Investigational COVID-19 Convalescent Plasma - Emergency INDs

A licensed physician must request the Emergency IND (eIND) and obtain the COVID-19 convalescent plasma from a blood center. FDA does **not** provide COVID-19 convalescent plasma for eINDs.

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The Food and Drug Administration (FDA or Agency) plays a critical role in protecting the United States from public health threats including the Coronavirus Disease 2019 (COVID-19) pandemic. FDA is committed to doing everything we can to provide timely response efforts to this pandemic and facilitate access to investigational drugs for use in patients with serious or immediately life-threatening COVID-19 infections.

One investigational treatment being explored for COVID-19 involves the use of convalescent plasma collected from recovered COVID-19 patients. It is possible that convalescent plasma that contains antibodies to SARS-CoV-2 (the virus that causes COVID-19) might be effective against the infection. Use of convalescent plasma has been studied in outbreaks of other respiratory infections, including the 2009-2010 H1N1 influenza virus pandemic, 2003 SARS-CoV-1 epidemic, and the 2012 MERS-CoV epidemic. Although promising, convalescent plasma has not been shown to be effective in every disease studied. It is therefore important to determine through clinical trials, before routinely administering convalescent plasma to patients with COVID-19, that it is safe and effective to do so. Investigators wishing to study the use of convalescent plasma are encouraged to submit requests to FDA for investigational use under the traditional IND regulatory pathway (21 CFR 312).

Although participation in clinical trials is one way for patients to obtain access to convalescent plasma, these may not be readily available to all patients in potential need. Therefore, given the public health emergency that the expanding COVID-19 outbreak presents, while clinical trials are being conducted, FDA is facilitating access to COVID-19 convalescent plasma for use in patients with serious or immediately life-threatening COVID-19 infections through the process of single patient emergency Investigational New Drug Applications (eINDs) for Individual patients under 21 CFR 312.310. This process allows the use of an investigational drug for the treatment of an individual patient by a licensed physician upon FDA authorization. This does not include the use of COVID-19 convalescent plasma for the prevention of infection.

Healthcare providers interested in the emergency use of investigational COVID-19 convalescent plasma under a single patient emergency IND should consider the following:

- **COVID 19 Convalescent Plasma**

COVID-19 convalescent plasma must only be collected from recovered individuals if they are eligible to donate blood (21 CFR 630.10, 21 CFR 630.15). Required testing must be performed (21 CFR 610.40) and the donation must be found suitable (21 CFR 630.30).

Additional considerations for donor eligibility should be addressed, as follows:

- Prior diagnosis of COVID-19 documented by a laboratory test
- Complete resolution of symptoms at least 14 days prior to donation
- Female donors negative for HLA antibodies or male donors
- Negative results for COVID-19 either from one or more nasopharyngeal swab specimens or by a molecular diagnostic test from blood. A partial list of available tests can be accessed at https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations (/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations).
- Defined SARS-CoV-2 neutralizing antibody titers, if testing can be conducted (e.g., optimally greater than 1:320)

The container label of COVID-19 convalescent plasma units must include the following statement, "Caution: New Drug--Limited by Federal (or United States) law to investigational use." (21 CFR 312.6 (a))

- **Eligible patients for use under expanded access provisions:**
    - Must have laboratory confirmed COVID-19
    - Must have severe or immediately life-threatening COVID-19, for example:[1]
        - Severe disease is defined as:
            - dyspnea,
            - respiratory frequency ≥ 30/min,
            - blood oxygen saturation ≤ 93%,
            - partial pressure of arterial oxygen to fraction of inspired oxygen ratio < 300, and/or
            - lung infiltrates > 50% within 24 to 48 hours
        - Life-threatening disease is defined as:
            - respiratory failure,
            - septic shock, and/or

        - multiple organ dysfunction or failure
    - Must provide informed consent

How to obtain authorization for use of COVID-19 convalescent plasma

- For request that are not highly time sensitive (response from FDA provided within 4 to 8 hours), the requesting physician may contact FDA by completing form 3926 (https://www.fda.gov/media/98616/download (/media/98616/download)) and submitting the form by email to CBER_eIND_Covid-19@FDA.HHS.gov (mailto:CBER_eIND_Covid-19@FDA.HHS.gov).
    - The completed form should include a brief clinical history of the patient, including: diagnosis, current therapy, and rationale for requesting the proposed investigational treatment in order to meet the expanded access use requirements of 21 CFR 312.305 and 312.310.
    - The form should include information regarding where the COVID-19 convalescent plasma will be obtained.
    - Providers should complete the form to the extent possible, and FDA will work with the provider if additional information is required.
    - FDA will review the request and, upon approval, FDA will send the requesting physician a confirmatory email that includes the emergency IND number.
- In the event of an emergency that is highly time sensitive (response required in less than 4 hours) or where the provider is unable to complete and submit form 3926 due to extenuating circumstances, the provider may contact FDA's Office of Emergency Operations at 1-866-300-4374 to seek verbal authorization.
    - If verbal authorization is given, the requestor must agree to submit an expanded access application (e.g., form 3926) within 15 working days of FDA's authorization of the use.

In addition to the above, FDA is continuing to work with its government partners including the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC) to develop master protocols for use by multiple investigators in order to coordinate the collection and use of COVID-19 convalescent plasma.

[1]*Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. Published online February 24, 2020. doi:10.1001/jama.2020.2648*