

# Ethical Framework to Allocate Remdesivir in the COVID-19 Pandemic

This framework has been updated since July 29, 2020 to:

- address updated clinical guidance from the FDA; and
- clarify allocation under conditions of both scarcity and sufficient supply of RDV

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## Introduction

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) on May 1, 2020, to permit the emergency use of the unapproved product remdesivir (RDV) for treatment of COVID-19. The FDA noted, “Remdesivir is a direct acting antiviral that inhibits viral RNA synthesis. It is an investigational drug and is not currently approved for any indication ... [However], it is reasonable to believe that the known and potential benefits of RDV outweigh the known and potential risks of the drug for the treatment of patients hospitalized with severe COVID-19.”<sup>1</sup> In May and June 2020, Gilead donated supplies of remdesivir to the U.S. government for distribution to states, and the Minnesota Department of Health distributed Minnesota’s portion of that supply to hospitals and health care systems. Subsequently, the U.S. government secured additional supplies of remdesivir for distribution to states under a structure that includes payment by hospitals. To date, a series of publications have addressed RDV safety and efficacy, and the FDA updated its EUA on August 28, 2020.<sup>2</sup> This guidance document updates the previous allocation procedures to address these changes.

This document was developed by the Minnesota Department of Health (MDH) working with a subgroup of the Minnesota COVID Ethics Collaborative (MCEC), including the co-leads, with additional clinical inputs, and will be subsequently reviewed by MCEC. The document addresses relevant past guidance developed at MDH, key ethical values, and how allocation should occur at two

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<sup>1</sup> U.S. Food and Drug Administration. May 1, 2020. Letter to Ashley Rhoades, MBS, RAC, Gilead Sciences, Inc.

<sup>2</sup> U.S. Food and Drug Administration, August 2020. Letter to Ashley Rhoades. MBS. RAC. Gilead Sciences Inc.

levels, under conditions of scarcity and conditions of sufficient supply: (1) allocation among health care facilities in Minnesota, and (2) allocation among patients within each health care facility.

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## Past guidance and ethical values

This document draws upon substantial ethical guidance that had already been developed for public health emergencies in the state of Minnesota, well before the COVID-19 crisis began. This established ethical guidance was created in two projects, sponsored by and completed in partnership with MDH: the [Minnesota Pandemic Ethics Project \(www.health.state.mn.us/communities/ep/surge/crisis/panethics.html\)](http://www.health.state.mn.us/communities/ep/surge/crisis/panethics.html), and [Ethical Considerations - Crisis Standards of Care \(www.health.state.mn.us/communities/ep/surge/crisis/ethical.html\)](http://www.health.state.mn.us/communities/ep/surge/crisis/ethical.html). The development of that ethical guidance involved significant stakeholder consultation and wide community engagement. Community engagement forums included discussion of allocation objectives, criteria for allocation, and strategies to promote equity in access and address health disparities. In the COVID-19 pandemic, as in other public health emergencies, response must focus on the overall benefit to the population, to try to save the most lives possible while also respecting rights and promoting fairness across our population.

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## Ethical values guiding COVID-19 response

This ethical framework for COVID-19 response is grounded in the fundamental ethical commitment that the response to a pandemic will pursue Minnesotans' common good in ways that:

- Are accountable, transparent, and worthy of trust.
- Promote solidarity and mutual responsibility.
- Respond to needs respectfully, fairly, effectively, and efficiently.

To honor these fundamental value commitments, pandemic response must promote Minnesotans' common good by balancing three ethical objectives:

- Protect the population's health by reducing mortality and serious morbidity.
- Respect individuals and groups.
- Strive for fairness and protect against systematic unfairness and inequity.

When supply of RDV is sufficient and not scarce, standard clinical ethical values guiding competent medical care, shared decision-making with patients, and appropriate stewardship of medications apply. However, when supply of RDV is scarce, additional considerations grounded in public health ethics for allocating scarce resources in a pandemic should guide response. Allocation of scarce resources should maximize the **number of lives saved**, taking into account both risk and expectation of benefit, while respecting individuals and groups and protecting against inequity. Evaluation of

clinical prognosis, construed here as survival to discharge from an acute care facility, should be based upon well-accepted clinical tools and individualized assessment. This framework provides guidance about allocation to health care facilities across the state, as well as to patients within a given facility.

In existing ethical guidance for public health emergency response in Minnesota, recommended allocation of antivirals has included some prioritization of key workers, both due to considerations of reciprocity (what is owed to workers by virtue of the risk they take on) and instrumentality (what is owed to workers based on their role in response and recovery). Guidance is being considered to address whether to operationalize a priority for key workers in allocation of RDV and if so, how. Key worker status should not be considered in RDV allocation at this time.

