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DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Health systems, medical products and innovation
Medical products: quality, safety, innovation

Briefing on Covid-19 Convalescent Plasma in the EU – 28 August 2020

Lines to take

- The European Commission strongly supports studying the therapeutic use of plasma from recovered Covid-19 patients, encouraged by the evidence of a very low incidence of adverse reactions and the signals of efficacy.

- The current evidence on the efficacy of CPP is promising, but limited. In particular, more information is needed on the optimal treatment protocol (timing and frequency of the transfusions, testing and selection of donations etc.). It is essential to continue gathering evidence. Randomised controlled trials, ongoing in a number of Member States, will provide the highest quality of evidence. However, as they also take significant amount of time, monitored use in observational studies should proceed in parallel.

- The EU has issued guidance on the collection and transfusion of convalescent COVID-19 plasma, endorsed by the 27 Member State Competent authorities for blood. The Commission is also supporting the health professionals to collect data through a dedicated platform and H2020 grants.

- Health Commissioner Kyriakides encouraged recovered Covid-19 patients to donate their plasma to support these efforts and the Emergency Support Instrument is providing grants to blood services across the EU to help them increase their plasma collection capacity.

Commission européenne/Europese Commissie, 1049 Bruxelles/Brussel, BELGIQUE/BELGIË - Tel. +32 22991111
Office: F101 08/070 - Tel. direct line +32 229-51936

Massimo.AMBROSIO@ec.europa.eu

Background

The European Commission strongly supports the collection of plasma donations from recovered Covid-19 patients and studying its possible therapeutic use, either by direct transfusion or as the starting material for a purified medicinal product. The hypothesis that the antibody rich plasma could help patients to fight the infection is science based and, even before the pandemic, there was evidence from other diseases, such as SARS, that it might work.

We are encouraged by the very low incidence of adverse reactions and the signals of efficacy that have emerged in the most recent US publications on CCP transfusion, while noting that some publications, including those from the FDA's Expanded Access Programme, are still awaiting peer review. Other smaller studies have also produced promising results. However, the guidance published by the Commission and ECDC, and endorsed by the 27 Member State Competent authorities for blood, has not changed from the version published on 19 June. Thus, the efficacy of convalescent plasma transfusion should continue to be tested in the EU, ideally in randomised controlled trials, and enrolment of patients in those trials should be favoured when they meet eligibility criteria. This is essential to ensure a full understanding of which patients should be transfused, when and how often they should be transfused and how the donations should be tested and selected to ensure the best outcome.

Given that randomised controlled trials take significant time to produce results and are not available for participation to all hospitals, monitored use in observational studies should proceed in parallel. Several ongoing trials in the EU, as well as monitored use studies, are supported by a database developed by the Commission, together with the European Blood Alliance, that facilitates the aggregation and analysis of the EU data.

Through Horizon 20:20, the Commission is funding research on CPP. A project led by the European Blood Alliance is about to be launched (SUPPORT-E). This project has partner organisations from 14 Member States together with the UK and Switzerland. It will support high quality clinical evaluation of Covid-19 convalescent plasma (CCP), work to achieve consensus on the appropriate use of CCP in the treatment of Covid-19 across EU Member States and to optimise the assessment of plasma potency. A second Horizon 20:20 project (ATAC) is working on the development of a CCP based hyper-immune medicinal product to treat Covd-19.

None of this work can proceed without large quantities of precious donations by patients that have recovered from Covid-19. On World Blood Donor day in June 2020, the Commission for Health and Food Safety, Dr Kyriakides, called on citizens to donate blood; in particular, she urged

recovered Covid-19 patients to donate their plasma to support the efforts to treat patients with Covid-19.

The best way for donors to donate plasma is by apheresis, a method that allows the donor to donate larger volumes and to donate more frequently than normal blood donation, because they keep their red cells. Many blood services have limited capacity to collect plasma in this way. To address this, the Commission's Emergency Support Instrument has allocated up to 40 million Euros to support blood centres to increase their plasmapheresis capacity across the EU. On 27 August, applications were received from 80 national, regional and local blood establishments in 15 Member States, and from the UK, for these grants and the evaluation process has just started.

