GOVERNMENT OF WEST BENGAL
DEPARTMENT OF HEALTH & FAMILY WELFARE
State Blood Transfusion Council, West Bengal
Swasthya Bhawan, Salt Lake, Block GN-29, Sector V, Kolkata- 700091

HFW-28013(99)/6/2020-SBTC SEC-Dept. of H&FW **Date. 02.09.2020**

Sub : Standard Operating Procedure (SOP) for Whole Blood derived Convalescent COVID-19 Plasma (WB-CCP)- for Off-Label use.

Enclosed please find herewith the approved SOP for Whole Blood derived Convalescent COVID-19 Plasma (WB-CCP) along with Annexure I, II, III for collection, preparation, processing, storage, distribution etc. of WB-CCP in 20 State run BCSUs.

All concerned are requested to take necessary action accordingly.

Special Secretary
MERT Branch (ME)
Dept. of H&FW
Govt. of West Bengal

HFW-28013(99)/6/2020-SBTC SEC-Dept. of H&FW/1(4) **Date. 02.09.2020**

Copy forwarded for information to:

1. Secretary, DoH&FW & MD, NHM
2. Secretary to Dept. of H&FW & Project Director, WBSAP&CS & Member Secretary, SBTC, WB
3. DHS, DoH&FW, GoWB
4. DME, DoH&FW, GoWB

HFW-28013(99)/6/2020-SBTC SEC-Dept. of H&FW/2(18) **Date. 02.09.2020**

Copy forwarded for information and taking necessary action to:

1. Principal/MSVP, ……..MCH (All)
2. Director, Drugs Control, West Bengal
3. Jt. Director (Finance), WBSAP&CS
4. Dy. Director, (Blood Safety), WBSAP&CS
5. State Programme Officer, State Blood Cell
6. Assistant Director (Medical), SBTC, WB
7. Assistant Director (VBD), WBSAP&CS
8. Quality Control Manager, WBSAP&CS
9. Quality Manager (Blood Safety), WBSAP&CS
10. CMOH, ……District (All)
11. Dy. CMOH-II, …… District & Nodal Officer of Blood Centre (All)
12. Director, IBTM&IH
13. Director, RBTC, ……..Blood Centre (All)
14. Superintendent, DH/SDH/SGH/SSH attached to Blood Centre (All)
16. The MOIC……..Blood Centre (All)
17. PA to the Principal Secretary, Dept. of H&FW
18. Office copy.

Special Secretary
MERT Branch (ME)
Dept. of H&FW
Govt. of West Bengal

GOVERNMENT OF WEST BENGAL
DEPARTMENT OF HEALTH & FAMILY WELFARE
State Blood Transfusion Council, West Bengal
Swasthya Bhawan, Salt Lake, Block GN-29, Sector V, Kolkata- 700091

STANDARD OPERATING PROCEDURE (SOP) OF WHOLE BLOOD DERIVED COVID-19 CONVALESCENT PLASMA (FOR OFF-LABEL USE ONLY)

1. PRINCIPLE & APPLICATION

The outbreak of severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), has become pandemic. To date, no specific treatment has been proven to be effective. Promising results were obtained in China and other countries using hyperimmune plasma from COVID-19 recovered patients. Use of convalescent plasma has also 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.

2. RESPONSIBILITY

It is the responsibility of the consultant/medical officer, technical supervisor/technologist and nurse posted in blood donation complex to select eligible donor, perform separation of plasma, and store processed and labeled plasma for use in indicated patients. These personnel are also responsible for documentation and record keeping of the product in computer system or in a dedicated register.

3. DEFINITION

This SOP describes donor eligibility, preparation / processing, labeling, storage, distribution and transfusion of Convalescent COVID-19 Plasma (CCP) obtained by whole blood separation.

