CIRCULAR OF INFORMATION

FOR THE USE OF CELLULAR THERAPY PRODUCTS

This Circular was preparated by Calabria Cord Blood Bank (Italy, Reggio Calabria). Is intended to provide general information to those who administer cellular therapy products, and serves as an extension and enhancement of the label found on the cellular therapy product. The task force has chosen to describe only those cellular therapy products that are most frequently used in clinical practice.

CALABRIA CBB
CORD BLOOD BANK
Reggio Calabria

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Notice to All Users

The Circular of Information for the Use of Cellular Therapy Products is intended to be an extension of the cellular therapy product label. It has been jointly prepared by the AABB Circular of Information Cellular Therapies Task Force, which includes a collaborative group of multiple non governmental organizations that represent the cellular therapy field. The US Food and Drug Administration and the Health Resources and Service Administration also participated in the development and review process.

General Information and Cellular Therapy Product Sources

The Task Force intentionally limited its scope to only include minimally manipulated cellular therapy products such as peripheral blood progenitor cells, bone marrow, cord blood and leukocytes. The group recognizes there are multiple cellular therapy products that could not be adequately covered in the Circular. To accommodate this, the Circular includes multiple blank pages at the end of the document to allow for the addition of product or facility specific information.

Indications

Allogeneic HPC products are intended to provide hematopoietic reconstitution after myeloablative or nonmyeloablative preparative regimens for a wide range of disease states. For patients with certain malignancies, the product is also intended to provide immune reconstitution and immune-mediated therapy. Autologous HPCs are collected and used following myeloablative or myelotoxic therapy to enhance hematopoietic reconstiution. The therapy is intended to treat the patient's underlying malignancy, and autologous HPC products are administered to minimize morbidity and mortality caused by the myelotoxic effects of the therapy. Additional applications may be used as indicated in clinical trials and research protocols.

Donors

Cellular therapy products descrive in this Circular have been collected from human donors for autologous or allogenic administration. Autologous HPC collection usually occurs after mobilization of the donor’s stem and progenitor cells with growth factors, chemoterapy, or both. Donors of the other cellular therapy products may or may not require stimulation by growth factors, depending on the protocol employed. Allogenic HPC collection usually occurs after mobilization with growth factors alone.

Dosage and Administration

The minimum number of HPCs necessary for engraftment in a myeloablated recipient has not been established for all HPC sources. However, eligibility criteria for some protocols may dictate a minimum number of cells to be collected and/or infused. Some examples of cell types measured to determine HPC dosage are CD34+ cells, nucleated or mononuclear cells, and colony-forming units–granulocyte-macrophage (CFU-GM). The dose for MNC(A) or NC(WB) is determined by institutional policies and is usually based on the number of T cells, nucleated cells, or mononuclear cells. Manufacturers may recommend that products be filtered using a 170- to 260-micron filter to remove clumps or aggregates. Some institutions may have specific policies regarding the use of these filters for cellular therapy products. (See facility-specific section at the end of this document.) Cellular therapy product infusion should begin slowly and with sufficient observation to detect symptoms and/or signs suggestive of acute immunologic or infectious complications. Thereafter, the rate of infusion may be as rapid as tolerated. The administration time will be determined by the total volume to be infused and by whether the cells are fresh or previously cryopreserved. If the thawed products have not been washed to remove DMSO, care should be taken not to exceed 1 mL of DMSO per kilogram of recipient weight per day administration (eg, 100 mL of a 10% solution contains 10 mL of DMSO).

Storage

Cellular therapy products may be transported for administration in a fresh or cryopreserved state. They may require either long-term or short-term storage before administration. Institutional policies and protocols dictate specific storage requirements for cellular therapy products. The recommended storage duration and temperature may be included in the product labeling and should indicate the cell dose, storage temperature, and duration of storage to ensure acceptable cell viability and function. If an expiration date has been defined, it should be included on the product label. Before infusion, products received for the treatment of a patient should be stored according to the instructions on the label or those supplied in accompanying documentation. If there is an unexpected delay in administration and the product must be held for infusion after the expiration period indicated on the label, if applicable, the distributing/issuing and/or local cell processing facility should be contacted for further handling and storage instructions.

Noncryopreserved Cellular Therapy Products

Fresh products may be transported from distant collection facilities or under go short term local storage before administration.

Cryopreserved Cellular Therapy Products

Cryopreserved products may be received and stored long term according to the manufacturer's directions or by a validated method. These products may be thawed at the local cell processing laboratory, with or without additional processing, or thawed at the bedside immediately before administration. These products should be infused as soon as possible after thawing occurs.

