# UKALL14

# Drug Supply Guidelines

**N.B. This document outlines the arrangements for ordering, storing and handling drug for randomised patients on UKALL14. Patients on the 'Registration only' Sub-study will receive no Investigational Medicinal Products (IMPs). Rather, they will receive drug from hospital stock and standard treatment of their treating clinicians' choice.**

## CONTACT DETAILS

For further information on trial drugs, trial protocol, dosing, supply drug and distribution queries please contact:


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**Chief Investigator**
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**Drug company**
Name: Baxalta/ Shire
IMP: Pegylated Asparaginase (Oncaspar)

**Drug Distributor**
Name: Shire

**Drug company**
***N.B. no further IMP to be supplied following closure of B randomisation in July 2017***
Name: Roche Ltd
IMP: Rituximab (Mabthera)

**Drug Distributor**
Name: Roche

**Drug company**
Name: Novartis
IMP: Nelarabine (Atriance)

**Drug Distributor**
Name: Novartis

**Drug company** (*stopped supplying April 2016*)
Name: Swedish Orphan Biovitrium (SOBI)
IMP: Palifermin (Kepivance)

**Drug Distributor**
Name: SOBI

## VERSION HISTORY

| Version number | Date | Summary of changes from previous version | Changes made by |
|---|---|---|---|
| 1.0 | 29.11.10 | First release of drug supply guidelines | N/A |
| 1.1 | 21.07.11 | Change to Palifermin Ordering Procedure | SP |
| 2.0 | 11.09.12 | Change to Rituximab delivery times and change to Oncaspar ordering procedure | JG |
| 2.1 | 25.02.14 | Removal of any statements relating to Rituximab coming off patent. | SP |
| 3.0 | 23.11.17 | • Clarification that sites can use own accountability logs upon CTC approval, and dose banding clarification & Minor administrative changes.<br>• Change to drug suppliers for nelarabine and pegylated asparaginase<br>• Amended to reflect cessation of supply for palifermin following closure<br>• Addition of clarification regarding closure of B randomisation and opening of 'Registration only' Sub-study at implementation of protocol v11 | EL |

**TABLE OF CONTENTS**

## 1. OVERVIEW

### 1.1 Applicability

These drug supply guidelines are applicable to the Lead Pharmacist and any other member of staff who has responsibilities in conducting UKALL14.

### 1.2 Trial Information

For detailed information on the UKALL14 trial, please refer to the current version of the protocol.

## 2. TRIAL DRUGS

### 2.1 IMPs (randomised patients)

In accordance with the Clinical Trial Authorisation (CTA) granted by the MHRA on the 13th January 2010 the following are classed as Investigational Medicinal Products (IMPs): **Rituximab** (Mabthera®), **Pegylated Asparaginase** (Oncaspar®), **Nelarabine** (Atriance®) and **Palifermin** (Kepivance®).

For UKALL14 the following IMPs will be provided **free of charge** to site pharmacies for the duration of the trial:

- Rituximab (Mabthera®) – provided by Roche Products Ltd until July 2017 – rituximab randomisation now closed.
- Nelarabine (Atriance®) – provided by Novartis Pharmaceuticals UK Ltd.
- Palifermin (Kepiance®) - provided by Swedish Orphan Biovitrum Ltd until April 2016 – palifermin randomisation now closed.

The following IMP will be provided **at sites' own cost** to site pharmacies for the duration of the trial:

Pegylated asparaginase (Oncaspar®) - provided by Baxalta UK Ltd, now part of Shire.

**National dose banding is not permitted for IMPs in UKALL14. Dosing should be as outlined in the protocol.**

### 2.2 Non-IMPs (randomised patients)

All other drugs specified in the protocol are standard treatment for this disease and are classified as Non Investigational Medicinal Products (NIMPs). NIMPs **will not be** provided for the trial and must be provided from pharmacy stock at participating sites. For avoidance of doubt, the NIMPs for the UKALL14 trial are:

- Daunorubicin
- Vincristine
- Dexamethasone
- Methotrexate
- Imatinib
- Cyclophosphamide
- Cytarabine
- Mercaptopurine
- Etoposide
- Fludarabine
- Melphalan
- Alemtuzumab
- Prednisolone

**Pharmacies must ensure they have adequate supplies at all times for trial patients.** Sites are responsible for putting systems for traceability of NIMPs in place (see section 11.1).