4. METHODS AND MATERIALS

TYPES OF BLOOD BAGS TO BE USED FOR COLLECTION

i. 350 ml (Double) SAGM + CPD Bag
ii. 450 ml (Double) CPDA Bag

DONOR ELIGIBILITY & RECRUITMENT

1. All recovered COVID-19 cases that once tested positive for COVID-19 or have had symptoms of the disease fulfilling the following criteria in order of preference (as per NBTC guidelines after COVID-19 pandemic for donor selection).

   i. Negative RT-PCR /True NAT/ Antigen test report at least 28 days prior to donation.

   Or

   ii. Complete resolution of symptoms at least 28 prior to donation as documented by discharge certificate.

   Or

   iii. Having certification by a doctor/any other competent authority regarding the end of the quarantine period at least 28 days before donation.

   Or

   iv. Self-declaration of donor indicating that duration of symptom-free period at least for 28 days before donation.

[Negative RT-PCR/True NAT/Antigen test report is not mandatory in case of (ii), (iii) & (iv)]

2. Prior diagnosis of COVID-19 by RT-PCR is not mandatory since detection of anti-SARS-CoV-2 IgG antibodies, being performed now, is a direct evidence of prior COVID-19 disease.
3. Maximum time limit of donation: up to 4 months from the onset of disease symptoms.
4. For donation in 350 ml Blood Bag, body weight of donor should be 45 Kg and above.
5. For donation in 450 ml Blood Bag, body weight of donor should be 60 Kg and above.
6. Only male and nulliparous female donor will be eligible.
7. Donor's Haemoglobin should be $\geq$ 12.5 gm/dl.
8. Any recovered COVID-19 patient who has had history of transfusion of CCP or any other blood component while admitted in hospital for treatment of COVID-19, will not be considered as eligible donor.
9. A written and informed consent of donor for voluntary blood donation and for using his/her plasma as CCP (Attached herewith as Annexure-I).
10. In addition, donor eligibility criteria for whole blood donation will be followed in accordance to the Drugs & Cosmetics Act 1940 and rules 1945 therein (as amended till March 2020).

COLLECTION OF WHOLE BLOOD FROM A DONOR

1. Collection can be done either inside the premises of a licensed BCSU or in a Blood Mobile vehicle or in a VBD camp compliant with the donor eligibility criteria mentioned above.
2. While collecting blood in 350 ml (Double) SAGM+CPD Bag, maximum limit of volume to be collected is 385 ml.
3. While collecting in 450 ml (Double) Bag, maximum limit of blood to be collected is 495 ml.
4. Usual universal safety precautions are to be followed strictly during collection.
5. Transportation of collected blood from a VBD camp to blood bank should be done maintaining cold-chain at 2-6°C. Maintenance of cold-chain at 2-6°C is also mandatory till separation.

COMPONENT SEPARATION

1. Separation shall be done within 6 (six) hours after collection, **at 4°C applying a hard spin** as per existing guidelines and departmental SOP.
2. Volume of plasma per unit to be used as CCP should not be less than 200 ml.
3. No pooling of plasma from different donors will be allowed.
4. **Each CCP should have its own Unique Identification Number (UIN) before entering into system.**
5. **After separation the PRBC component will be added to the existing inventory as usual** (as per NBTC guidelines after COVID-19 pandemic for donor selection).

TTI SCREENING

The CCP should be negative for infectious markers of HIV I&II, HBV, HCV by serology and Syphilis & Malaria should be tested as per departmental SOP.

DETECTION OF COVID-19 IgG (TESTING METHODS)

1. Plasma shall be tested for detection of Covid-19 IgG against S1-RBD using ELISA kits or CLIA kits as approved by the appropriate authority.
2. While detecting Covid-19 IgG by ELISA, plasma tested positive for Covid-19 anti-S1-RBD IgG, will be considered as CCP. On the other hand, test value (OD) of plasma negative for Covid-19 anti-S1-RBD IgG, will not be considered as CCP, but to be considered as FFP.