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## Determining Conditions of Scarcity or Sufficient Supply

Each facility or system should determine whether RDV is in sufficient supply or scarce supply within their institution(s). This determination should be reviewed at least weekly and communicated to frontline caregivers so that it is clear whether RDV should be allocated based on guidance for conditions of sufficient supply or conditions of scarcity, as outlined below.

RDV should be considered to be in **sufficient supply** when facilities or systems have sufficient RDV in reserve to treat 125% of weekly utilization rate for Priority Groups 1 - 3 below for one week OR when facilities or systems are able to obtain sufficient supply for that week to treat patients in all priority groups without needing to triage. Note that if facilities require additional courses of RDV to meet patient needs or additional doses to make up a treatment course, they should reach out to their regional healthcare coalitions for assistance in locating supply that can be transferred, with the receiving facility reimbursing the sending facility. Alternatively, facilities seeking additional supply may directly contact other facilities without working through the regional healthcare coalition. If they are unable to secure supply of RDV using these processes, they may contact Sarah Lim at MDH ([sarah.lim@state.mn.us](mailto:sarah.lim@state.mn.us)) to ascertain if MDH has any available supply. RDV should be considered in **scarce supply** if the criteria listed above for sufficient supply are not met. If RDV is scarce in some facilities but not all, those facilities should make reasonable efforts to secure additional supply from other facilities or MDH so that they can meet patient needs.

When supply is sufficient, facilities and systems should allocate RDV in line with competent medical care, shared decision-making with patients, and appropriate stewardship of medications. Antimicrobial stewardship aims to ensure the appropriate use of antimicrobials, typically using facility or system-level programs that promote and monitor appropriate antimicrobial prescribing under the oversight of pharmacy staff and/or infectious disease physicians. Additionally, provisions below for Triage team management and secondary review do not apply when supply is not scarce. However, if there is not sufficient RDV in reserve, triage should occur based on the clinical priority groups as listed on page 6.

## Ethical criteria for allocation of remdesivir

### Ethical strategy for distribution throughout the state

Whether supply of RDV is sufficient or scarce, distribution of RDV to health care facilities across the state should be proportional to a **5-day average of the total number of COVID-positive patients currently admitted to the facility who are not currently on ventilators**. In other words, more resources should be sent to facilities with greater numbers of recipients in the highest priority tier, so that these patients have maximal access to the scarce resources. When supply of RDV is sufficient and not scarce, this strategy for distribution throughout the state will still ensure that supply tracks demand.

### Process for allocation among facilities in Minnesota

For allocation of RDV to health care facilities, MDH should estimate how many patients at each facility (or system, if facility data are unavailable) fit the allocation criteria listed immediately above. Based on those numbers, MDH should calculate the proportion of that total associated with each facility (or system), and notify each facility (or system) of their proportional allocation. The facility (or system) should promptly respond by indicating how much of that allocation they are willing to buy. If a facility (or system) declines to purchase its full allocation, MDH may purchase the resulting surplus (if funds allow). Alternatively, MDH may query other facilities (or systems) to determine if any are willing to purchase the surplus. If more than one facility (or system) is willing to purchase the surplus, MDH should decide where to direct the surplus to optimize availability of the drug in regions with especially limited supply relative to need.

Once each facility's (or system's) allocation has been determined, MDH will notify Amerisource Bergen Corporate (ABC) of the quantity to ship to each facility (or system) and to MDH (if applicable). ABC will then contact receiving facilities or systems to coordinate the delivery of remdesivir and arrange payment from them. If an allocation of RDV goes to a system instead of a single facility, that system should allocate proportionately to its facilities based on the number of prioritized patients in each facility.

In the event that a patient receives RDV or is ordered RDV under this framework and is later transferred to another facility inside or outside of Minnesota, the remainder of the course should follow that patient. Systems that have facilities located outside of Minnesota should be allocated RDV only for their in-state facilities. In addition, given that facilities/systems have access to RDV through the state's allocation from the federal government, they should reserve their full supply of the drug for patients presenting for care at their in-state facilities.

Each facility (or system) should identify points of communication for MDH to contact with information about 1) pending shipments and 2) to inform MDH of their facility's (or system's) purchasing decision. This guidance recommends that RDV status be recorded in patients' Electronic Health Record for ease of access to information.