**National dose banding is permitted for NIMPs only**. This should be undertaken as per local practice.

### 2.3 Status of drugs for 'Registration only' sub-study patients

Because 'registration only' sub-study patients are being treated with the standard of care regimen of their treating clinician's choice, and are entered in the trial for observation/data collection and sample collection only, the drugs used to treat these patients are not regarded as IMPs or NIMPs for the purposes of the UKALL14 trial.

Drugs which have been supplied for the UKALL14 trial for randomised patients **must not** be used to treat 'registration only' sub-study patients. All drugs must be sourced from hospital stocks and traceability must be maintained as per local standard practice.

## 3. PHARMACY REGISTRATION & SET-UP

The Principal Investigator must ensure that pharmacy is informed about the trial and that pharmacy related duties are delegated appropriately.

A designated member of the pharmacy staff, who takes overall responsibility for all pharmacy aspects of the clinical trial, should be identified and will be assigned the Lead Pharmacist. This person will be listed on the main Site Delegation Log.

The Pharmacy Lead is responsible for ensuring all members of staff undertaking trial related activities have completed the Delegation Log.

## 4. PHARMACY ACTIVATION

The following stages are required prior to site authorisation:

- Clinical Trial Authorisation
- REC Approval
- Local R & D approvals
- Signed Clinical Trial Site Agreement.
- Confirmation of receipt of Investigator Site File and Pharmacy Site File documentation.
- Site (Principal Investigator & Research Team) & Pharmacy Initiation.

UCL CTC will perform a Site Initiation meeting with the lead Pharmacist (or delegate). This will take place prior to authorisation to recruit patients.

Once a site is ready for activation (pending Site Initiation), a Pharmacy File will be sent to the Lead Pharmacist from UCL CTC. The contents of the file will include copies of forms for drug ordering and accountability logs for UKALL14. All trial related documentation should be retained in the Pharmacy Site File (or include a statement of its location if documentation is held outside of the PSF).

All sites will need to provide UCL CTC with the following information prior to activation:

- Site Name
- PI Name
- PI GMC Number
- Site Address
- Pharmacy Contact Name, telephone number, email address
- Pharmacy Delivery Address
- Pharmacy specific drug delivery instructions
- Movianto order number (If site does not have an account with Movianto, pharmacy will need to set one up) – No longer applicable as of 01.03.2018

When all stages listed above are complete, UCL CTC will formally notify the Research team and Pharmacy team that potential trial participants can be approached, by sending a site activation letter. The Site Pharmacy will then be able to order the initial supply of trial specific **pegylated asparaginase** only. (Please see Section 7).

## 5. RANDOMISATION

Once the site is activated, patients may be recruited into the trial. Once an eligible patient has been identified, the site research team will contact UCL CTC to randomise the patient into the trial. When a patient is randomised, UCL CTC will provide randomisation confirmation details to the research team and to the pharmacy contact person named on the randomisation form. **Ensure that any changes in pharmacy staff are communicated to the research team promptly to ensure randomisation confirmation reaches the correct person(s).** File the confirmation in section 4.7 of the Pharmacy Site File.

Pharmacy should review the randomisation confirmation and ensure that there is sufficient stock of IMP, and/or place any necessary trial specific drug orders as required.

*N.B. Please take into consideration that various non-IMPs are required within each treatment phase, therefore ensure stock levels of these are sufficient.*

Please refer to the current version of the protocol for complete guidance on randomising patients into the trial.

From the implementation of protocol version 11.0 (dated 11.09.2017), UKALL14 includes provision for B-cell patients to be entered on a 'registration only' sub-study. **IMPs (defined as pegylated asparaginase, rituximab, nelarabine and palifermin that have been supplied specifically for use in UKALL14) must not be dispensed to 'registration only' sub-study patients.**

All treatment for 'registration only' sub-study patients must be sourced from local hospital stock, and they will receive standard of care treatment of their treating clinician's choice.

It is possible that clinicians will opt to treat patients with the standard arm of UKALL14, in which case please note the following:

1. Treatment for 'registration only' sub-study patients should not be prescribed on trial prescriptions.
2. Pegylated asparaginase supplied for the trial **must not** be used to treat 'registration only' sub-study patients.
3. Rituximab is not currently licensed or funded for use in newly-diagnosed ALL, but may come into routine use in due course. In any event, Rituximab supplied for the trial **must not** be used to treat 'registration only' sub-study patients.

