Remdesivir: Availability and Frequently Asked Questions Expanded Access for Treatment Programs of a Test Article

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Remdesivir Availability

Remdesivir is manufactured by Gilead Lifesciences and is only available through one of the pathways listed below:

1. Through a clinical trial
2. Through an Expanded Access Program
3. Through a Single Patient Emergency Investigational New Drug (EIND) use
4. Through FDA's Emergency Use Agreement (EUA)

More information on each of these options is presented below.

1. Clinical Trials (research)

There are currently several trials underway with the use of Remdesivir. Gilead has initiated two Phase 3 clinical studies to evaluate the safety and efficacy of Remdesivir in adults diagnosed with COVID-19. These randomized, open-label, multicenter studies began enrolling patients in March 2020 and will enroll a total of approximately 1,000 patients in the initial phase of the studies in countries with high prevalence of COVID-19.

One study will evaluate the safety and efficacy of both a 5-day and a 10-day dosing duration of remdesivir, in addition to standard of care, for patients with severe manifestations of COVID-19. More information on the Gilead study in patients with moderate disease can be found at https://clinicaltrials.gov/ct2/show/NCT04292730

The second study will evaluate the safety and efficacy of both a 5-day and a 10-day dosing duration of remdesivir in addition to standard of care for patients with moderate manifestations of COVID-19, compared to standard care alone. More information on the Gilead study in patients with severe disease can be found at https://clinicaltrials.gov/ct2/show/NCT04292899

The U.S. National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, has initiated a Phase 2 adaptive, randomized, double-blind, placebo-controlled trial into remdesivir as a potential treatment for hospitalized adult patients diagnosed with COVID-19. More information on the NIAID study can be found at https://clinicaltrials.gov/ct2/show/NCT04280705

These studies require review and approval by your local Institutional Review Board (IRB) prior to enrolling patients.
Due to the overwhelming interest in these studies it is not known if additional sites are being accepted for clinical trials. To learn more about becoming a site, reach out to the contact listed under the “Contact” section of the web listings.

2. Expanded Access Program (non-research)

In late March 2020 Gilead introduced an Expanded Access Program for remdesivir. This program provides sites with access to remdesivir on an emergency access basis, for a group of patients that meet the protocol criteria. More information on this program, and the patient criteria, can be found at https://clinicaltrials.gov/ct2/show/NCT04323761

While the Expanded Access Program is not research, it does require IRB review and approval prior to enrolling patients.

Due to remdesivir’s Emergency Use Authorization (EUA) approval on May 1, 2020, no additional sites are being accepted into the Expanded Access Program. Gilead has stated that once the drug distribution system for the EUA is in place, remdesivir’s EAP will be discontinued.


In late March 2020 Gilead significantly curtailed the criteria for requesting remdesivir for a single patient expanded access EIND. At this time this pathway is only available for pregnant women and children < 18 years of age with significant clinical manifestations. More information on this program, and the patient criteria, can be found at https://rdvcu.gilead.com/

See "Remdesivir Work Flow Expanded Access" document for further details on this program, including required IRB reporting for every patient use.

4. FDA’s Emergency Use Authorization (EUA) (non-research)

The U.S. FDA announced on May 1, 2020 that remdesivir had been granted Emergency Use Authorization (EUA) for the treatment of COVID-19. The U.S. government will coordinate the distribution of Gilead’s remdesivir supply to hospitals most heavily impacted by COVID-19, working with AmerisourceBergen as the exclusive distributor.

Information on the availability of remdesivir under the EUA for specific locations is pending and will be communicated through the distributor or your state public health department.

No IRB reporting is required for remdesivir administration under an EUA; however, under the terms of the EUA, a "Fact Sheet" must be made available to patients and healthcare providers. See the COVID-19 "Treatment Guidance" for additional details on the documentation of this process.

Healthcare providers should refer to FDA's "Fact Sheet for Health Care Providers: Emergency Use Authorization (EUA) of Remdesivir (GS-5734)" for details on the mandatory requirements for remdesivir administration under and EUA, including required reporting of adverse events. https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#covidtherapeutics

**Frequently Asked Questions**

This Frequently Asked Questions (FAQ) document has been created to provide operational guidance on Expanded Access for Treatment Programs and guidance for informed consent when PPE is in place for droplet or airborne precautions.

**Q1.** Is Expanded Access of a test article considered research? There are instructions in the recommended workflow about having to report to the IRB.

**A1.** There are three types of Expanded Access:
- For individual patients, including Single Emergency Use
- For intermediate-size patient populations
- For wide-spread use

The main distinction between expanded access and the ‘usual’ clinical trial/study of an investigational drug under an IND is that expanded access uses are not primarily intended to obtain information about the safety or effectiveness of a drug. However, there are activities in each type of expanded access that requires involvement of the Institutional Review Board (IRB).

