# Use of Remdesivir in COVID-19 for Pregnant Women and Children < 18 years

How to Request Single Patient Expanded Access ("Compassionate Use")
Emergency Investigation New Drug (IND)

**Recommended Work Flow**
(Version dated 3/22/20)

**Update (3/22/20):** Due to overwhelming demand, Gilead has suspended single patient expanded access to remdesivir. Gilead is working to transition to an expanded access program, which will remove the requirement for review of each individual patient request. Gilead's goal is to make this transition as quickly as possible. Details on how to request remdesivir will be shared as soon they become known. **The process below is being maintained by Gilead only for pregnant women and children younger than 18 years of age with confirmed COVID-19 and severe manifestations of disease**. Gilead's online compassionate use portal, https://rdvcu.gilead.com/ has been updated to reflect this change.

## Work Flow:

A patient must meet the clinical criteria set out by the drug manufacturer (Gilead), as determined by the treating physician. Once approved by Gilead, the process for single patient expanded access IND can commence. Currently Gilead is assessing requests on a case-by-case basis. The key inclusion/exclusion criteria from Gilead are listed below. If patients do not meet these minimal criteria, a request to Gilead by the treating physician should not be submitted as it will likely be rejected. **Note: these criteria are only applicable to pregnant women and children younger than 18 years of age with confirmed COVID-19 and severe manifestations of disease, as defined below.**

**Key Inclusion Criteria**:
- Hospitalization
- Confirmed SARS-CoV-2 by Polymerase Chain Reaction (PCR)
- Invasive Mechanical Ventilation

**Key Exclusion Criteria**:
- Evidence of Multi-organ failure
- Pressor requirement to maintain blood pressure
- ALT levels > 5 X ULN
- Cr Clearance < 30 mL/min or dialysis or Continuous Veno-Venous Hemofiltration
- Remdesivir cannot be used in conjunction with other experimental antiviral agents

These criteria are subject to change without notice and may be subject to additional considerations and limitations by Gilead. Meeting these minimum criteria does not guarantee approval of a request for Remdesivir. See the following web link for current details on criteria:

https://rdvcu.gilead.com/
(click on the "I'm a healthcare professional" button to advance to the criteria screen).

Once a treating physician has confirmed the above criteria have been met, the following steps are required for each patient:

1. Request approval from Gilead for drug by completing all the required documentation.
2. Request FDA approval
3. Treat Patient
4. Notify appropriate IRB of drug use (must occur within 5 days following 1st infusion administration)

Each step requires clinical knowledge from the treating physician to complete the necessary forms.

See detailed workflows that follow for more information on each step, and associated resources.

## 1. Request Approval from Gilead or "Letter of Authorization" (LOA)

If the treating physician determines that a patient meets the inclusion criteria above, then the treating physician must submit the expanded access request on behalf of a patient, via an online submission form. The form can be accessed at:

https://rdvcu.gilead.com/
*(click on the "I'm a healthcare professional" button to advance to the criteria screen, then click on the "next" button).*

There is no specific request template to complete, as the online form serves as the submission form.

Gilead's email contact for questions is: CompassionateAccess@gilead.com
An alternate Gilead email contact for general questions regarding the response to COVID-19 is: coronavirus.response@gilead.com

All individual patient use requests submitted by a treating physician using the online submission form will be asked to provide the following information:

- Contact information for Requestor (name, phone, email, cell number)
- Institution/Treating Physician (institution name & address, physician phone & email)
- Pharmacy (name, address, phone)
- Pharmacist (name, email, cell number)
- Patient information:
  - demographics
  - description of clinical course

- current clinical status
- imaging results
- physical exam findings/vital signs (must include current supplemental oxygen requirement)
- labs (must include unit of measure and include BUN, Creatine, Creatinine Clearance, ALT, AST, Alkaline Phosphatase, Total Bilirubin)

Gilead uses the following criteria for considering requests to provide access to individual patients for expanded access. The patient must be suffering from a serious/life-threatening condition, and:

- There is a strong biological rationale or clinical data that support the possibility that the potential benefits of administration of the investigational drug to the patient for that serious/life-threatening condition could outweigh the potential risks.
- The patient's physician has determined that treating the patient with the investigational drug is in the patient's best interests.
- The investigational drug will be administered in accordance with applicable laws and regulatory requirements of the country where the patient is treated.
- The patient is not eligible or able to participate in a clinical trial or similar sponsored access program.
- No therapeutic alternative is available.

If the request is approved, the following documents will be provided from Gilead to the treating physician:

- Single Patient Protocol
- Investigator's Brochure
- Pharmacy Manual
- Prescriber Agreement (requires sign off by treating physician)
- Informed Consent template

Note that Gilead has up to 15 days to provide the LOA to a requesting site. If an LOA is not provided, note this in communication to FDA when requesting EIND.