In order to avoid IMP being dispensed to 'registration only' sub-study patients in error, please note the patient numbers associated with each patient group and ensure local procedures reflect which patients may be dispensed IMP:

- 14-1-xxx: Randomised B-cell patient – IMP may be dispensed to these patients
- 14-2-xxx: Randomised T-cell patient – IMP may be dispensed to these patients
- 14-3-xxx: 'Registration only' sub-study B-cell patient – IMP must not be dispensed to these patients

**Summary of IMPs required for each arm for <u>randomised patients</u>:**

| Arm | Pegylated asparaginase | Rituximab | Nelarabine | Palifermin |
|---|---|---|---|---|
| **B1**† | X* | | | |
| **B2**† | X* | X | | |
| **T1** | X* | | | |
| **T2** | X* | | X | |
| **P1**** | | | | X |
| **P2**** | | | | X |

* Not to be dispensed if patient has Philadelphia positive disease; different schedule for patients aged ≥41

** Palifermin randomisation arms closed April 2016

† B-cell randomisation arm closed July 2017

## 6. RITUXIMAB

### 6.1 Ordering Rituximab

*The rituximab randomisation closed on 10th July 2017 when the recruitment target was reached. All patients randomised to arm B2 have now received rituximab treatment and no further ordering can take place.*

Copies of completed **Rituximab Drug Order forms** must be retained in section 4.3 of Pharmacy Site File.

### 6.2 Receipt of Rituximab

No further supplies of rituximab are expected.

All correspondence relating to delivery should be located in section 4.3 of the Pharmacy Site File.

### 6.3 Labelling of Rituximab

No further supplies of rituximab expected.

Approved wording for labels used when rituximab arm was open is provided in section 4.2 of the Pharmacy Site File.

### 6.4 Handling & Storage of Rituximab

Rituximab which has been previously supplied for the trial should be appropriately segregated from hospital stock drug and stock for other trials. Details of the storage location should be recorded in the Pharmacy Site File.

Please refer to the current SmPC for Rituximab for details of storage, handling and incompatibilities.

**Details of excursions within permitted range must be documented in Pharmacy Site File. For temperature excursions see section 10 for full reporting details.**

Details of temperature monitoring systems for the area where the trial specific Rituximab is stored should be retained in the Pharmacy Site File.

### 6.5 Dispensing & Ordering of Rituximab

No further dispensing of rituximab to take place.

Copies of completed prescriptions can be located in section 4.5 of the Pharmacy Site File.

Completed Rituximab **Accountability Logs should** located in section 4.6 of the Pharmacy Site File.

### 6.6 Accountability of Rituximab

No further dispensing of rituximab to trial patients will take place, however destruction accountability is still applicable.

It is the responsibility of the pharmacist to maintain drug accountability records for Rituximab. Sites can use their own logs providing they capture the same information as the UCL CTC supplied logs and a copy is sent to UCL CTC for approval prior to site activation.

The pharmacist must record the receipt, dispensing, return and destruction of Rituximab on the appropriate **Stock Balance log** and **Accountability Log** found in section 4.6 of the Pharmacy Site File.

UCL CTC will request copies of the logs as necessary during the course of the trial, in accordance with the trial monitoring plan.

### 6.7 Recall of Rituximab

Rituximab randomisation closed in July 2017. No further drug ordering to take place.

### 6.8 Reconciliation of Rituximab

Rituximab reconciliation will be performed by UCL CTC, in accordance with the trial monitoring plan. To facilitate this, pharmacists must provide the following documents to UCL CTC upon request:

- **Rituximab Drug Order form** (section 4.3 of the Pharmacy Site File)
- **Certificate of Clinical Trial Supply** - drug receipt (section 4.3 of the Pharmacy Site File)
- **Stock Balance Log** for Rituximab (section 4.6 of the Pharmacy Site File)
- **Accountability Log** for Rituximab (section 4.6 of the Pharmacy Site File)