**Single Emergency Use**

Single Emergency Use of a test article does NOT require prospective review and approval by the IRB. The treating physician is required by regulation to report the emergent single use to the IRB within five (5) working days of first administration of the test article.

**Expanded Access – Intermediate and Wide-spread Use**

Intermediate Use and Wide-spread Use Expanded Access requires prospective review and approval by the IRB before treatment with the investigational drug may begin. Wide-spread Use Expanded Access typically has a protocol with an informed consent; both documents are to be reviewed (along with all other documents provided by the sponsor) and approved by the IRB before treatment may begin.

**Q2.** What form needs to be completed for Single Emergency Use?

**A2.** Complete the SJMHS IRB No. 1 *PERMISSION FOR EMERGENCY USE OF TEST ARTICLE* form https://www.stjoeshealth.org/assets/documents/irb/sjmhs-emergency-use-
permission-fillable-word.doc (the PERMISSION form) must be completed and filed with the SJMHS IRB No. 1 within five (5) working days of first administration of the test article.

Q3. How is Informed Consent obtained for Single Emergency Use when the patient is unable to consent and there is no Legally Authorized Representative (LAR) / Healthcare Power of Attorney (HPOA)?

A3. FDA regulations permit emergency use of a test article without informed consent by the patient or LAR/HPOA. In this instance, the signing of the informed consent is waived and replaced by the PERMISSION FOR EMERGENCY USE OF TEST ARTICLE form.

   A. Complete the form.
   B. Scan the completed original PERMISSION form in the EMR.
   C. File the original PERMISSION form with the other documents collected for the emergent use.

Q4. Our ministry has a patient who is being treated with remdesivir under Single Emergency Use; what is the best way to file the PERMISSION form with IRB No. 1?

A4. Submit a copy of the completed PERMISSION form to: asjirbsubmissions@stjoeshealth.org.

The lead pharmacist may also submit a weekly summary report to IRB No. 1 listing the patients, dosage, adverse events, outcomes, etc. to: asjirbsubmissions@stjoeshealth.org

Q5. The patient who has been selected to participate in an expanded access program is in a negative-pressure isolation room. The paper informed consent, once in the room, is considered contaminated by infectious material and cannot be taken out of the room. If we follow the patient verbal informed consent process, that requires 2 colleagues to gown/mask up and enter the room (1 to explain and discuss the informed consent, 1 to witness the verbal consent). What logistical / operational recommendations do you have to deliver the informed consent?

A5. Follow your ministry's normal work instructions for garnering verbal consent, the FDA Guidance On Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic, and the guidance provided in the Collection of Patient Verbal Consent (3/19/20) (on COVID-19 Pulse page) to ensure colleague safety and conservation of supplies.

Remember that the person who obtains the consent is the one who signs. If the treating physician has delegated the responsibility to a research coordinator to obtain the consent, this delegation is to be recorded on a delegation log kept in the expanded access program/study record.

We do not recommend having the patient sign a paper copy of the informed consent and subsequently have a digital image taken of the signed consent (e.g., photograph on a healthcare colleague’s cell phone). If this is the only option available at the ministry, discuss with the ministry's Privacy Officer on how to compliantly achieve capturing a digital image.
Best practice is to utilize an electronic method for obtaining the informed consent, such as having the consent document on a tablet or similar electronic device that is in the patient's room where the patient can sign it electronically. The e-signed document can then be stored in the EMR and the expanded access program/study record.

Remote Consent Process via Phone Call/Video Conference with Patient using a Tablet, Computer, or Other Device (The patient is able to give consent.)

- A health care colleague enters the room during the normal course of clinical care and brings up on the device the informed consent for the patient.
  - This colleague may be the witness to the informed consent process; if so, the colleague remains in the room.
- Treating physician/designee conducts a phone call/video conference with the patient, a witness, and any additional participants as selected by the patient (e.g., LAR/HPOA, next of kin).
- The phone call/video conference:
  - Identify and introduce each person who is on the call.
  - Physician/Designee reviews the consent with the patient and answers all questions.
  - Patient agrees to participate in the study and signs and dates the consent electronically on the device.
- Health care colleague who has been present in the patient room during consent process signs and dates the consent electronically on the device as a witness.
- The e-signed consent is emailed to the physician/designee by the health care colleague.
- Physician/Designee signs electronically as a person obtaining consent.
- Fully signed e-consent is saved electronically into the EMR record and the expanded access program/study record.
- Send a copy of the signed and dated e-consent to the patient (e.g., email, fax, mail, etc.).