Thawing and Washing

The Transplant Centre decides if the thawed product must be washed to remove DMSO or must be administered immediately after thawing, using a specific device at the bedside in the presence of aggregates (if necessary). The Processing Facility of GOM Reggio Calabria sets up a washing solution consisting of 10 % ACD, 20% human albumin and 70% saline solution (NaCl 0.9%). After having thawed the bag inside a thermostatic bath at 37°, connect the thawed bag to the bag with the washing solution and with a transfer bag.
Slowly, add the washing solution. Wait few minutes, no more than five, and transfer the content of the frozen bag to the empty transfer bag.
Centrifuge at 1800 x G for 10 minutes at 4°C without brake.

Cellular Therapy Product Labeling and Supporting Documents

At the time of issue, cellular therapy products will have the following information either on the affixed product label, on an attached label, or in accompanying documentation:
• Proper name of the product, including an indication of any qualification or modification.
• Unique identifier.
• Approximate volume.
• Name and volume of anticoagulant or other additives.
• Date and end time of collection.
• Expiration date and time (if applicable).
• Recommended storage temperature.
• Identity and address of collection facility or donor registry.
• Identity and address of processing/distributing facility.
• Statements regarding transmission of infectious diseases.
• Statement indicating "Do Not Irradiate."
• Biohazard or other warning label(s) (if applicable),
• Statements regarding recipient identification,
• Donor identifier and (if applicable) name.
• Recipient name and identifier.

• ABO group and Rh (D) type of donor or the ABO group and Rh (D) type of a cord blood product.
• Red cell compatibility testing results (if applicable).
Many products will be accompanied by additional records that are included to meet regulatory requirements. These accompanying records will include:
• A statement indicating whether the donor has been determined to be eligible or ineligible, or that the donor eligibility determination is incomplete.
• A summary of the records used to make the donor eligibility determination.
• Infectious disease testing results and supporting documents.
• For ineligible donors, a statement noting the reasons for ineligibility.

Biohazard and Warning Labels

When abnormal results of any donor screening or testing are identified in the donor, the transplant physician is notified of those results. Urgent medical need must be documented when a donation is used for transplantation from a related or an unrelated donor with an incomplete eligibility status, or when a donation is used for transplantation from an unrelated donor with an "ineligible" eligibility status.
Questions about the interpretation of any label on a specific product should be directed to the facility distributing the product.

Side Effects

Some side effects and complications may require reporting to a relevant national competent authority. Infusion of cellular therapy products can result in mild, moderate, or serious infusion reactions.
The following side effects and hazards pertain to administration of cellular therapy products.
Signs and symptoms of acute hemolytic reactions may include one or more of the following: Chills, fever, headache, CRS, facial flushing, tachicardia, shock, febrile Non-hemolytic reactions, allergic reactions, GVHD, alloimmunization to antigens, DMSO toxicity, septic infusion reactions, Transfusion-Related Acute Lung Injury (TRALI), Fat Emboli, Transmission of Infectious Disease and/or Disease Agents.

Reporting of Adverse Reactions

Any adverse reaction that is defined as a suspected or proven unfavorable response to administration of cellular therapy products and is manifested by signs and symptoms (including microbial contamination of a product or suspected disease transmission during or after product administration) must be documented and reported in accordance with the facility's policies and/or applicable laws and regulations. At a minimum, any such event must be reported to the patient's physician and to the medical director of the facility that issued the product. The reporting requirements vary based on the regulatory oversight required by the type of product and manufacturing process. The user must contact the manufacturing/distributing facility for specific requirements. Entities involved in the manufacture of the product must be contacted in the investigation/reporting of an adverse reaction, as applicable.

Specific Product Information

This page is intended to be blank to provide space for the distributing institution to give additional product information as applicable to its product.

As indicated in General Information section, the distributing institution is responsible for providing specific information not already included in this Circular about the cellular therapy product, including but not limited to the following:

Description.

Action.

Indications.

Controindications.

Storage.

Dosage.

Administration.

Activity Calabria Cord Blood Bank:

Manipulation and cryopreservation of Hematopoietic Stem Cells of different origin (from peripheral, bone marrow and cord blood) and lymphocytes.

Distribution of Hematopoietic Stem Cells for transplantation purposes.

Pre-transplant qualitative evaluation of cell products.

Manipulation of autologous lymphocytes for CAR-T use, since January 2020.

Production of blood components for topical and infiltrative use: platelet concentrate for the treatment of patients with vascular lesions: Cord Blood Platelet Gel (platelet gel from cord blood).

Production of autoserum eye drops and serum eye drops from cord blood applicable for the treatment of dry eye syndromes (GVHD, Sjogren's syndrome) and ocular epitheliopathy disorders.

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https://calabriacord.wixsite.com/ccbb
www.gomrc.it/banca-del-cordone
lab.cse@ospedalerc.it
calabriacord@ospedalerc.it
Instagram: banca_del_cordone

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