### 6.9 Destruction of Rituximab

Once reconciliation is complete, UCL CTC will give Pharmacy authorisation to destroy remaining Rituximab supplied for UKALL14 in accordance with approved local pharmacy policy.
Ensure the relevant documentation is completed and copies are sent to the CTC:

- Complete a **destruction log**, found in section 4.6 of the Pharmacy Site File, and file a copy
- Record the destruction on the **Stock Balance Log**, found in section 4.6
  *N.B Do not return trial drug to Roche*

Expired trial specific Rituximab must be quarantined. Notify UCL CTC who will liaise with Roche for advice on its use. CTC will communicate destruction confirmation back to sites. Expired vials should be destroyed in accordance with approved local pharmacy policy, and ensure relevant documentation is completed and filed as listed above.

Please include a copy of the local Drug Destruction Procedure/Policy in section 4.6 of the Pharmacy Site File.

## 7. PEGYLATED ASPARAGINASE

### 7.1 Ordering Pegylated asparaginase – for randomised patients

Pegylated asparaginase (Oncaspar®) will be supplied at cost to sites by Baxalta/ Shire.

Pegylated asparaginase must be ordered using the **Oncaspar Drug Order form**. This form will be forwarded to the Lead Pharmacist (or delegate) when a Site is activated and authorised to approach patients. Please ensure that the correct version of the order form is used. The current order form can be located via the CTC website (www.ctc.ucl.ac.uk).

**Placing an initial order:**

Following activation of a site, the Lead Pharmacist will be instructed to order an initial supply of 2 vials of pegylated asparaginase for the site.

1. Complete the **Oncaspar Drug Order form** provided to the Lead Pharmacist in the Pharmacy Site File and email the form to Shire at **servicecs.uk@baxalta.com**, copying in ctc.ukall14@ucl.ac.uk. Please check carefully to ensure that the correct pharmacy delivery address is entered to ensure the delivery is not delayed or misdirected.
2. If email is not possible, the **Oncaspar Drug Order form** may be faxed to Shire on **0203 655 2602** and CTC on **0207 679 9861**
3. Orders placed before 4pm will be processed for next day delivery. Orders received on a Friday will be delivered on the following Monday.

**To re-order:**

Site pharmacies will be responsible for maintaining an adequate supply of pegylated asparaginase for each patient randomised on the UKALL14 Trial at their site. Pharmacy staff should monitor levels regularly, in particular when a new patient is randomised at Site, and place re-orders as necessary.

**Minimum re-order:**

When re-ordering pegylated asparaginase, please note that there is a minimum order of 2 vials.

1. Complete the **Oncaspar Drug Order form** located section 4.3 of the Pharmacy Site File and email the form to Shire at **servicecs.uk@baxalta.com**, copying in ctc.ukall14@ucl.ac.uk. Please check carefully to ensure that the correct pharmacy delivery address is entered to ensure the delivery is not delayed or misdirected.
2. If email is not possible, the **Oncaspar Drug Order form** may be faxed to Shire on **0203 655 2602** and CTC on **0207 679 9861**
3. Orders placed before 4pm will be processed for next day delivery. Orders received on a Friday will be delivered on the following Monday.

Copies of completed **Oncaspar Drug Order forms** must be retained in section 4.3 of Pharmacy Site File.

If an order for pegylated asparaginase has not arrived by the expected date and time, pharmacy must contact UCL CTC in the first instance. Contact details can be found at the beginning of this document.

### 7.2 Receipt of Pegylated asparaginase

It is important to log receipt of each batch of pegylated asparaginase received on the **Stock Balance Log** for Oncaspar in a timely manner and store the drug appropriately.

If pegylated asparaginase arrives damaged, pharmacy must quarantine the product, and contact UCL CTC. All correspondence relating to delivery problems or any other problem with respect to pegylated asparaginase should also be documented and filed in section 4.3 of the Pharmacy Site File.

### 7.3 Labelling of Pegylated asparaginase

Pegylated asparaginase will be delivered labelled as commercial stock. Pharmacy **MUST** add a label upon receipt to designate its use in a clinical trial, and ensure it is segregated appropriately from hospital stock or

IMPs for other trials. Approved wording for labels is provided in section 4.2 of the Pharmacy Site File. Pharmacy must supply a copy of the label to be used to UCL CTC.

