The Christie NHS
NHS Foundation Trust

5.65 Pharmacy/Pathology Management of Cellular Therapy Products (CTPs) as Advanced Therapy Medicinal Products (ATMPs)

Purpose:
To describe the procedure for managing CTPs used as ATMP which are manufactured outside The Christie NHS Foundation Trust, received, stored and issued by The Stem Cell Laboratory at The Christie Pathology Partnership which has been prescribed by an appropriate prescriber.

Policy Application:
Pharmacy Department and The Christie Pathology Partnership - Stem Cell Team

Responsibilities for implementation:
Pharmacy Department and Stem Cell Pathology Team

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Author:
Nisa Khan (Lead Clinical Trials Pharmacist)

Authorisation:

Authorised by (Name and title)	Date Authorised
Adrian Bloor	20/09/18
Robert Duncombe	20/09/18
Diane Sweeney	20/09/18

Version History:

Version	Date	Author	Reviewer	Comments
1.0		Nisa Khan		

References (if applicable):
Foundation for the Accreditation of Cellular Therapy (FACT) Joint Accreditation Committee ISCT and EBMT (JACIE).*International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration* 7th Edition. Nebraska Medical Centre: United States of America

HTA guide to Quality and Safety Assurance for Human Tissue and Cells for Patient Treatment v2 April 2018

Medicines and Healthcare products Regulatory Agency (MHRA). (2012) *Good Clinical Practice Guide.*

London: The Stationery Office.

Number and location of any copies:
The Pharmacy Department
Q-Pulse
Stem Cell Lab SOP file

Definitions:
Advanced Therapy Medicinal Product (ATMP): A medicine for human use that is based on genes, cells or tissue engineering.

Advanced Therapy Investigational Medicinal Product (ATIMP): an ATMP as defined in Article 2(1) of Regulation 1394/2007 which is tested or used in a clinical trial (in accordance with Article 2(d) of Directive 2001/20/EC).

Cellular therapy: The administration of products with the intent of providing effector cells in the treatment of disease or support of other therapy.

Cellular therapy product (CTP): Somatic cell-based product (e.g., mobilized HPC, mononuclear cells, cord blood cells, mesenchymal stromal cells, T cells, natural killer cells) that is procured from a donor and intended for processing and administration.

Cytokine release syndrome (CRS): A non-antigen-specific toxicity that occurs as a result of high-level immune activation.

Designated Individual (DI): Individuals under whose supervision the Human Tissue Act licensed activity is authorised to be carried. They also implement the requirements of the Human Tissue Act.

Donor: A person who is the source of cells or tissue for a cellular therapy product.

Immune Effector Cell (IEC): A cell that has differentiated into a form capable of modulating or effecting a specific immune response.

Storage: Holding a cellular therapy product for future processing, distribution, or administration.

Traceability: The ability to track any product through all stages of collection, processing, and Administration.

Scope
This procedure outlines the arrangements agreed by the Pharmacy Department and the Christie Pathology Partnership for storage of ATMPs which are prescribed for use in a named patient. For the purpose of this SOP, ATMP will only include CTPs. Other products within the ATMP definition are beyond the scope of this SOP.

Background
ATMPs are medicines as defined within Directive 2001/83/EC. The Chief Pharmacist is responsible for their use with the same responsibility as all other medicines used in the Trust.

Cells procured from a donor at the Trust and manufactured externally are classed as tissues and cells for human application until made available by the Laboratory as starting material for a medicinal product and become an ATMP at the point of manipulation of the cells. The ATMPs are stored in a designated Nitrogen

tank within the Stem Cell Laboratory.

It is the responsibility of the Pharmacy Department to ensure the Stem Cell Laboratory has adequate systems for traceability, release of the ATMP under a HTA Designated Individual and quality management systems which enable reporting of non-conformance.

The chain of custody for ATMPs must be clear and this will be audited by Pharmacy on a quarterly basis for robust oversight of these products.

The Pharmacy Department are also responsible for ensuring appropriate therapy required to treat cytokine release syndrome is available for patients receiving the ATMP and supplied in a timely manner due to the high risk nature of ATMP infused in the recipient.

Pharmacy oversight of ATMPs

The HTA Designated Individual for Tissues and Cells for Human Use and the appropriate Lead in Pharmacy will meet on a quarterly basis to discuss the storage facility, the Quality Management System and processes in place for ATMPs, as well as reviewing the training records of the laboratory personnel and reports of non-conformance and or storage issues encountered.

New therapies will be discussed at the Cellular Therapies Programme Board and/or DTC, and between the HTA Designated Individual and relevant Lead in Pharmacy prior to the treatment being approved for use at The Trust to ensure appropriate documentation can be created and arrangements are in place between Pharmacy and the Stem Cell Laboratory. An SLA will be drafted by the DI for each trial/drug defining the responsibilities of the teams involved.