The intense efforts by the national blood authorities, blood service professionals, the industry that manufactures plasma-based medicinal products and the Commission will continue until there is clear evidence of the role that CCP might optimally play in the treatment or prevention of Covid-19.

Q&A

Q: How is the use of CCP authorised in the EU?

A: In line with EU blood legislation, blood establishments are inspected and authorised by their national competent authority for blood and blood components. In some Member States, this is also the authority for medicinal products. The Member States take slightly different approaches to authorising new components, many requiring clinical studies before authorisation. Many of these authorities are working together in an EU-funded Joint Action to standardise and optimise the approach to the authorisation of new blood components for transfusion as well as new preparations of tissues and cells for transplantation or assisted reproduction (GAPP Joint Action).

There is no system for centralised authorisation of blood components, such as plasma, in the EU and the European Medicines Agency does not have a mandate for this activity.

Q: How will the use of CCP to manufacture a medicinal product be regulated?

A: When blood components are used as the starting material for the manufacture of a medicinal product, the donation, procurement and testing is regulated by the blood legislation but all subsequent steps are regulated by the EU pharmaceutical legislation. Thus, requirements for clinical trials and authorisation of products are regulated as medicines and these activities fall under the mandate of the European Medicines Agency.

Q: Are blood establishments in the EU currently collecting CCP?

A: Yes, there is a high level of collection activity across the EU. Forty-two blood establishments from 18 countries have joined the CCP database hosted by the Commission and developed in co-operation with the European Blood Alliance (EBA). New registrations continue to arrive and these blood establishments are entering data on their protocols as well as individual donations and transfusions. The data will be analysed and summaries published by the EBA. The platform, parts of which are still being developed, will have a dashboard where activity data can be viewed by any interested organisation or citizen.

Q: Does the EU support increased collection of CCP?

A: Yes. The Commission considers that CCP should be collected from recovered patients across the EU. The plasma can be stored frozen for up to 3 years and, as donors should meet all normal blood donor eligibility criteria, it will not be wasted if not used for transfusion in Covid-19 patients

or for the manufacture of a Covid-19 plasma based medicine. It is likely that the level of antibodies in recovered patients will fall over time, so it is very important that collection proceeds as rapidly and efficiently as possible. This approach is supported by ECDC and WHO.

This is why the Emergency Support Instrument has allocated up to 40 million Euros to help public blood services and NGOs such as the Red Cross to increase their CCP collection capacity. By the deadline of 27 August 2020, 80 grant applications from national, regional and local blood establishments in 15 EU Member States, and the UK, for these grants. The applications will be evaluated during September and grants signed in October.

Q: Is there a standardised approach to collecting, storing and supplying CCP in the EU?

A: Yes. The Member State blood competent authorities worked together with ECDC and the European Commission to develop guidance to standardise the approach to collection, testing and supply. This guidance is published and is updated as needed.

Q: Are there research projects on CCP ongoing in the EU?

A: Yes. There are randomised controlled trials ongoing in France, Germany, the Netherlands, Denmark, Italy, Belgium and Spain (at least); some of these countries have more than one trial ongoing. The UK is also conducting a randomised clinical trial. A number of non-randomised trials and observational studies are also being carried out.

Q: Is the safety of CCP considered to be established?

A: Some studies with large numbers of transfused patients indicate that the adverse incidents associated with CCP are similar to the low level of incidents that are reported for plasma transfusion in general. Blood establishments in the EU have a legal requirement to report adverse reactions in all patients receiving blood components and the Commission publishes aggregated summaries of the data on an annual basis.

Q: Is the efficacy of CCP considered to be established?

A: No. The Commission considers that considerable work is still needed to establish efficacy and optimal selection and use of CCP. Horizon 20:20 has funded a project that will soon be launched. Called SUPPORT-E, and co-ordinated by the European Blood Alliance, it will aim to bring together the data from the multiple clinical studies across the EU to achieve more robust conclusions. The project will also investigate the optimal methods for testing of plasma to characterise it more precisely.