Convalescent Plasma

Background

Responding to the unprecedented challenge of fighting coronavirus disease 2019 (COVID-19), the U.S. Government is supporting a national Expanded Access Program (EAP) to collect and provide convalescent plasma to patients in need across the country. Plasma from recovered COVID-19 patients contains antibodies that may help fight the disease.

Working collaboratively with industry, academic, and government partners, Mayo Clinic will serve as the lead institution for the program.[1]

The Mayo protocol requires the patient or family member to consent to receiving plasma from someone who has recovered from COVID-19. Their plasma contains substances that could improve chances of recovery. Only hospitalized patients referred by their health care provider will participate in this protocol.

Following registration on the protocol in one of the participating centers and provision of informed consent, patients will be given a transfusion with one unit of ABO-compatible convalescent plasma obtained from an individual who has recovered from documented infection with SARS-CoV-2.

nThrive has focused on the EAP process through Mayo and has endeavored to consolidate the detailed information for registration, of not only the patient, but the physician and facility as well. More expansive information is defined under the following links.

https://www.uscovidplasma.org

https://www.fda.gov/vaccines-blood-biologics/investigational-new-drug-ind-or-device-exemption-ide-process-cber/recommendations-investigational-covid-19-convalescent-plasma

In addition, the us-covid-plasma website indicates that if adhering to the Mayo terms is not acceptable, local IRB and institution may apply for an emergency IND and use their own product and protocol and refers such providers to the FDA website for more information.

According to the us-covid-plasma website institutions wanting to participate in the EAP agree to:

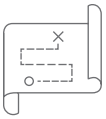
- ✓ Rely upon Mayo Clinic IRB by checking the box on the site and Physician/PI enrollment form.
- ✓ Abide by all US and state regulations and the Principles in the Belmont report.
- ✓ Use the approved consent form. (https://uscovidplasma.org/#consent).
- ✓ Not ask for any other written agreements. The FDA has waived certain requirements for us to allow the EAP to proceed as quickly as possible as exceptions to policy. The use of REDCap is one example. The use of typical written reliance agreements is another.

In addition, a site must be registered first, but only once, by either the physician/PI or their regulatory/IRB staff at https://www.uscovidplasma.org/ and then each physician/PI must register themselves. Each medical facility within a health system must also be registered.[2] Following that, they can consent and subsequently register patients for EAP enrollment following the guidelines below.

FDA has issued guidance to provide recommendations to health care providers and investigators on the administration and study of investigational convalescent plasma collected from individuals who have recovered from COVID-19 (COVID-19 convalescent plasma) during the public health emergency.

The guidance provides recommendations on the following:

- ✓ Pathways for use of investigational COVID-19 convalescent plasma.
- ✓ Patient eligibility.
- ✓ Collection of COVID-19 convalescent plasma, including donor eligibility and donor qualifications.
- ✓ Labeling.
- ✓ Record keeping.



Pathways

Because COVID-19 convalescent plasma has not yet been approved for use by the FDA, it is regulated as an investigational product. As such, administration of COVID-19 convalescent plasma by a health care provider must be under an Investigational New Drug (IND):

- ✓ Traditional institutional clinical trial IND.
- ✓ Mayo EA IND.
- ✓ Single-patient emergency IND application.[3]

Eligibility

To facilitate requests for eINDs for use of COVID-19 convalescent plasma to treat patients, health care providers seeking an emergency IND may want to consider the eligibility criteria used for the National Expanded Access Treatment Protocol. These criteria include:

- ✓ Laboratory confirmed COVID-19.
- ✓ Severe or immediately life-threatening COVID-19.
  - – Severe disease is defined as one or more of the following:
    - » shortness of breath (dyspnea)
    - » respiratory frequency ≥ 30/min
    - » blood oxygen saturation ≤ 93%
    - » partial pressure of arterial oxygen to fraction of inspired oxygen ratio < 300
    - » lung infiltrates > 50% within 24 to 48 hours
  - – Life-threatening disease is defined as one or more of the following:
    - » respiratory failure
    - » septic shock
    - » multiple organ dysfunction or failure
- ✓ Informed consent provided by the patient or health care proxy.