3. While detecting Covid-19 anti-S1-RBD IgG by CLIA, plasma can be labeled as CCP based on the test result of specific Signal/Cut-off value in accordance with the concerned manufacturer's instruction and also with the departmental SOP such that the established value thus obtained, would be corroborative with the value of IgG titre, already established to be effective in the treatment of Covid-19 patients published in various international studies. Conversely, the plasma yielding result below the accepted value will not be considered as CCP but as FFP.
4. Titration of anti-COVID-19 (both IgG and IgM) antibodies and SARS- CoV-2 neutralizing antibodies may be done depending on availability of facilities at the time of testing. (Desired titre for IgG antibodies > 640 or neutralizing antibodies >40). Doubling dilution of donor serum will be done and titration will be done using ELISA. If not done at the time of plasma collection the donor samples will be stored in aliquots at - 80°C and to be tested at a later date when technology becomes available.

UNIQUE IDENTIFICATION NUMBER CREATION

1. After separation of whole blood into PRBC and Plasma, segregation of CCP and FFP will be done based on the IgG testing result either by ELISA or CLIA (Vide-DETECTION OF COVID-19 IgG TESTING METHODS).

2. A Unique Identification Number of CCP has to be created subsequently preferably in following manner:

   For example: XYZ-2020/camp code/donor number/CCP; (XYZ = Name of the Blood Bank)

   Or

3. Unique Identification Number of CCP may also be created as per the facility's own SOP.

LABELLING AND STORAGE OF CCP

1. The unit will be issued with minimal labeling requirements as follows:

   i. Unique Identification Number
   ii. ABO Group
   iii. TTI negative results

iv. Name of the product: **WHOLE BLOOD DERIVED COVID-19 CONVALESCENT PLASMA**
v. Date of Collection (dd/mm/yy)
vi. Date of Expiry (dd/mm/yy)
vii. Volume of product (in ml)

2. In addition, the label may include - a. SARS-CoV-2 antibody test/titre result b. Cautionary statement like "Caution: New Drug - Limited by National law to investigational use only"
3. In case, not being used immediately, freeze the plasma immediately below – 30^0C or preferably colder and stored frozen until distribution.
4. Separate deep freezer or dedicated drawer / rack in existing deep freezer may be used for storage of CCP. Proper **signage** is needed to locate these CCP storage sites more easily.

STORAGE OF CCP AND SHELF-LIFE

1. CCP has to be stored in a temperature below –30°C and shelf-life of such CCP will be for 1(one) year.
2. Convalescent Plasma thus collected from whole blood will be frozen within 8 hours of collection and stored as "Convalescent Frozen Plasma -- for COVID patient only" below –30° C.
3. The unit may be quarantined in "Untested" if any test result is pending. It should be moved to "Tested" compartment once the testing results are satisfactory.
4. Separate shelf of deep freezer should be dedicated for CCP.
5. After thawing at 37°C, CCP may be used for transfusion up to 5 days, if thawed plasma is stored at 2-6° C.
6. CCP should always be transported in temperature-controlled condition.

DISTRIBUTION / ISSUE OF CCP

1. CCP will be issued to prescribed patient only against valid requisition and samples.
2. The patient's request form should mention **"Off-Label" use of CCP**.
3. If frozen, CCP has to be thawed at 37°C before its issuance, following departmental standard operating procedure (SOP).
4. **ABO & Rh (D) Blood Group Compatibility**: Only ABO blood group compatibility is required. Rh (D) blood group can be ignored, provided Anti-D antibodies are not present in Rh (D) negative donors.

Compatibility of CCP:

Patient Blood Group	Compatible CCP Donor
A	A, AB
B	B, AB
AB	AB
O	O, A, B, AB

4. Minor cross matching must be done at AHG phase using CAT/CTT method.

5. Before issuing CCP, it has to be checked for product appropriateness, labeling, blood group, volume and expiry. Proper documentation and records to be maintained in the blood & component issue register.

