Advancing Transfusion and Cellular Therapies Worldwide

Toolkit for COVID-19 Convalescent Plasma (CCP) under Emergency Use Authorization (EUA)

Updated: August 28, 2020, 315pm

This toolkit will continue to be updated.

Refer to NEW INFORMATION on page 3 - AABB has added an Overview of the EUA for CCP:

- ✓ intended to assist AABB members until an FDA guidance for the EUA is available
- ✓ which includes both:
  - EUA Requirements from the Letter of Authorization, and
  - Comments from FDA on August 26, 2020.

The rapidly evolving information related to the Emergency Use Authorization for CCP is expected to result in updates to the current recommendations:

- FDA's May 1, 2020 Investigational CCP Guidance for Industry, and
- FDA's webpage, Recommendations for Investigational COVID-19 Convalescent Plasma.

NEW INFORMATION:
Overview of the EUA for CCP, 08 28 2020, 315pm

The Overview, linked here:

- ✓ Is intended to assist AABB members until an FDA guidance for the EUA is available
- ✓ Includes both:
  - EUA Requirements from the Letter of Authorization, and
  - Comments from FDA on August 26, 2020.

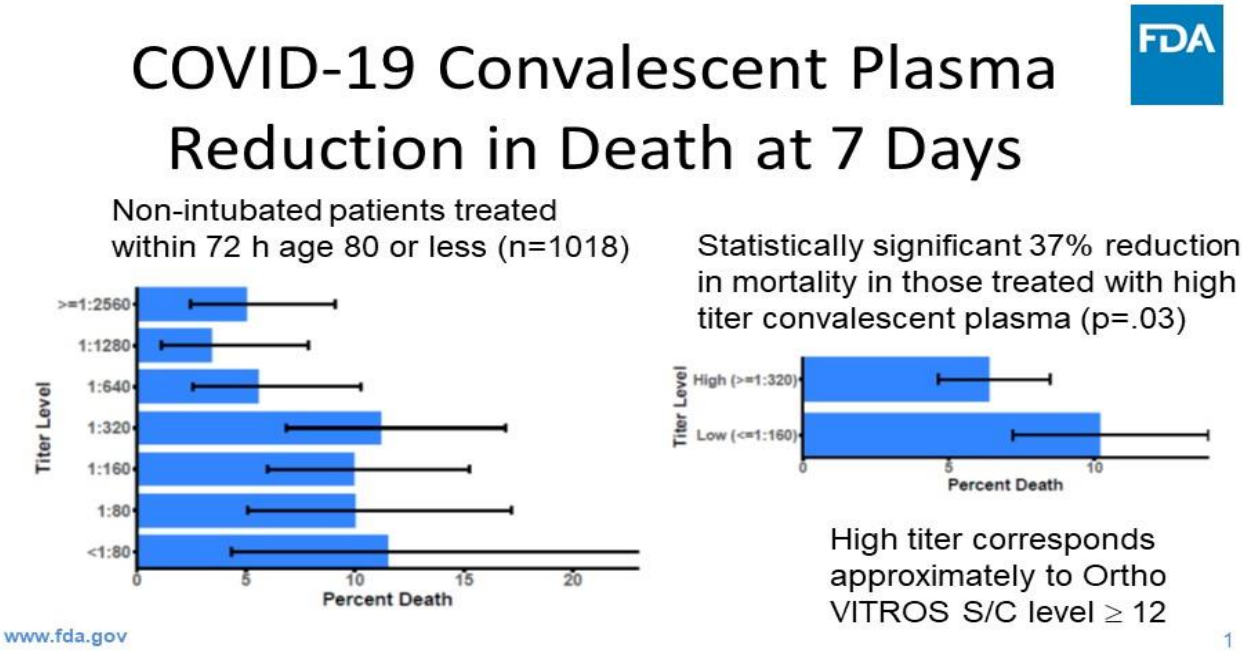
Events of August 23, 2020

1- FDA provided this statement:
"One investigational treatment being explored for COVID-19 is the use of convalescent plasma collected from individuals who have recovered from COVID-19. On August 23, 2020 FDA issued an Emergency Use Authorization (EUA) for COVID-19 Convalescent Plasma. In addition, the Recommendations for Investigational COVID-19 Convalescent Plasma page provides information on the pathways available outside of the EUA for administering or studying the use of COVID-19 convalescent plasma. It is critical to continue to enroll and complete randomized clinical trials to fully answer the questions about the effectiveness of convalescent plasma…Health care providers or acute care facilities should obtain COVID-19 convalescent plasma from an FDA-registered blood establishment."

