FACT SHEET FOR HEALTH CARE PROVIDERS

EMERGENCY USE AUTHORIZATION (EUA) OF COVID-19 CONVALESCENT PLASMA FOR TREATMENT OF CORONAVIRUS DISEASE 2019 (COVID-19)

AUTHORIZED USE

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product, COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies, for the treatment of COVID-19 in patients with immunosuppressive disease or receiving immunosuppressive treatment, in either the outpatient or inpatient setting.

This EUA is based on results from clinical trials of convalescent plasma and related passive immune therapies conducted during the current outbreak and data obtained from the National Expanded Access Program (EAP) sponsored by the Mayo Clinic. Data suggest that use of COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies may be effective in treating COVID-19 in patients with immunosuppressive disease or receiving immunosuppressive treatment.

For the purposes of this EUA, immunosuppressive treatment does not include immunosuppressive treatment administered specifically for the purpose of treating COVID-19 (e.g., systemic corticosteroids, interleukin-6 inhibitors).

FDA will continue to evaluate this authorization based on additional data that become available.

Given that the clinical evidence in patients with immunosuppressive disease or receiving immunosuppressive treatment remains limited, data from additional randomized, controlled trials are needed.

LIMITATIONS OF AUTHORIZED USE

COVID-19 convalescent plasma is not authorized to treat immunocompetent patients with COVID-19. Results from randomized controlled trials in hospitalized patients indicate that these patients are unlikely to benefit from COVID-19 convalescent plasma. In addition, alternative therapies in immunocompetent patients prior to hospitalization are authorized for emergency use and have more consistently demonstrated clinical benefit.

INSTRUCTIONS FOR HEALTH CARE PROVIDERS

As the healthcare provider, you must communicate to your patient or parent/caregiver, as age appropriate, information consistent with the "Fact Sheet for Patients and Parents/Caregivers" (and provide a copy of the Fact Sheet) prior to the patient receiving COVID-19 convalescent plasma, including:

1. FDA has authorized the emergency use of COVID-19 convalescent plasma, which is not an FDA-approved biological product, in patients with immunosuppressive disease or receiving immunosuppressive treatment.

2. The patient or their caregiver has the option to accept or refuse administration of COVID-19 convalescent plasma.

3. The significant known and potential risks and benefits of COVID-19 convalescent plasma and the extent to which such risks and benefits are unknown.

4. Information on available alternative treatments and the risks and benefits of those alternatives, including information from clinical trials.

If providing this information will delay the administration of COVID-19 convalescent plasma to a degree that would endanger the lives of patients, the information must be provided to the patients as soon as practicable after convalescent plasma is administered.

For information on clinical trials that are testing the use of COVID-19 convalescent plasma for COVID-19, please see www.clinicaltrials.gov.

PRODUCT DESCRIPTION

COVID-19 convalescent plasma is human plasma collected by FDA registered or licensed blood establishments from individuals whose plasma contains high titers of anti-SARS-CoV-2 antibodies, and who meet all donor eligibility requirements (21 CFR 630.10 and 21 CFR 630.15) and qualifications. Convalescent plasma is qualified and labeled as having high titer anti-SARS-CoV-2 antibodies based on testing accepted by FDA under this EUA. Qualification of COVID-19 convalescent plasma as high titer is based on serologic correlates of neutralizing activity, i.e., the ability of the donor antibodies to block infection by reference strains of the SARS-CoV-2 virus in laboratory tests.

DOSAGE, ADMINISTRATION, AND STORAGE OF COVID-19 CONVALESCENT PLASMA

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 unit of COVID-19 convalescent plasma (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 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°C or colder and has an expiration date of one year from the date of collection. Once thawed, it can be refrigerated for up to 5 days prior to patient transfusion.

DRUG INTERACTIONS

COVID-19 convalescent plasma may be contraindicated in patients with a history of severe allergic reactions or anaphylaxis to plasma transfusion.

SIDE EFFECTS, RISKS, BENEFITS, AND RISK-BENEFIT ASSESSMENT

Side Effects
Known side effects and hazards associated with plasma transfusion include transfusion-transmitted infections (e.g., HIV, hepatitis B, hepatitis C), allergic reactions, anaphylactic reactions, febrile nonhemolytic reactions, transfusion-related acute lung injury (TRALI), transfusion-associated cardiac overload (TACO), and hemolytic reactions. Hypothermia, metabolic complications, and posttransfusion purpura have also been described. Additional information on risks of plasma can be found in the (Association for the Advancement of Blood & Biotherapies (AABB) Circular of Information (http://www.aabb.org/tm/coi/Documents/coi1017.pdf).

Adverse event monitoring in studies of COVID-19 convalescent plasma has shown low overall rates of serious adverse events, and risks do not appear to exceed those associated with plasma transfusion in general.

Risks
A theoretical risk of administration of convalescent plasma is the phenomenon of antibody-dependent enhancement of infection (ADE). ADE has been described in other viral infections, such as dengue, and involves an enhancement of disease in the presence of certain antibodies. For coronaviruses, several mechanisms of ADE have been proposed, including the theoretical concern that antibodies to one type of coronavirus could enhance infection to another strain. Preparations with high titers of antibody against the same virus strain are thought to be less likely to cause ADE.

Another theoretical risk is that antibody administration may attenuate the immune response and make patients more susceptible to re-infection.