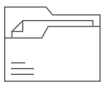
Plasma Collection

Health care providers or acute care facilities seeking to use COVID-19 convalescent plasma should include information in the IND submission that the COVID-19 convalescent plasma will be obtained from an FDA-registered blood establishment that follows the donor eligibility criteria and donor qualifications specified in collecting plasma from donors.

Labeling

The container label of COVID-19 convalescent plasma units must include the following.

- ✓ The following statement, "Caution: New Drug--Limited by Federal (or United States) law to investigational use."
- ✓ A reference to the circular of information.
- ✓ Use of a uniform container label. The FDA recommends the use of the International Society of Blood Transfusion (ISBT) format specified in the United States Industry Consensus Standard for the Uniform Labeling of Blood and Blood Components Using ISBT 128.
- ✓ The manufacturing process used and the expiration date.



Record Keeping

A health care provider who is participating in an IND, including an expanded access IND or eIND, must maintain the following records.

- ✓ For the COVID-19 convalescent plasma unit(s) administered to the COVID-19 patient.
  - – Include the unique identification number(s) (e.g., the ISBT donation identification number(s) of the unit(s).
- ✓ A 4-hour post infusion data form capturing the essential data on serious adverse events that are required by the Sponsor and US Government.
- ✓ Two additional short, data forms at days 7 and 30 if your patient(s) remain hospitalized.

nThrive contacted the us-covid-plasma organization regarding the cost of obtaining convalescent plasma. The consent form required by the Mayo EAP indicates that the plasma is free, and the patient is only liable for cost-sharing related to testing and other services related to care.

The response nThrive received stated: "There will be no charge associated with the unit of plasma to hospitals or to patients. The federal program will reimburse for plasma collection costs, regardless of the supplier (i.e., Red Cross, Vitalant, OneBlood, ABC, New York Blood Center, or another local supplier).

In regard to shipping and administrative efforts with plasma transfusion, please follow standard operating procedures for billing to patient of blood products. Thus, we cannot advise further.

This is an Expanded Access Program protocol and is not a qualifying clinical trial; a coverage analysis was not completed. There is no associated site funding for this project as the goal is to streamline the IND process for convalescent plasma therapy and reduce administrative burdens for clinicians."

As the protocol requires the patient be admitted to inpatient care and of high acuity to be eligible for receiving convalescent plasma, the addition of a specific HCPCS would not be necessary. Even though the convalescent plasma is collected and frozen as is plasma for other use it is being provided in this context as investigational and if billed would need a means of indicating such on the claim. CMS is also providing a higher DRG rate, based on diagnosis code U07.1 on the claim, for patients admitted with COVID-19 Coronavirus which would seem to cover the cost of transfusion as part of routine nursing care.

Other programs or insurances may provide different instruction but based on the Mayo EAP guidance available, nThrive is not recommending adding the product to the CDM as a chargeable item. If an order-entry mechanism is needed the product could be linked to a non-billable charge of $0.00.

Guidance

- ✓ Take actions now to determine how the hospital will procure convalescent plasma.
- ✓ Ensure adherence to FDA guidelines.
- ✓ If registering to receive plasma from Mayo, identify requirements for each step outlined and register each medical facility within the health system where convalescent plasma will be transfused.
  - – Review protocol for transfusion with medical staff and implement procedures to identify patients that meet criteria prior to convalescent plasma being ordered.
  - – Create a zero-dollar charge for convalescent plasma.
  - – Determine if transfusion charges will be captured based on guidance provided.
- ✓ Implement strategies to ensure record keeping and documentation meet the required protocols.

Sources

1. https://www.uscovidplasma.org/#why
2. https://www.uscovidplasma.org/faq.html
3. https://www.fda.gov/vaccines-blood-biologics/investigational-new-drug-ind-or-device-exemption-ide-process-cber/recommendations-investigational-covid-19-convalescent-plasma ■