For dispensing, Pharmacy must label the drug with the minimum suggested labelling content as below:

**FOR CLINICAL TRIAL USE ONLY**
**UKALL14** (EudraCT No 2009-012717-22)
**Principal Investigator** (Provide name of the Site PI for the UKALL14 Trial as drug information contact)
**Subject Number** (patient's trial number)
**Treatment phase/day details (e.g. phase 1, day 4)**

### 7.4 Handling & Storage of Pegylated asparaginase

Pegylated asparaginase supplied for the trial should be appropriately segregated from hospital stock drug and stock for other trials. Details of the storage location should be recorded in the Pharmacy Site File.

Please refer to the current SmPC for Oncaspar for details of storage, handling and incompatibilities.

**Details of excursions within permitted range must be documented in Pharmacy Site File. For temperature excursions see section 10 for full reporting details.**

Details of temperature monitoring systems for the area where the trial specific pegylated asparaginase is stored should be retained in the Pharmacy Site File.

### 7.5 Dispensing & Recording of Pegylated asparaginase

The Investigator/additional clinician are responsible for ensuring pegylated asparaginase is prescribed appropriately for a patient on the trial. Please refer to the trial protocol for dosing schedules for pegylated asparaginase.

Sites should develop their own trial specific prescriptions and a copy should be sent to CTC for information. Prescriptions must be signed by an appropriate member of staff (as detailed on the staff delegation log) and a copy must be retained in the Pharmacy Site File.

**Before dispensing pegylated asparaginase to randomised patients, please check the following:**

- The patient's age. On day 4 of phase 1 induction, pegylated asparaginase is to be omitted in patients aged ≥41
- The patient's Philadelphia status. Pegylated asparaginase is to be omitted in patients with Philadelphia chromosome positive disease

The **Accountability Log** must be completed to record each dose of pegylated asparaginase dispensed for each trial participant. This must be retained in section 4.5 of the Pharmacy Site File, and a copy must be returned to UCL CTC upon request.

**Pegylated asparaginase supplied for UKALL14 must not be given to non-trial patients or 'registration only' substudy patients, and randomised trial patients must not be given hospital stock.**

### 7.6 Accountability of Pegylated asparaginase

It is the responsibility of the pharmacist to maintain drug accountability records for pegylated asparaginase. Sites can use their own logs providing they capture the same information as the UCL CTC supplied logs and a copy is sent to UCL CTC for approval prior to site activation.

The pharmacist must record the receipt, dispensing, return and destruction of pegylated asparaginase on the **Stock Balance Log** and **Accountability Log** for Oncaspar found in section 4.6 of the Pharmacy Site File.

UCL CTC will request copies of the accountability logs during the course of the trial in accordance with the trial monitoring plan.

### 7.7 Recall of Pegylated asparaginase

In the event of Pegylated asparaginase recall, UCL CTC will notify pharmacies of actions required, and liaise with Baxalta to ensure replacement product is supplied.

### 7.8 Reconciliation of Pegylated asparaginase

Pegylated asparaginase reconciliation will be performed by UCL CTC in accordance with the trial monitoring plan. To facilitate this, pharmacists must provide the following documents to UCL CTC upon request:

- **Oncaspar Drug Order form (section 4.3 of the Pharmacy Site File)**
- **Delivery confirmation** documents (section 4.3 of the Pharmacy Site File)
- **Stock Balance Log** for Pegylated asparaginase (section 4.6 of the Pharmacy Site File)
- **Accountability Log** for Pegylated asparaginase (section 4.6 of the Pharmacy Site File)

### 7.9 Destruction of Pegylated asparaginase

Once reconciliation is complete, UCL CTC will give Pharmacy authorisation to destroy remaining pegylated asparaginase supplied for UKALL14 in accordance with approved local pharmacy policy. Ensure the relevant documentation is completed and copies are sent to the CTC:

- Complete a **destruction log**, found in section 4.6 of the Pharmacy Site File, and file a copy
- Record the destruction on the **Stock Balance Log**, found in section 4.6
  *N.B Do not return trial drug to Shire*

Expired trial specific pegylatyed asparaginase must be quarantined. Notify UCL CTC who will liaise with Baxalta, for advice on its use. CTC will communicate destruction confirmation back to sites. Expired vials should be destroyed in accordance with approved local pharmacy policy, and ensure relevant documentation is completed and filed as listed above.

