| | Expanded Access Program | Emergency Use Authorization |
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| **Description** | An Expanded Access Program **(EAP)** is a potential pathway for a patient with a serious or immediately life-threatening disease or condition to gain access to an investigational medical product (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy option is available. Expanded access requires submission of an expanded access protocol to an existing investigational new drug **(IND)** application or a new expanded access IND, and is subject to certain IND requirements such as IND safety reporting, IRB approval and informed consent.<br><br>**The Mayo Clinic EAP:** Mayo Clinic received permission from the FDA on 1 April 2020 to start an EAP for COVID-19 convalescent plasma for administration to patients with COVID-19 (see USCOVIDplasma.org). The Mayo Clinic EAP was designed primarily to provide patient access to convalescent plasma, secondarily to examine safety , and finally to examine efficacy within the limits of the study design (i.e., the EAP is not a randomized clinical trial/ **RCT**). | In certain types of emergencies, the HHS Secretary may issue a determination and declaration under the Food, Drug and Cosmetic Act which permits the FDA to issue an emergency use authorization **(EUA)** to facilitate access to medical countermeasures (drugs, biologics, vaccines, and/or devices) that can be used to diagnose, treat or prevent a serious disease or condition in a public health emergency.<br><br>The FDA decides whether the use of the product is likely to be more helpful than harmful for the emergency situation (i.e., the agency determines that the known and potential benefits of the medical product for its intended use outweighs any known and/or potential risks). This authorization is reserved for the *emergency situation* and is NOT the same as FDA approval or licensure to use a product/device.<br><br>**What this means for the Mayo Clinic EAP:** The Mayo Clinic EAP has shown that convalescent plasma for COVID-19 patients in serious or life-threatening condition is safe to use and can reduce mortality if 1) given early (within 3 days of diagnosis) and 2) has a higher antibody content. These findings are part of the consideration the FDA makes when deciding to transition from an EAP to EUA. *Once the FDA decides that enough evidence exists to safely administer the product under an EUA they will authorize stopping the Mayo Clinic EAP and starting a EUA.* |

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| **Criteria** | **Criteria to enroll in the Mayo Clinic EAP:** COVID-19 convalescent plasma is available in the US and its territories through the EAP to qualified registered treating physicians at registered sites for patients that have met specific inclusion and exclusion criteria and provided informed consent. COVID-19 convalescent plasma is considered an *investigational product*. The EAP is *not* a clinical trial. | An EUA allows COVID-19 convalescent plasma to be distributed and used by licensed health care providers to treat adults with serious or life-threatening COVID-19. Treating patients with convalescent plasma under the EUA is considered *part of the practice of medicine* in a temporary *emergency* situation as long as the declaration of the public health emergency exists. The EUA is *not* a clinical trial. |
| **Consent** | **Obtaining consent in the Mayo Clinic EAP:** *Consent is required.* Mayo Clinic is the central IRB for the EAP. Informed consent must be obtained from the patient or LAR prior to enrollment in the program and receipt of convalescent plasma using the Mayo Clinic EAP-specific IRB approved consent form. | **Consent is required**<br>The site is responsible for obtaining informed consent per institutional policy. |
| **Serious Adverse Event (SAE) Reporting (i.e., reporting side effects)** | **Reporting SAEs under the Mayo Clinic EAP:** *Reporting SAEs is a Federal Requirement.* Treating physicians in the EAP agree to provide information on SAEs and to fill out all forms, etc. for the EAP when they join the study. It is a Federal Requirement that physicians report SAEs to the Sponsor (Mayo Clinic) who will evaluate the nature of the adverse event and report to the FDA as a part of the IND requirement. | **Reporting Adverse Events**<br>Health care providers must maintain records and conduct a thorough investigation of adverse reactions after transfusion of convalescent plasma, and must report fatalities related to transfusion, as required under 21 CFR 606.170. |
| **Detailed Information about the Product (i.e., COVID-19 convalescent plasma)** | Information about the product such as use, dosing, administration and risks is available in the EAP Protocol, Consent and Investigator's Brochure and is provided to the treating physicians participating in the EAP.<br><br>**Mayo Clinic's EAP:** Information about the product (i.e., COVID-19 convalescent plasma) can be found in the Mayo Clinic EAP Protocol, Consent and Investigator's Brochure are available on the website USCOVIDplasma.org. | The details of the product (i.e., COVID-19 convalescent plasma) including its use, dosing, administration and risks are provided in a Fact Sheet by the FDA to health care providers and patients. |
| **FDA IND Required?** | Yes | No |

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| **IRB Approval Required?** | Yes, approval by the local or a central IRB is required prior to initiation of the EAP.<br>**Mayo Clinic serves as the central IRB for the COVID-19 convalescent plasma EAP.** | No, IRB Approval is **not** required. |
| **Ordering, Billing and Charging** | Patients may not be charged for the use of an investigational product unless prior approval has been obtained from the FDA under 21 CFR 312.8.<br><br>**Mayo Clinic EAP:** Patients are not charged for the use of COVID-19 convalescent plasma in the Mayo Clinic EAP. | CMS Announces New Hospital Procedure Codes for Therapeutics in Response to the COVID-19 Public Health Emergency effective August 1, 2020 (including convalescent plasma).<br><br>ICD-10 MS-DRGs Version 37.2 Effective August 1, 2020 |

***How does a EUA differ from Expanded Access ?***

An EUA is a temporary measure, pursuant to a Secretary of Health and Human Services declaration, in which the FDA Commissioner may authorize unapproved medical products (i.e., COVID-19 convalescent plasma) or unapproved uses of approved medical products for use in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by chemical, biological, radiological or nuclear (CBRN) threat agents. In issuing an EUA, the FDA must determine, among other things, that the product may be effective in diagnosing, treating, or preventing a serious or life-threatening disease or condition caused by the CBRN agent; that the known and potential benefits outweigh the known and potential risks for the product; and that there are no adequate, approved, and available alternatives.

While EUAs may only be issued while the Secretary of Health and Human Services declaration justifying emergency use is in effect, requests for **expanded access** to an investigational drug may be submitted to the FDA and considered at any time. **Expanded access** is a potential pathway for a patient with a serious or immediately life-threatening disease or condition to gain access to an investigational medical product (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available. **Expanded access** requires submission of an expanded access protocol to an existing investigational new drug (IND) application or a new expanded access IND, and is subject to certain IND requirements such as IND safety reporting, IRB approval and informed consent.

***With an EUA in place, will COVID-19 Convalescent Plasma continue to be available through Expanded Access?***

**Yes**. If a patient does not qualify for access under the EUA but may benefit from the use of COVID-19 convalescent plasma and meets the criteria for Expanded Access, the treating physician may submit a request to the FDA for an Expanded Access IND or request treatment under an emergency investigational new drug (eIND) application. Examples of situations where this might be the case include a **child or adolescent** who is not an adult and so does not qualify for the EUA but is experiencing severe or life-threatening disease, or a patient who is **not yet considered to be in a life-threatening condition** but is rapidly progressing to that state.

***With a EUA in place, will COVID-19 Convalescent Plasma continue to be available through the Mayo Clinic EAP?***

**No**. Once the FDA transitions the availability of COVID-19 convalescent plasma from an EAP to a EUA, enrollment in the Mayo Clinic EAP will stop. All patients that were enrolled in the Mayo Clinic EAP prior to the transition will be able to provide convalescent plasma under the EAP and are required to complete all of the SAE reporting and other forms that are associated with the EAP. This is a Federal Requirement.