

## New Mexico Medical Advisory Team (MAT) Assessment

MAT Workgroup Name: Clinical – Drugs and Therapeutics

Date: April 9, 2020

### Question or request:

1. What is the role of Convalescent plasma treatment for COVID-19 patients?
2. When might Convalescent Plasma treatment become available?

### Recommendation/s or Response/s in bullet form:

1. **We recommend** this treatment be restricted to those organizations that are either participating in the Mayo Clinic Expanded Access Program described below, or in the context of an ongoing clinical trial, given the onerousness of the current available processes to obtain Convalescent Plasma.
  - Currently, providers can obtain and transfuse Convalescent Plasma by: 1.) submitting a Single Patient Emergency Investigational New Drug application to the FDA, 2.) by participating in an Expanded Access Program through the Mayo Clinic, and/or 3.) by participating in a clinical trial.
  - Both expanded access and clinical trials require Institutional Review Board (IRB) preapproval for human subjects research (21 CFR 56). The expanded access program gives enrolled sites the opportunity to use Mayo's IRB eliminating the need to seek approval from an independent IRB (UNM and Presbyterian IRBs will still review the package and will cede review to Mayo).
2. **We recommend** that interested facilities work with their local blood supplier to determine what method to obtain Convalescent Plasma works best for them. Currently, the FDA recommends that interested facilities who are expecting to transfuse Convalescent Plasma in more than a few patients should enroll in the Mayo Clinic Expanded Access Program, which may facilitate more rapid availability of these units and enable additional patients to receive Convalescent Plasma (See [www.uscovidplasma.org](http://www.uscovidplasma.org)).
3. **Be aware** that coordination between healthcare organizations, Tricare and DOH is under way to identify potential plasma donors in NM.

### Assessment:

Convalescent plasma collected from individuals who have recovered from COVID-19 is being explored as one potential treatment option.

The FDA is currently exploring the efficacy of convalescent plasma collected from individuals who have recovered from COVID-19, which contains antibodies to SARS-CoV-2, as a possible treatment.<sup>4</sup> Recent small studies from China show a potential benefit of transfusing convalescent plasma to critically ill patients with COVID-19.<sup>8,9</sup> 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.<sup>1, 2, 3</sup> The FDA is currently working with the Mayo Clinic to allow for an expanded access protocol to facilitate access to COVID-19 convalescent plasma under an existing IND for acute care facilities ([www.uscovidplasma.org](http://www.uscovidplasma.org))

The FDA has also allowed access to COVID-19 convalescent plasma for use in patients with serious or immediately life-threatening COVID-19 infections. In these cases, physicians must request a single patient emergency Investigational New Drug Application (eIND) for the individual patient.

Providers wishing to request an eIND should specify the following in the application:

- Laboratory confirmed COVID-19

## New Mexico Medical Advisory Team (MAT) Assessment

- Severe or immediately life-threatening COVID-19 evidenced by respiratory failure, septic shock and/or multiple organ dysfunction or failure. Signs of this can include one or more of the following:
  - Dyspnea, respiratory frequency  $\geq 30/\text{min}$ , blood oxygen saturation  $\leq 93\%$ , partial pressure of arterial oxygen to fraction of inspired oxygen ratio  $< 300$ , and/or lung infiltrates  $> 50\%$  within 24 to 48 hours
- Informed consent to receive convalescent plasma must be obtained and documented in accordance with 21 CFR 50.

### Convalescent Plasma Donor Criteria

To be eligible to donate convalescent plasma, an individual must have:

- Evidence of COVID-19 documented either through a diagnostic test at the time of illness or a positive serological test for SARS-CoV-2 antibodies after recovery if prior diagnostic testing was not performed at the time COVID-19 was suspected.
- Complete resolution of symptoms at least 28 days prior to donation OR complete resolution of symptoms at least 14 days prior to donation AND negative results for COVID-19 either from one or more nasopharyngeal swab specimens or by a molecular diagnostic test from blood.
- Male donors and female donors who have not been pregnant or female donors who have been testing since their most recent pregnancy and results interpreted as negative for HLA antibodies.
- Defined SARS-CoV-2 neutralizing antibody titers (e.g. greater than 1:80). If neutralizing antibody titers cannot be obtained in advance, a retention sample from the convalescent plasma donation should be stored for determining antibody titers at a later date.

Providers wishing to request an eIND should specify the following in the application:

- Laboratory confirmed COVID-19
- Severe or immediately life-threatening COVID-19 evidenced by respiratory failure, septic shock and/or multiple organ dysfunction or failure. Signs of this can include one or more of the following:
  - Dyspnea, respiratory frequency  $\geq 30/\text{min}$ , blood oxygen saturation  $\leq 93\%$ , partial pressure of arterial oxygen to fraction of inspired oxygen ratio  $< 300$ , and/or lung infiltrates  $> 50\%$  within 24 to 48 hours
- Patients must provide informed consent to receive convalescent plasma.

