Advanced Therapy Treatment Centres

Midlands-Wales Advanced Therapy Treatment Centre

Example SOP: Procurement of Advanced Therapeutic Medicinal Products (ATMPs) – CAR-T cells

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Background

An advanced therapy medicinal product (ATMP) is a medicinal product which is:

- a gene therapy medicinal product
- a somatic cell therapy medicinal product
- a tissue engineered product
- or combination product

Trusts are required to have defined governance processes in place for their use.

There are several licensed ATMPs - CAR-T cell therapy products and gene therapy medicinal products. This SOP will consider the procurement process for licensed products using two CAR-T products as exemplars.

Investigational ATMPs are typically referred to as ATIMPs and are outside the scope of this SOP.

As the name suggests ATMPs are medicines and their safe use is the responsibility of the Chief Pharmacist. The Chief Pharmacist may choose to delegate some of the duties involved in their use to other departments in the Trust.

Procurement will typically be through the Pharmacy Department but will usually involve input from other departments such as legal and finance teams, cell laboratories and other health care professionals

CAR-T products are cellular products (classed as ex-vivo gene therapy) and, as such, considered to be high risk medicines for many reasons including the possibility of giving the patient unmatched cells.

All of the current ATMPs are costly and so involve a significant financial risk. Trust Standing Financial Instructions may require a higher level of order authorisation than other medicines.

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Example SOP for Procurement of ATMPs by a Pharmacy Department

Effective shared care between the treatment centre and the referring centre is essential before, during and after therapy. This requires:

- Good communication between the treatment centre and referring centre, with designated individuals for each centre.
- Intensity of post treatment care is patient dependent and flexibility may be required
- The treatment centre should be contacted to discuss management of any complications after the patient returns to the referring centre

1. Scope

Pharmacy Department

2. Purpose

To provide guidance for procurement of ATMPs using CAR-T as exemplars.

Authorised personnel/training required

Named Pharmacists and Technicians should attend product specific training. This is usually provided by the company manufacturing the ATMP. Training records should be maintained e.g. as evidence for JACIE

Prior to any procurement, senior Pharmacy staff must review and agree the terms and conditions of the manufacturer. They may choose to seek advice from Trust Legal or Finance Teams.

In particular, they should review the facilities required for product handling, the terms relating to out of specification product, the terms for payment in the event of a product not being used and the point in the procurement process when the Trust becomes liable to pay the invoice.

Chief Pharmacists and Deputy Chief Pharmacists should make themselves aware of the Trust Standing Financial Instructions as to the level of authorisation required for high value orders. They should also consider insurance cover for any situation where a high value product might be rendered unusable. Supply agreements should be reviewed and SOPs for product cancellation/credit should be in place.

3. Products and manufacturers.

a) Kite

Yescarta (axicabtagene ciloleucel) and Tecartus (autologous anti-CD19-transduced CD3+ cells) are prepared by Kite Ltd and are ordered on the KiteKonnect portal.

The portal is at https://kitekonnect-eu.force.com

Username and password can be obtained from the local company CAR-T representative after training in its use.

Access to the portal should be attained by several members of the Pharmacy Team to allow for cover in the event of absence.

Typically other members of the CAR-T clinical team will require access e.g. nurses, members of cell therapies laboratories (CTL). It is useful, but not essential for haematologists to have access to the portal.

NHS patients should be approved by the national panel. A record should be kept of the panel approval number.

The patient should be enrolled onto the CAR-T programme on KiteKonnect. This generates a Kite ID number which is unique to the patient and product. Kite will use this number in all correspondence about the patient and product. (Most Kite employees do not have sight of patient information.) This step does not constitute a contract between the Trust and Kite.

A member of the clinical team should complete the first Blueteq form. Pharmacy should verify this and can then raise an order number. (Verifying the Blueteq is not mandatory but is recommended to avoid any accidental omission.) The order number can be added to the patient's KiteKonnect record by the Kite Case Manager. To maintain a robust chain of identity, it is highly desirable that a second check occurs of the patient and product details, the Blueteq number, the order number and the Kite ID number. It is important to match the order number to the patient to ensure that the correct order is goods received and invoiced.

CAR-T products require the patient's lymphocytes to be harvested. Once an apheresis date has been planned, a coordination call will be scheduled by Kite. This will be to arrange collection of the patient cells from the Trust. It is usually most convenient that a member of the Cell Therapy Laboratory (CTL) is on this call and would often also include specialist nursing staff or process co-ordinator. Pharmacy do not need to be on the call but may choose to do so.