If facilities require additional courses of MDH to meet patient needs or additional doses to make up a treatment course, they may reach out to their regional health care coalitions for assistance in locating supply that can be transferred, with the receiving facility reimbursing the sending facility. Alternatively, facilities seeking additional supply may directly contact other facilities without working through the regional health care coalition. If they are unable to secure supply of RDV using these processes, they may contact Sarah Lim at MDH ([sarah.lim@state.mn.us](mailto:sarah.lim@state.mn.us)) to ascertain if MDH has any available supply.

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## Allocation within institution

### Ethical strategy for distribution within a facility

**Clinical prognosis should ground allocation decisions.** Prognosis should be understood to include both need for the resource (i.e., risk of serious morbidity or mortality if the patient were not to receive the resource), and the likelihood that the patient will benefit from access to the resource by recovery to hospital discharge. **Substantial differences** in prognosis are what is ethically relevant in differentiating between patients; small differences should be viewed as morally equivalent and should not be used to allocate resources to or withhold resources from patients.

After discussion with infectious disease experts and members of the MCEC, and updated with preliminary data from the published Beigel et al. RDV trial published on May 22<sup>3</sup>, data from the Gilead open-label RDV trial comparing a 5-day and 10-day course in a subset of patients<sup>4</sup> treatment guidelines issued by NIH,<sup>5</sup> and data from the published Spinner et al. trial of RDV in patients with moderate illness,<sup>6</sup> clinical criteria for RDV allocation was determined based on risk and likelihood of greatest benefit. This guidance is based on evidence available at the time it was produced; changes in available evidence may require changes in allocation among patients within a facility.

**For all potential recipients of RDV**, the current recommended dose for adults and pediatric patients weighing >40 kg is a single loading dose of 200mg on Day 1 followed by 100mg once daily

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<sup>3</sup> Published online May 22, 2020, by the New England Journal of Medicine by Beigel et al., "[Remdesivir for the Treatment of Covid-19 – Preliminary Report](https://www.nejm.org/doi/full/10.1056/NEJMoa2007764)" (<https://www.nejm.org/doi/full/10.1056/NEJMoa2007764>)

<sup>4</sup> Published online May 27, 2020, by the New England Journal of Medicine by Goldman et al., "[Remdesivir for 5 or 10 Days in Patients with Severe COVID-19](https://www.nejm.org/doi/full/10.1056/NEJMoa2015301)" (<https://www.nejm.org/doi/full/10.1056/NEJMoa2015301>)

<sup>5</sup> Updated July 24, 2020, by the National Institutes of Health (NIH), [COVID-19 Treatment Guidelines: Remdesivir](https://www.covid19treatmentguidelines.nih.gov/antiviral-therapy/remdesivir/) (<https://www.covid19treatmentguidelines.nih.gov/antiviral-therapy/remdesivir/>)

<sup>6</sup> Published online August 21 by the Journal of the American Medical Association "Spinner, et al. Effect of Remdesivir vs Standard Care on Clinical Status of Patients with Moderate COVID-19"

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for Days 2 through 5 (for a total 5-day course). **At five days, patients can be evaluated for possible continuation of RDV if needed**, for a possible total 10-day course.

**During conditions of scarcity, the following applies:**

- Patients being considered for RDV treatment should have laboratory-confirmed COVID-19 (by RT-PCR testing on a respiratory specimen).
- Patients should meet other clinical inclusion criteria as specified by the FDA EUA for RDV (GFR  $\geq$  30ml/min, ALT  $<$  5 times upper limit of normal).

**During conditions of sufficient supply, the following applies:**

- Patients being considered for RDV may have laboratory-confirmed or suspected COVID-19 infection.
- Patients with renal or hepatic impairment may be considered for RDV if the potential benefit outweighs the risk as specified by the FDA EUA for RDV.

**When RDV is not a scarce resource** in line with the criteria stated above, facilities and systems should allocate RDV in line with competent medical care, shared decision-making with patients, and appropriate stewardship of medications, but not a triage model. The provisions below for Triage team management and secondary review do not apply when supply is not scarce. However, when RDV is a **scarce resource**, triage should occur based on the following Priority Groups.

**Priority 1 Patients:** patients receiving the highest priority for allocation of RDV are those with the following characteristics:

- $<$  94% oxygen saturation on room air OR using supplemental oxygen, and
- Lung infiltrates on imaging.
- And are NOT on advanced respiratory support (high flow nasal cannula, CPAP, or BIPAP).