6. Requisition, issue slip and related documents may be stored in a separate folder / file/box.

7. There should not be any delay in the transportation of product. A system may be developed such that the blood bank is updated once the product reaches the patient.

8. If necessary, bulk transfer or single unit transfer of CCP from one BCSU to another BCSU/non-BCSU blood bank/BSU may be done as and when required in order to ensure its availability in remote areas of the state and to prevent unnecessary wastage of CCP as well. While transferring the CCP between the facilities, maintenance of cold-chain must be ensured at 2-6 °C, whether in frozen state or in liquid state after thawing and such convalescent plasma can be used for patient transfusion up to 5 days, if stored at 2-6°C.

RECOMMENDATIONS FOR CCP TRANSFUSION

1. The treating physician or the doctor in-charge of the patient should check and confirm the plasma product, related documents and the designated patient before initiation of transfusion.

2. Patient may receive an initial dose of 200-250 ml followed by one or two additional doses of 200-250 ml at 24 hrs interval according to disease severity and tolerance of infusions. The second plasma will be preferably from different ABO compatible donor based on availability.

3. Blood/serum/plasma samples of the patient prior to and after transfusion of CCP may be collected for future potential scientific investigations like checking of the changes in anti-SARS-CoV-2 antibody titer.

4. Complete documentation of CCP transfusion should be done by the treating physician / doctor.

5. Any adverse event related to CCP transfusion should be managed by the treating doctor and must be notified to the blood bank by the concerned facility.

PATIENT SELECTION CRITERIA FOR WB-CCP USE

The use of convalescent plasma could improve the clinical outcomes in hospitalized COVID-19 patients with moderate to severe disease and limit further disease associated complications. To date, the strongest signals of benefit of CCP in terms of survival benefit has been observed in association with transfusion of high-titer unit (greater than 1:1350) within 72 hours of admission due to clinical symptoms of COVID-19.

Patient should be provided WB-CCP therapy under the following conditions:

1. Age ≥18 years
2. Adult patient of any sex
3. Laboratory confirmed diagnosis of infection with SARS-CoV-2
4. Clinical features of dyspnoea and or hypoxia, fever, cough, including-

Any two of the followings (optional if unavailable at treatment center):

a. $PaO_2/ FiO_2 < 300$
b. Respiratory Rate > 24/min and $SaO_2 \leq 94\%$ on room air
c. Requiring supplemental oxygen or high-flow oxygen, non-invasive or invasive mechanical ventilation at time of admission.

5. Evidence of lung infiltrates on chest radiography (CXR and CT-Chest)
6. Severe COVID-19 disease; judged by the treating physician as at high risk of progression to life-threatening disease **

** Life threatening disease defined as any of the following:

a. Respiratory failure
b. Septic shock
c. Multiple organ dysfunction or failure

WB-CCP NOT TO BE TRANSFUSED IN PATIENTS

1. Pregnant women
2. Breastfeeding women
3. Known hypersensitivity to blood products or past history of severe transfusion reaction
4. Receipt of pooled immunoglobulin (IvIg etc.) in last 30 days
5. Receipt of any anti-viral agent(s) with possible activity against SARS-CoV-2 <24 hours prior to CCP transfusion.
6. Mechanically ventilated (including veno-venous (VV)-ECMO) ≥ 5 days
7. Shock (Requiring vasopressor to maintain a MAP ≥ 65mm Hg or MAP below 65)
8. End-stage multi-organ failure

DOCUMENTATION

1. Enter the details of donors in the computer system / dedicated register.
2. Photocopies of investigations, treatment prescriptions / papers may be preserved and recorded.
3. Enter details of product labeling, storage and distribution / issue in prescribed register
4. Following Registers will be maintained:

i). COVID positive donor register
ii). CCP Stock Register
iii). Cross-match and Issue Register for CCP