The CTL will arrange the pick-up of the cells from the Trust with Kite.

After collection, Kite will put an estimated date for the product's readiness on KiteKonnect. This will be of the order of 28 days. This estimated date can be used for planning purposes but cannot be relied on for definite.

When the product has been manufactured and tested by the KITE Qualified Person, the Qualified Person Certificate of Release for Authorized ATMP is prepared and posted on KiteKonnect. An email is sent to the CAR-T team. (Strictly speaking, it is at this point that the product becomes a medicinal product.)

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3. Products and manufacturers.

The product is now ready to be delivered and a second coordination call is initiated by Kite to arrange delivery. The choice of delivery date is influenced by several factors –

The patient's condition and / or any bridging chemotherapy given.

Bed availability

CTL opening hours

Availability and timing of leucodepletion chemotherapy.

(Most Trusts prefer to have the CAR-T product available on site prior to starting leucodepleting chemotherapy. This avoids the possibility of giving the chemotherapy and then discovering a product defect. However, this is not mandatory and in certain clinical circumstances may be waived).

b) Novartis

Kymriah (tisagenlecleucel) is prepared by Novartis Ltd and is ordered on the Novartis Cellchain portal.

The portal is at https://cellchain.force.com

Username and password can be obtained from the local company CAR-T representative after training in its use.

Access to the portal should be attained by several members of the Pharmacy Team to allow for cover in the event of absence.

Typically other members of the CAR-T clinical team will require access e.g. nurses, members of cell therapies laboratories (CTL). Haematologists generally do not need access but may choose to use the portal for information.

NHS lymphoma patients should be approved by the national panel. A record should be kept of the panel approval number. There is no panel for ALL patients and treatment is typically decided by Blueteq eligibility and peer discussion.

The patient should be enrolled onto the CAR-T programme on Novartis Cellchain. This generates a Novartis Batch ID which is unique to the patient and product. Novartis will use this number in all correspondence about the patient and product. (Most Novartis employees do not have sight of patient information.) This step does not constitute a contract between the Trust and Novartis.

A member of the clinical team should complete the first Blueteq form. Pharmacy should verify this and can then raise an order number. (Verifying the Blueteq is not mandatory but is recommended to avoid any accidental omission.) The order number can be added to the patient's Novartis Cellchain record.

To maintain a robust chain of identity, it is highly desirable that more than one person checks the patient details against the Blueteq number, the order number and the Novartis batch ID number, indeed it is usual for the pharmacist to act as a second check, the details having been entered by a member of the clinical team.

CAR-T products require the patient's lymphocytes to be harvested. Once an apheresis date has been planned, a coordination call will be scheduled by Novartis. This will be to arrange collection of the patient cells from the Trust. It is usually most convenient that a member of the Cell Therapy Laboratory is on this call. Pharmacy do not need to be on the call but may choose to do so.

As the cells are cryopreserved, pickup will invariably be from the CTL. The CTL will arrange the pick-up of the cells from the Trust with Novartis.

After collection, Novartis will put an estimated date for the product's readiness on Novartis Cellchain. This will be of the order of 28 days. This estimated date can be used for planning purposes but cannot be relied on for definite.

When the product has been manufactured and tested by the Novartis Qualified Person, the Certificate of Conformance/EU QP Batch certification/confirmation is prepared and posted on Novartis Cellchain. An email is sent to the CAR-T team. (Strictly speaking, it is at this point that the product becomes a medicinal product).

The product is now ready to be delivered and a second coordination call is initiated by Novartis to arrange delivery. The choice of delivery date is influenced by several factors –

The patient's condition and / or any bridging chemotherapy given.

Bed availability

CTL opening hours

Availability and timing of leucodepletion chemotherapy.

(Most Trusts prefer to have the CAR-T product available on site prior to starting leucodepleting chemotherapy. This avoids the possibility of giving the chemotherapy and then discovering a product defect. However, this is not mandatory and in certain clinical circumstances may be waived.)

4. Acknowledgements

The MW-ATTC wish to thank Cambridge University Hospitals NHS Foundation Trust for sharing their procedures as a basis for this exemplar SOP.

5. Supporting Documents/Further Information

Further information may be provided in the company supply agreements, product specific SOPs, risk assessments, and Summary of Product Characteristics/risk materials as well as from the company representatives.