### New Mexico Convalescent Plasma Treatment

TriCore is exploring opportunities to implement convalescent plasma treatment with regional blood supplier, Vitalant, to treat critically ill patients with COVID-19. Vitalant will soon be collecting plasma from recovered COVID-19 donors. Additionally, Presbyterian and UNMH's transfusion services are exploring opportunities to leverage their participation in the Mayo Clinic Expanded Access Program to obtain units from both Vitalant and the American Red Cross. Additional details about the expected time to treatment and anticipated capacity for this mode of treatment will be shared as they become available.

### **Red flags and Concerns:**

While treatment with convalescent plasma has been successfully used for other outbreaks, it is not without risk. As with other blood transfer procedures, risks include inadvertent infection with another infectious disease agent and reactions to serum constituents, including immunological reactions such as serum sickness. Many of these risks are mitigated with the modern blood banking techniques used to screen for blood-borne pathogens and match the blood type of donors and recipients, so this risk is considered low. There is a higher risk, however, in treating individuals with pulmonary disease with plasma transfusion, as it can result in transfusion-related acute lung injury (TRALI). Blood centers have worked to mitigate the risk of TRALI as much as possible by only collecting from either female donors without HLA antibodies or male donors. This risk should be considered in the risk-benefit assessment for each patient.

There is also the theoretical risk of causing antibody-dependent enhancement of infection (ADE), which can enhance the disease in the presence of certain antibodies. Since the proposed use of convalescent plasma in the COVID-19 epidemic would rely on preparations with high titers of neutralizing antibody against the same virus, this risk is

## New Mexico Medical Advisory Team (MAT) Assessment

thought to be low. Additionally, there is a risk that antibody administration to those exposed to SARS-CoV-2 may prevent disease by attenuating the immune response, leaving individuals vulnerable to subsequent reinfection. While additional studies are needed, if this risk proves real, these individuals could be vaccinated against COVID-19 when a vaccine becomes available.

Given the high mortality of COVID-19, particularly among the elderly and vulnerable individuals, the benefits are thought to outweigh the risks for its use in those at high risk for or with early disease. However, a risk-benefit assessment should be conducted for all cases where convalescent plasma administration is considered to assess individual variables. Additionally, caution and vigilance will be required to identify any evidence of enhanced infection and monitor patients for signs of reinfection.<sup>5, 6, 7</sup> Under the expanded access protocol, serious adverse events judged by the treating physician to be potentially related to the administration of the convalescent plasma must be reported to the Principal Investigator.

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### Resources/Reference:

<sup>1</sup> Cheng, Y., Wong, R., Soo, Y. O. Y., Wong, W. S., Lee, C. K., Ng, M. H. L., ... & Cheng, G. (2005). Use of convalescent plasma therapy in SARS patients in Hong Kong. *European Journal of Clinical Microbiology and Infectious Diseases*, 24(1), 44-46.

<sup>2</sup> Chen, L., Xiong, J., Bao, L., & Shi, Y. (2020). Convalescent plasma as a potential therapy for COVID-19. *The Lancet Infectious Diseases*, 20(4), 398-400.

<sup>3</sup> Van Griensven, J., Edwards, T., de Lamballerie, X., Semple, M. G., Gallian, P., Baize, S., ... & Lomas, C. (2016). Evaluation of convalescent plasma for Ebola virus disease in Guinea. *New England Journal of Medicine*, 374(1), 33-42.

<sup>4</sup> U.S. Food and Drug Administration Revised Information for Investigational COVID-19 Convalescent Plasma Available from: <https://www.fda.gov/vaccines-blood-biologics/investigational-new-drug-ind-or-device-exemption-ide-process-cber/revised-information-investigational-covid-19-convalescent-plasma> [Accessed April 7, 2020].

<sup>5</sup> Gajic O, et al. Transfusion-related acute lung injury in the critically ill: prospective nested case-control study. *Am J Respir Crit Care Med*. 2007;176(9):886–891.

<sup>6</sup> China puts 245 COVID-19 patients on convalescent plasma therapy. News release. Xinhua. February 28, 2020. Accessed March 10, 2020. [http://www.xinhuanet.com/english/2020-02/28/c\\_138828177.htm](http://www.xinhuanet.com/english/2020-02/28/c_138828177.htm).

<sup>7</sup> Casadevall, A., & Pirofski, L. A. (2020). The convalescent sera option for containing COVID-19. *The Journal of clinical investigation*, 130(4).

<sup>8</sup> Shen, C. et al. Treatment of 5 critically ill patients with COVID-19 with Convalescent Plasma. *JAMA*. 2020.

<sup>9</sup> Duan K, et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. *PNAS*. 2020.