Gilead requires that the "Prescriber Agreement" be signed by the treating physician. If the treating physician is employed by Trinity Health or one of its hospitals, please note that the "Prescriber Agreement" has been reviewed by Trinity Health Legal and does not require further review by local legal counsel. Please sign where indicated, and return a copy to your legal department to obtain your hospital executive's signature of approval or confirmation of delegation of signature authority. A copy of the contract will then be returned to you, and a copy will be sent to the Trinity Health IRB of Record. The treating physician will also be required to return a copy of the signed "Prescriber Agreement" to Gilead, before the investigational drug will be shipped. If you have any questions about this process, please contact legal team member Liza Brooks (Liza.Brooks@trinity-health.org). **Please note that Trinity Health's legal department does not provide legal**

**advice to non-employed medical staff members.** If the treating physician is not employed by Trinity Health or one of its hospitals, then he or she may wish to seek legal advice from his or her own legal counsel.

Gilead's "Informed Consent" template has been reviewed by Trinity's IRB of Record, and has been modified to meet our institutional requirements (i.e. Ethical and Religious Directives for Catholic Health Care Services). HIPAA authorization has been incorporated into the consent. Each ministry will need to include their site specific contact information in the appropriate areas of the consent form. The consent template to use is available on the Trinity Health website, click here to access it.

## 2. Request FDA Approval

Once approval has been received from Gilead, an Emergency IND (EIND) must be requested from the FDA. To obtain this, complete the following steps:

- Complete FDA Form 3926: https://www.fda.gov/media/98616/download This form is designed specifically for use by physicians when submitting requests for single patient expanded access to investigational drugs, including in emergencies.
- Attach Gilead's "Letter of Authorization" (LOA), if available. Note this can be submitted to FDA up to 15 days after request is made.
- Assemble completed Form 3926, and a curriculum vitae (CV) for the treating physician, and submit using the following instructions:

**To obtain an EIND during regular business hours** (8:00 am - 4:30 pm Eastern Time, Monday - Friday):

- Send the completed required forms and CV to the FDA, Division of Antivirals (DAV) by fax (301-796-9883) or email (DAVPEINDREQUEST@fda.hhs.gov). Please include telephone and fax numbers where the treating physician can be reached in case the FDA has additional questions or needs additional information to support granting of the EIND. **If sending the paperwork by fax, please call the Division (301-796-1500) to inform them the fax has been sent.**

**To obtain an EIND after regular business hours** (weekdays after 4:30 pm or before 8:00 am Eastern Time; weekends or holidays):

- Call the FDA Emergency Coordinator at 1-866-300-4374 or 301-796-8240 or call the Center for Drug Evaluation and Research (CDER) Emergency Coordinator at 301-796-9900. The treating physician will be placed into contact with an FDA staff member who can facilitate or grant the request. Please note that the requester will not be provided with an EIND number if the request is

granted outside of regular business hours. Provide the drug manufacturer with the name of the person who authorized the EIND for release of the drug.
- Send the completed required forms and CV to DAV by fax (301-796-9883) or email (DAVPEINDREQUEST@fda.hhs.gov). Please include telephone and fax numbers where you can be reached.

**Note**: You will need to provide documentation of the FDA's approved EIND to Gilead, before drug will be shipped to you.

### 3. Treat Patient

Arrange for treatment of patient at your ministry. Treating physician is responsible for obtaining informed consent for use of investigational medication.

Some operational considerations that will need to be specified include:

- Investigational drug is administered over a 10 day time frame, 30-60 minutes daily IV infusion.
- Specifying a pharmacist to receive shipment of the investigational drug, and dispense, ensuring 24/7 pharmacy coverage

### 4. Notify IRB

The Trinity Health IRB of Record is represented by the Saint Joseph Mercy Health System (SJMHS) IRB #1 (Ann Arbor). This IRB provides regulatory oversite for all Remdesivir single patient expanded access emergency use submissions for Trinity Health locations*. All local IRB leaders, as well as designated Institutional Officials / Chief Medical Officers (for those ministries without an IRB / Institutional Official), have been informed, and are in agreement with, this coordination of services. Documentation of acknowledgement is maintained by the IRB of Record housed in the Research Compliance Department, Michigan.

*Exceptions are: Loyola University Medical Center (Maywood, IL), Catholic Health (Buffalo, NY), and MercyOne Des Moines Medical Center (Des Moines, IA). These sites will use their local IRB for this work.

Notify the appropriate IRB of Record by completing and submitting the SJMHS "Permission for Emergency Use of Test Article" form: https://www.stjoeshealth.org/assets/documents/irb/sjmhs-emergency-use-permission-fillable-word.doc

Note there are two parts to this form. **If possible**, please submit Part I *prior to* emergency use of Remdesivir. Part II *must be submitted within five working days after the first use of Remdesivir*. For purposes of completing the IRB form, the "first use of the test article" will commence at the time of first infusion of Remdesivir.

Submit form to: aasjirbsubmissions@stjoeshealth.org

For additional details on the IRB of Record process see SJMHS policy on "Expanded Access to Investigational Drugs and Biologics and Off-Label Use" below: https://saml.policymedical.net/policymed/anonymous/docViewer?stoken=f1e162db-50b4-4a1e-a457-797ef23c7500&dtoken=8037a83b-c714-48e8-8ae2-d8096bebebb2

Contact the SJMHS IRB of Record with any questions regarding the submission at 734-712-5470.