The Stem Cell Laboratory Manager will send quarterly quality reports to the Lead Clinical Trials Pharmacist and the Lead Haematology Pharmacist to provide regular oversight of storage of ATMPs. Exceptions and non-conformance will be discussed at the Trust transplant combined meeting with the Stem Cell laboratory manager, Lead Clinical Trials Pharmacist and Lead Haematology Pharmacist present in the meeting.

A record of all patients (regardless of whether or not they are receiving the ATMP as a clinical trial) will be kept in the pharmacy department as a log and this will be updated during each oversight visit to identify how much ATMP activity is occurring in the Trust.

Any issues or concerns identified by either of the lead pharmacists will be discussed with the Chief Pharmacist and HTA DI should these be of a recurrent or serious nature.

Storage of ATMPs

1. ATMPS are stored in the secure storage area of the Stem Cell Laboratory in the vapour phase of liquid Nitrogen below -160°C, or in the shipper they are received in. Each ATMP is stored in a segregated area of a dedicated ATMP tank.
2. The nitrogen tank is continually monitored for temperature and for faults and externally alarmed in the Blood bank, where there are staff available to investigate at all times. (POLICY SCL/POL/CRYO: Storage Policy for Cryopreserved Cells)

Procedure for supply of an ATMP

1. A proforma will be written by a suitably experienced clinician, as per FACT-JACIE Standards, and prescribed on an in-patient drug chart or electronically on iQEMO as appropriate.
2. The specialist haematology pharmacist will sign the proforma and screen the in-patient drug chart or iQEMO prescription and will review the drug chart during the patient's admission on the ward.

3. The Stem Cell lab will issue the ATMP for the named patient following the receipt of a request for issue form and the proforma detailing pharmacy oversight and agreement to the release.
4. Designated Laboratory staff will complete appropriate documentation to record the batch number and product expiry of the issued product.
5. The product will be supplied to the ward where the recipient is admitted and administered in accordance with relevant procedures.
6. A suitably trained nurse will administer the ATMP, in accordance to the directions on the prescription and document receipt and administration on the appropriate forms (See Infusion of Cellular Products SOP WRD-5).

Additional steps for supply of an ATIMP

1. A Sponsor approved paper clinical trial prescription will also be completed and signed by the clinician. This clinical trial prescription will be sent to the clinical trials pharmacy team at least 48 hours prior to the ATIMP infusion date.
2. A clinical trials pharmacist trained in the study will clinically screen the clinical trial prescription and take the signed prescription to the Stem Cell Laboratory for the clinical trial prescription to be processed.
3. The section of the clinical trial prescription designated for the laboratory staff will be completed by the laboratory personnel processing the request for issue and the clinician and pharmacist sections of the clinical trial prescription will be stored in the study-specific folder in the Stem Cell Lab with the accountability logs.
4. A photocopy of the clinician and pharmacist sections of clinical trial prescription and the remaining blank sections of the clinical trial prescription will be supplied with the ATIMP to the ward on receipt of a request for issue form and the proforma.
5. The HTA DI or designee will also complete the Sponsor accountability logs which will record the ATIMP batch number and expiry.
6. The product will be supplied to the ward where the recipient is admitted at the temperature at which it has been stored by the Laboratory.
7. A suitably trained nurse will administer the ATIMP, in accordance to the directions on the prescription and document receipt and administration on the appropriate forms (See Infusion of Cellular Products SOP WD-5). The clinical trial prescription will also be completed and stored in the Trial Master File.

Administration and handling of ATMPs on the ward

Staff handling and administering ATMPs should follow the *WRD-5 "Infusion of Cellular Products"* SOP.

Management of therapy for Cytokine Release Syndrome

The Guidelines for the Management of Cytokine Release Syndrome Associated with Cancer Immunotherapies outlines the prescribing guidance to clinically manage cytokine release syndrome. Pharmacists involved in coving the haematology ward and involved in setting up ATIMPs must ensure they have read and understood this SOP.

The Specialist Haematology Pharmacist will ensure adequate stock levels of tocilizumab are maintained and will ensure there is a minimum physical stock level of 2 doses per patient, following notification that a patient due to receive an ATMP should this be required.

For a patient receiving an ATMP which is an ATIMP, the clinical trials pharmacist will ensure tocilizumab is available for the clinical trial that the patient is a participant in, and clearly labelled for use in accordance to the protocol guidelines. Sponsors mostly supply tocilizumab on a named-patient basis to ensure it is available for use for patients recruited into the trial and therefore careful stock management and regular stock inventory must be carried out. If there is a sufficient stock holding of tocilizumab at the Trust, reimbursement arrangements will be made with the Sponsor if used for a patient on a clinical trial.

Unused ATMPs

The Trust Genetically Modified Micro-organisms Policy must be followed for the handling and management of unused ATMPs where appropriate. The Biological Safety Officer can advise for non-GMO ATMPs
Disposal of materials from trials must be authorised by the sponsor. Disposal of clinical material is authorised by the Laboratory Medical Director.