Benefits
COVID-19 is a serious and potentially fatal or life-threatening human disease. The potential benefits of COVID-19 convalescent plasma with high antibody titers in patients with

immunosuppressive disease or receiving immunosuppressive treatment could include improvement in symptoms, reduced need for supplemental oxygen and mechanical ventilation, and reduced mortality. Support for the safety and effectiveness of COVID-19 convalescent plasma is derived from past human experience with convalescent plasma, evidence of preclinical safety and efficacy in animal models, published studies on the safety and efficacy of COVID-19 convalescent plasma and related passive immune therapies in COVID-19 patients.

Risk-Benefit Assessment
Based on the totality of scientific evidence available at this time, the known and potential benefits of COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies outweigh the known and potential risks when administered to patients with immunosuppressive disease or receiving immunosuppressive treatment.

COVID-19 convalescent plasma is not authorized to treat immunocompetent patients who are hospitalized due to COVID-19. Results from randomized controlled trials indicate that these patients are unlikely to benefit from COVID-19 convalescent plasma. Transfusion of blood components, including COVID-19 convalescent plasma, is associated with several known risks. Therefore, the known and potential benefits of COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies do not outweigh the known and potential risks when administered to hospitalized patients who do not have immunosuppressive disease or are not receiving immunosuppressive treatment.

FDA has authorized other treatments for emergency use for the treatment of COVID-19 in adults and pediatric patients in the outpatient setting. These products have more consistently demonstrated clinical benefit in this population, and do not carry some of the risks associated with transfusion of blood components. Therefore, considering the availability of these products, the known and potential benefits of COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies do not outweigh the known and potential risks when administered to immunocompetent patients who are not hospitalized with COVID-19.

USE IN SPECIFIC POPULATIONS

Pediatric
Safety and effectiveness of COVID-19 convalescent plasma in the pediatric population has not been evaluated. The decision to treat patients <18 years of age with COVID-19 convalescent plasma should be based on an individualized assessment of risk and benefit. As with other blood components, pediatric patients may be at an increased risk of transfusion associated circulatory overload (TACO).

Geriatric
Safety and effectiveness of COVID-19 convalescent plasma has been evaluated in several randomized controlled trials and expanded access protocols that included geriatric patients. In the National Expanded Access Program sponsored by the Mayo Clinic, 105,717 patients were enrolled. 26,305 (24.9%) were 60-69 years of age, 21,585 (20.4%) were 70-79 years of age, and 13,229 (12.5%) were 80 years of age or older. These trials indicate that adverse event rates for COVID-19 convalescent plasma in the geriatric population are consistent with those expected for transfusion of blood components. Geriatric patients may be at increased risk of TACO.

Pregnancy
There are insufficient data to evaluate the risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes associated with COVID-19 convalescent plasma. COVID-19 convalescent plasma should only be used during pregnancy if the potential benefit outweighs the potential risk for the mother and the fetus.

Lactation
While maternal IgG is known to be present in human milk, there are insufficient data to evaluate whether or not transfused anti-SARS-CoV-2 antibodies in COVID-19 convalescent plasma are excreted in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COVID-19 convalescent plasma and any potential adverse effects on the breastfed infant from COVID-19 convalescent plasma.

REPORTING ADVERSE EVENTS

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.

APPROVED AVAILABLE ALTERNATIVES

There is no adequate, approved, and available alternative to COVID-19 convalescent plasma for the treatment of COVID-19 in patients with immunosuppressive disease or receiving immunosuppressive treatment. Additional information on COVID-19 treatments can be found at http://www.covid19treatmentguidelines.nih.gov/. The healthcare provider should visit https://clinicaltrials.gov/ to determine whether the patient may be eligible for enrollment in a clinical trial.

COUNTERMEASURES INJURY COMPENSATION PROGRAM

The Countermeasures Injury Compensation Program (CICP) is a federal program that has been created to help pay for related costs of medical care and other specific expenses to compensate people injured after use of certain medical countermeasures. Medical countermeasures are specific vaccines, medications, devices, or other items used to prevent, diagnose, or treat the public during a public health emergency or a security threat. For more information about CICP regarding the COVID-19 convalescent plasma used to prevent COVID-19, visit www.hrsa.gov/cicp, email cicp@hrsa.gov, or call: 1-855-266-2427.

AUTHORITY FOR ISSUANCE OF THE EUA

The Secretary of the U.S. Department of Health and Human Services (HHS) has declared a public health emergency that justifies the emergency use of drugs and biological products during the COVID-19 pandemic. In response, the FDA has issued an EUA for the unapproved product, COVID-19 convalescent plasma, to treat COVID-19 in patients with immunosuppressive disease or receiving immunosuppressive treatment.

Based on the totality of the scientific evidence available to date, it is reasonable to believe that COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies may be effective for the treatment of COVID-19 in patients with immunosuppressive disease or receiving immunosuppressive treatment, as specified in this Fact Sheet. You may be contacted and asked to provide information to help with the assessment of the use of the product during this emergency.

This EUA for COVID-19 convalescent plasma will end when the Secretary of HHS determines that the circumstances justifying the EUA no longer exist, if additional data were to become available to no longer support the product's use under an EUA, or when there is a change in the approval status of the product such that an EUA is no longer needed.