**Priority 2 Patients:** if facilities have met the needs of all of the patients in the highest priority group, facilities should then allocate RDV to the following groups of patients:

- Patients who are on advanced respiratory support (high flow nasal cannula, CPAP, or BIPAP)  
AND
- Patients who have been mechanically ventilated for 5 days or less or have been on ECMO for 5 days or less

**Priority 3 Patients:** if facilities have met the needs of the first and second priority groups of patients, facilities should then allocate RDV based on the following criteria:

- Patients with signs or symptoms of COVID-19 pneumonia (e.g., with cough and lung infiltrates on chest imaging), but who do not require supplemental oxygen.

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**For all of the above priority groups: when patients are otherwise of equal priority within a priority group of patients** (i.e., there is no substantial difference in risk and likelihood of benefit) and there is not sufficient RDV for all patients in that priority group, the Triage Officer or Team should use a random process to allocate the resource (as explained below).

**In any of the priority groups:** patients who have started a course of RDV who later **no longer meet clinical criteria for eligibility** because of worsening kidney or liver function should be considered for discontinuation of RDV. It should not be discontinued for purposes of reallocating to other patients.

**Also in all of the priority groups:** in addition to prognosis of surviving current illness to hospital discharge, allocation decisions should consider **whether the patient is imminently and irreversibly dying or terminally ill with life expectancy under 6 months** (e.g., eligible for admission to hospice). If supply of RDV is scarce, patients in this group should not receive priority for access. If supply is sufficient, then patients who are terminally ill with life expectancy under 6 months should be considered as candidates for RDV.

**Patient ability to pay should not control access to RDV, under circumstances of scarcity or of sufficient supply.** Facilities (or systems) should work with patients to identify sources of payment for RDV, including based on patient eligibility for insurance, subsidized care, or any program that will enable access.

In order to maximize benefit of this resource, **if facilities project with reasonable confidence that their supply of RDV will likely be insufficient to meet patient needs** across all priority tiers until the next shipment arrives, they may consider holding supply to treat only patients in the highest priority tier(s). Alternatively, if supply allows treatment of patients in the highest priority tier(s) and some but not all patients in the second or third priority tier, then a fair random process for allocating among those patients in the second or third priority tier should be employed. **Conserving supply in this way, and thus limiting which patients receive treatment, is permissible only if facilities will be unable to secure RDV from other facilities to address their shortage.**

Such a projection regarding (in) sufficiency of supply requires that facilities consider amounts of available supply, the timing of the next expected shipment, the ability to transfer RDV from other facilities to alleviate shortages, and the trends in caseloads across the priority tiers. Under conditions of sufficient supply, facilities should not withhold treatment from current patients who meet allocation criteria to hold some supply in reserve for possible future use.

### **Patient decision-making and consent to RDV**

Under all circumstances – scarcity or sufficient supply – on intake, clinical teams should discuss the patient’s interest in receiving therapies not yet approved by the FDA but available under an EUA, should they become available, and document the discussion in the EHR. In addition, patients may be asked whether they would be interested in receiving investigational therapies, if they qualify for access through compassionate use or a clinical trial (access and consent to those investigational uses are not addressed by this framework).

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Patients should be informed if they have been deemed eligible for and selected to receive an RDV course under this RDV framework, even if they had previously indicated they were not interested in receiving unapproved therapies. A patient who is capable of decision-making is entitled to partner with their care team in deciding whether to consent to administration of RDV.

Patients should be informed that RDV is not FDA-approved but is available under an Emergency Use Authorization. For patients who are not capable of making decisions, their authorized decision-maker should be consulted. To promote equity, consent forms/patient information sheets should be available in the diverse languages of a facility's patient populations, and appropriate translation services should be available to foster appropriate consent discussions.

**If the patient lacks decision-making capacity but no authorized decision-maker is available,** clinicians should provide the RDV if the patient is eligible in keeping with the best interests of the patient, unless the patient previously refused to consent to unapproved therapies. The authorized decision-maker should be the person appointed by the patient to make decisions on their behalf. If the patient has not indicated who that person should be, the clinical team should work with the patient's spouse, partner, family, or close friend.

Clinicians and health care organizations should work to follow Minnesota guidance and law on surrogate decision-making. If patients or their authorized decision-makers express interest in accessing RDV treatment but have concerns about ability to pay, facilities should work with patients to identify sources of payment for RDV.

