanded access programs. This approach will both accelerate access to remdesivir for severely ill patients and enable the collection of data from all participating patients. These programs are currently under rapid development in conjunction with national regulatory authorities worldwide. More details on how to participate in the expanded access programs will be forthcoming.

During this transition period, we are unable to accept new individual compassionate use requests due to an overwhelming demand over the last several days. We are focused now on processing previously approved requests and anticipate the expanded access programs will initiate in a similar expected timeframe that any new requests for compassionate use would have been processed.

Exceptions will be made only for pregnant women or children less than 18 years of age with confirmed COVID-19 and severe manifestations of disease.

Given the importance of data generation, we urge you to enroll patients in clinical trials if reasonably possible rather than pursue an emergency treatment request. Please refer to the links below for information on current clinical trials investigating the use of remdesivir in COVID-19:

- NCT04286705
- NCT04292730
- NCT04292899
- 2020-000936-23

Expanded Access Protocol: NCT04323761
References

21. Chin-Hong, Peter (PCH_SF). We have fielded a lot of requests from around the country for our experience with getting #compassionateuse #remdesivir from #Gilead for critically ill #COVID19 pts. Pears:1)~72 hrs if approved 2)Many steps but doable 3)Model of #interprofessional ID/IDPharm aloha. We are all in.” 3/16/20:20:16. Tweet.
Updates Log

3/24/2020 – Original version posted
4/5/2020 – Community transmission case report; ongoing trial info updated
4/12/2020 – Compassionate use case series added; ongoing trial info updated
4/17/2020 – Updated trial info
4/29/2020 – Lancet Severe Trial, NIAID/SIMPLE prelim data, Updated trial info
5/1/2020 – Emergency Use Authorization
Questions

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