The guidance below assumes that there is no electronic method for obtaining the informed consent at the ministry.

Verbal Consent with the LAR/HPOA (The patient is unable to give consent and their LAR/HPOA is not able to be physically present in the hospital.)

- Phone Call/Video Conference with the LAR/HPOA:
  - Identification and introduction of each person who is on the call.
  - The treating physician/designee reviews the consent with the LAR/HPOA and answers all questions.
  - Witness confirms with the LAR/HPOA that all questions have been answered.
  - LAR/HPOA verbally gives consent.
- The physician/designee and the witness each sign and date the consent with the attestation statement VERBAL CONSENT OBTAINED FROM LAR/HPOA written on the consent.
- Document in the EMR the attestation statement 'Verbal consent obtained' with the names of the physician, witness, and LAR/HPOA, and date/time stamp.
- Scan the original signed and dated consent in the EMR.
File the original signed and dated consent with other documents associated with the expanded access program/study record.

Send a copy of the signed and dated e-consent to the LAR/HPOA (e.g., email, fax, mail, etc.).

**Remote Consent Process via Phone Call/Video Conference with Patient** (The patient is able to give consent. This option does not require any of the participants to be in the patient's room.)

A health care colleague enters the room during the normal course of clinical care and, *if allowed per ministry work instructions for negative-pressure isolation rooms*, brings a paper copy of the informed consent to the patient.

Treating physician (or designee) conducts a phone call/video conference with the patient, a witness, and any additional participants as selected by the patient (e.g., LAR/HPOA, next of kin). Likely the physician and witness are together (in the same room) for the phone call/video conference.

- The phone call/video conference:
  - Identify and introduce each person who is on the call.
  - Physician/Designee reviews the consent with the patient and answers all questions.
  - Witness confirms with the patient that all questions have been answered.
  - Physician/Designee verbally confirms that the patient is willing to receive treatment and participate in the expanded access program/study; physician/designee documents VERBAL CONSENT OBTAINED on the informed consent document, signs and dates the document while the witness is listening on the phone/video conference. Witness signs and dates the document.
  - Patient verbally confirms that they would like to participate in the expanded access program/study; signs and dates the informed consent document that is in their possession.

Attestation by physician/designee and witness on a copy of the informed consent document:

- The physician/designee and witness each sign and date the consent with the attestation statement VERBAL CONSENT OBTAINED VIA PHONE/VIDEO CONFERENCE written on the consent.
- Document in the EMR and the expanded access record the attestation statement *'Verbal consent obtained via phone/video conference'* and the statement *'informed consent document signed by the patient was not retained due to contamination of the document by infectious material'*; with the names of the physician and witness, date/time stamp.

Scan the original signed and dated consent in the EMR.

Place the original signed and dated consent into the expanded access program/study record.

Paper copy of the informed consent remains in the room until it is properly disposed of per ministry work instructions for disposal of contaminated items in a negative-pressure isolation room.
Q6. Who is responsible for managing the data and reporting back to the FDA regarding the EIND?

A6. The physician who submitted the Expanded access IND or EIND is responsible for managing the data and reporting back to the FDA regarding the status of the patient and report any serious adverse events that occurred during treatment.

Per FDA Guidance *Individual Patient Expanded Access Applications*: Form FDA 3926 (October 2017), "Under individual patient expanded access INDs, the physician who submits an IND is considered a sponsor-investigator (as defined in § 312.3) and is responsible for complying with the responsibilities for both sponsors and investigators to the extent they are applicable to the expanded access use, including submitting IND safety reports and annual reports and maintaining adequate drug disposition records. The responsibilities of sponsors and investigators are described in subpart D of 21 CFR part 312 and in related guidance documents, for example, in the guidance for industry *Investigator Responsibilities—Protecting the Rights, Safety, and Welfare of Study Subjects.*"

**References and Other Materials:**

21 CFR 312 Subpart I — *Expanded Access to Investigational Drugs for Treatment Use*

Expanded Access: [https://www.fda.gov/news-events/public-health-focus/expanded-access](https://www.fda.gov/news-events/public-health-focus/expanded-access)

How to submit Expanded Access forms (all types): [https://www.fda.gov/news-events/expanded-access/expanded-access-how-submit-request-forms](https://www.fda.gov/news-events/expanded-access/expanded-access-how-submit-request-forms)


SJMHS IRB Policy & Procedure *Expanded Access to investigational Drugs and Biologics and Off-Label Use*
SJMHS IRB No. 1  *PERMISSION FOR EMERGENCY USE OF TEST ARTICLE* form
https://www.stjoeshealth.org/assets/documents/irb/sjmhs-emergency-use-permission-fillable-word.doc