2- EUA request for CCP sponsored by the Office of the Assistant Secretary for Preparedness and Response.

3- FDA News Release: FDA Issues Emergency Use Authorization, stating:
"Today, the U.S. Food and Drug Administration issued an emergency use authorization (EUA) for investigational convalescent plasma for the treatment of COVID-19 in hospitalized patients as part of the agency's ongoing efforts to fight COVID-19. Based on scientific evidence available, the FDA concluded, as outlined in its **decision memorandum**, this product may be effective in treating COVID-19 and that the known and potential benefits of the product outweigh the known and potential risks of the product."

"The EUA remains in effect until the termination of the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biologics for prevention and treatment of COVID-19. The EUA may be revised or revoked if it is determined the EUA no longer meets the statutory criteria for issuance."



*MORE INFORMATION is provided in the **news release**.*

4- FDA posted the Clinical/decision memorandum - REFER to the memorandum for detailed information supporting these **Conclusions:**

- COVID-19 Convalescent Plasma meets the eligibility criteria for Emergency Use Authorization.
- COVID-19 Convalescent Plasma **may be effective** in the treatment of COVID-19 and it is reasonable to believe that the known and potential benefits of CCP outweigh the known and potential risks of the product for the proposed EUA.
- Current evidence suggests **clinical benefit is most likely in patients treated early in the course** of the disease (e.g., prior to intubation) and with the use of CCP with higher antibody levels or neutralization activity.
- Current data are limited by the unavailability of validated assays of antibody levels or neutralization activity in CCP. Based on the available data, it is **reasonable to use the Ortho VITROS IgG assay with an S/C cutoff of 12 or greater** as a manufacturing potency test to qualify high titer units of CCP.
- Based on the available evidence, CCP without a result of 12 or greater in the Ortho VITROS assay meets the criteria for issuance of an EUA because, among other things, it is reasonable to believe it may be effective in treating COVID-19 and the **known and potential benefits of the product outweigh its known and potential risks**. Such units must be labeled as "COVID-19 Convalescent Plasma of Low Titer." Health care providers can decide whether to use these units based on an individualized determination of potential benefit and risk.
- **Randomized controlled trials are required to show definitive evidence of safety and efficacy** and to determine the optimal product attributes and appropriate patient populations for the use of COVID-19 Convalescent Plasma.

5- Fact Sheets – "**The EUA requires that fact sheets** providing important information about using COVID-19 convalescent plasma in treating COVID-19 be **made available to health care providers and patients**, including dosing instructions and potential side effects. Possible side effects of COVID-19 convalescent plasma include

allergic reactions, transfusion-associated circulatory overload, and transfusion associated lung injury, as well as the potential for transfusion-transmitted infections."

- The Fact Sheet for **health care providers** includes a description of the product and information such as drug interactions, side effects, risks, benefits and risk-benefit assessment. The Fact Sheet also includes the following:

  Dosage
  Health care providers will administer COVID-19 convalescent plasma according to standard hospital procedures and institutional medical and nursing practices.
  Clinical dosing may first consider starting with one convalescent plasma unit (about 200 mL), with administration of additional convalescent plasma units based on the prescribing physician's medical judgment and the patient's clinical response.
  Patients with impaired cardiac function and heart failure may require a smaller volume or more prolonged transfusion times.

  Administration
  Administer COVID-19 convalescent plasma infusion through a peripheral or central venous catheter according to standard institutional medical and nursing practices for the administration of plasma (http://www.aabb.org/tm/coi/Documents/coi1017.pdf).

  Storage
  COVID-19 convalescent plasma, may be stored frozen at -18℃ or colder, and has an expiration date one year from the date of collection. Once thawed, it can be refrigerated for up to 5 days prior to patient transfusion.

- The Fact Sheet for **patients** provides general information to inform the patient and patient's parents/caregivers.

6- The EAP website www.USCOVIDplasma.org has posted an updated message:

> **"The Mayo Clinic-led expanded access program will be discontinuing new physician and new patient enrollments effective 1159 pm local time August 28, 2020. COVID-19 convalescent plasma remains available through emergency use authorization."**