**Facilities should make sure to note in the patient's records how to reach the authorized decision-maker rapidly,** whether supplies of RDV are scarce or sufficient

**Children and pregnant women** were previously eligible to receive RDV through compassionate use from Gilead, but it is not clear if that remains the case. If and when Gilead ceases providing compassionate use access to patients in these groups, they should have access under the criteria and processes stated in this framework. If a patient is approved for RDV under the compassionate use program but a delay in initiating therapy is expected (e.g., due to the time needed to ship RDV) that may adversely affect the patient's clinical course, a facility may use their EUA supply to start the patient on treatment, as long as 1) there is sufficient supply available to allocate to other patients until the compassionate use RDV arrives, 2) the excess supply received under the compassionate use program is used to replenish the EUA supply, and 3) initiation of therapy complies with applicable institutional and FDA rules, including IRB involvement.

**Patients who are already receiving RDV** (e.g., through clinical trials or compassionate use) will not be eligible to receive doses from this round of drug allocation.

**Key workers** will not receive prioritization during this round of allocation, for the reasons noted earlier in the document.

**Allocation decisions should not consider or be based upon:**



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- Race, ethnicity, gender, gender identity, sexual orientation or preference, religion, citizenship or immigration status, or socioeconomic status.
- Ability to pay.
- Age as a criterion in and of itself (this does not limit consideration of a patient's age in clinical prognostication of likelihood to survive to hospital discharge).
- Disability status or comorbid condition(s) as a criterion in and of itself (this does not limit consideration of a patient's physical condition in clinical prognostication of likelihood to survive to hospital discharge).
- Predictions about baseline life expectancy beyond the current episode of care (i.e., life expectancy if the patient were not facing the current crisis), unless the patient is imminently and irreversibly dying or terminally ill with life expectancy under 6 months (e.g., eligible for admission to hospice).
- First-come, first-served (should not distinguish between patients when treatment has not yet been started on equivalent patients).
- Judgments that some people have greater "quality of life" than others.
- Judgments that some people have greater "social value" than others.

### Process for allocation within a facility

#### Separation of roles: triage decision-making and bedside care

Randomization decisions that become necessary in the triage process **when RDV is scarce**, should be made by a **Triage Officer or Team** that is separate from the clinicians providing care at the bedside. This approach to decision-making promotes the ability of bedside clinicians to advocate for their patients, thus protecting the integrity of the patient/provider relationship. Bedside clinicians will be expected to follow the outcomes of the randomization process completed by the Triage Officer or Team, so that resources may be ethically stewarded.

**Facilities that do not yet have Triage Officers or Teams established should set up an ad hoc triage process for the June 2020 shipment of RDV to maintain separation of roles, for example, using the administrative head of pharmacy to randomize among eligible patients.**

#### Importance of documentation

Under all circumstances – scarcity or sufficient supply - patients who receive RDV should have the order (including length of course) documented in the patient's electronic health record (EHR). Allocation decisions should be logged and recorded by facility to allow for transparency and retrospective review. Under conditions of scarcity, when RDV is allocated via triage, this log should include which patients were eligible for RDV, which patients received the RDV allocation, and how randomization occurred. Documentation is important to ensure appropriate care of the patient across clinicians and shifts, to ensure transparency and accountability to the patient and family, to

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allow triage processes to work properly, and to enable retrospective review to spot and resolve problems.

Importance of retrospective review: [Allocation of Ventilators & Related Scarce Critical Care Resources During the COVID-19 Pandemic](https://www.health.state.mn.us/communities/ep/surge/crisis/ventilators.pdf) ([www.health.state.mn.us/communities/ep/surge/crisis/ventilators.pdf](https://www.health.state.mn.us/communities/ep/surge/crisis/ventilators.pdf)) recommends the establishment of Secondary Review Teams that are responsible, among other things, for retrospective review of rationing decisions **when resources are scarce**. For RDV allocation, the Secondary Review Team will perform retrospective review of the full set of allocation decisions at least monthly. If the Secondary Review Team has not yet been established, then a facility may use an ad hoc process for Secondary Review.

This type of review is important to ensure that the allocation processes are working appropriately and in keeping with this framework. Problems discovered should be resolved immediately. The Secondary Review Team should develop a means to document retrospective reviews and problem resolution, and should have access to additional patient identifiers at this time to check that decisions are being made fairly.

A significant function of retrospective review is to ensure that decisions are made without bias, including on the basis of race, ethnicity, ability to pay, or other characteristics identified above as impermissible to consider in decision-making. Retrospective review should also consider whether any groups are being disproportionately impacted in a way that leads to systematic disadvantage or worsens existing inequities. Data should be gathered at the state level as well as the level of health systems and institutions to assess impact and ensure fairness and equity.



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