5. REFERENCES

- Clinical Management Protocol: COVID-19, Govt. of India, Ministry of Health & FW; Director General of Health Service; Version 3, 13.06.2020 & Version 5, 03.07.2020.
- Information on convalescent plasma in COVID-19, Central Drugs Standard Control Organization (Biological Division), DGHS, GOI, 01.07.2020
- Advisory on COVID-19 case management, Dept. of Health & FW, Govt.of West Bengal; 12.08.2020
- COVID-19 Convalescent plasma collection: Donor eligibility, processing, labeling and distribution. AABB, updated on 04/04/2020
- National Guidance to blood transfusion services in India in light of COVID-19 pandemic. National Blood Transfusion Council; Ministry of H&FW, GOI, 25.03.2020.
- U.S. Dept. of Health and Human Services (HHS), Determination of public health emergency and declaration that circumstances exist justifying authorizations pursuant to Section 564(b) of the Federal, Food, Drug and Cosmetic Act, Emergency use authorization declaration for convalescence plasma, 23.08.2020.
- A phase II, Open Label RCT to assess the safety and efficacy of convalescent plasma in COVID-19, Version 1.5, 11.05.2020
- Mayo Clinic US, Expanded Access Program for Convalescent Plasma therapy for COVID-19. https://doi.org/10.1101/2020.08.12.20169359
- AABB Update on CCP: Benefit of Early Transfusion, 01.09.2020.

------END OF DOCUMENT-----

Date. 02.09.2020

Annexure – 1

COVID-19 CONVALESCENT PLASMA DONATION CONSENT FORM

I certify that I (name) ----------aged _____ years, had suffered from COVID-19 based on Clinical Diagnosis / RT-PCR / True NAT/ Antigen tests from (date):_____ to (date) _____. I was declared cured on (date): _____, as per my attached test reports / my symptoms disappeared for more than 28 days. I have been explained thoroughly about the process of whole blood collection and the risks involved in it in the language that I understand. I am aware that my plasma may be used as an off-label therapy to treat a COVID-19 patient. Having fully learned and understood all that, I am willingly giving my consent to the donation procedure

Donor's Name_____ Sign _____Date & Time _____

---------- 0 ----------

Date. 02.09.2020

Annexure - II

GOVERNMENT OF WEST BENGAL

DEPARTMENT OF HEALTH AND FAMILY WELFARE

STATE BLOOD TRANSFUSION COUNCIL, WB

Request for "Off-Label" use of Convalescent Covid19 Plasma

Name.....Age.....Sex.....

Hospital.....Date of Admission.....

Registration No.....Ward.....Bed no.....

Clinical Condition:

Mild ARDS / Moderate ARDS / Severe ARDS/ Others (Pl. Specify) - *Encircle the condition applicable*

Any h/o pregnancy at present.....Co-morbidity.....h/o Allergy/Anaphylaxis.....

****ABG Report: FiO2..... PaO2..... PCO2..... HCO3..... pH.....**

BLOOD GROUP..... (Please send 3 ml EDTA blood sample to reconfirm), **BP .....**

Declaration of treating Doctor:

I have provided the relevant information related to patient's clinical condition as per requirement for "Off –Label" use of **Convalescence Covid19 Plasma. Its Off- Label use had been approved by the competent authority of the facility.**

HFW-28013(99)/6/2020-SBTC SEC-Dept. of H&FW

Date. 02.09.2020

The patient / next to kin have been fully explained of its application, adverse potential and given the consent to transfuse Convalescence Covid19 Plasma under me / my team. Under the event of any adverse event related to its transfusion to be reported to the concerned blood centre immediately.

Signature of treating specialist Doctor with date and time

Medical Registration No:

Name in Block letters **Mobile no:**

To be filled by Blood Centre only:
Unit No.
Date Of expiry.

****Data may be provided where the facility of ABG is available.**

Annexure - III

WORK FLOW OF WB-CCP (FOR OFF-LABEL USE)