Please include a copy of the local Drug Destruction Procedure/Policy in section 4.6 of the Pharmacy Site File, and ensure the UCL CTC has been sent a copy.

## 8. NELARABINE

### 8.1 Ordering Nelarabine

Nelarabine (Atriance®) will be supplied free of charge by Novartis.

Nelarabine must be ordered from Novartis using the **Nelarabine Drug Order form**. This form will be provided to the Lead Pharmacist (or delegate) when a Site is activated and authorised to approach patients.

Upon receipt of confirmation that a patient has been randomised to arm T2* (Phase 2 Induction plus Nelarabine) please follow the process below:

1. Complete the **Nelarabine Drug Order** form and email to **ctc.ukall14@ucl.ac.uk** or send by fax on **0207 679 9861**. Please check carefully to ensure that the correct pharmacy delivery address/number is entered to ensure the delivery is not delayed or misdirected
2. UKALL14 Trial team will confirm by return email that the order has been received and processed. **If you have not received a confirmation email within 1 business day, please call UCL CTC on 020 7679 9860** and speak to the UKALL14 Trial team.
3. The UKALL14 Trial team will forward your order on to Novartis. If the order form is received later in the day (>4pm) or after business hours (9-5pm) the order will be forward to Novartis the following day. Give at least 5 working days' notice when ordering to avoid delays in receiving drug.
4. Nelarabine stock should be delivered within 5 working days of receipt of drug order by Novartis.

**although nelarabine is given at the end of phase 2 induction, nelarabine drug orders should be placed as soon as possible after randomisation to T2 arm.*

If an order of Nelarabine has not arrived by the expected date and time, pharmacy must contact UCL CTC in the first instance. Contact details can be found at the beginning of this document.

Copies of all completed **Nelarabine Drug Order forms** must be retained in section 4.3 of Pharmacy Site File.

### 8.2 Receipt of Nelarabine

It is important to log receipt of each batch of Nelarabine received on the **Stock Balance Log** in a timely manner and store the drug appropriately.

If the Nelarabine arrives damaged, pharmacy must quarantine the product, and contact UCL CTC. All correspondence relating to delivery problems or any other problem with respect to Nelarabine should also be documented and filed in section 4.3 of the Pharmacy Site File.

### 8.3 Labelling of Nelarabine

Nelarabine will be delivered labelled as commercial stock. Pharmacy **MUST** add a label upon receipt to designate its use in a clinical trial, and ensure it is segregated appropriately from hospital stock or IMPs for other trials. Approved wording for labels is provided in section 4.2 of the Pharmacy Site File. Pharmacy must supply a copy of the label to be used to UCL CTC.

For dispensing, Pharmacy must label the drug with the minimum suggested labelling content as below:

**FOR CLINICAL TRIAL USE ONLY**
**UKALL14** (EudraCT No 2009-012717-22)
**Principal Investigator** (Provide name of the Site PI for the UKALL14 Trial as drug information contact)
**Subject Number** (patient's trial number)
**Treatment phase/day details (e.g. Nelarabine day 1)**

### 8.4 Handling & Storage of Nelarabine

Nelarabine supplied for the trial should be appropriately segregated from hospital stock drug and stock for other trials. Details of the storage location should be recorded in the Pharmacy Site File.

Please refer to the current SmPC for Nelarabine for details of storage, handling and incompatibilities.

Details of excursions within permitted range must be documented in Pharmacy Site File. **For temperature excursions see section 10 for full reporting details.**

Details of temperature monitoring systems for the area where the trial specific Nelarabine is stored should be retained in the Pharmacy Site File.

### 8.5 Dispensing & Recording of Nelarabine

The Investigator/additional clinicians are responsible for ensuring Nelarabine is prescribed appropriately for a patient on the trial. Please refer to the trial protocol for dosing schedules for Nelarabine.

Sites should develop their own trial specific prescriptions and a copy should be sent to CTC for information. Prescriptions must be signed by an appropriate member of staff (as detailed on the staff delegation log) and a copy must be retained in the Pharmacy Site File.

**Before dispensing nelarabine to randomised T2 arm patients, please check the following:**

- The patient has achieved count recovery; neutrophils >0.75 x $10^9$/l and platelets >75 $10^9$/l
- Should not be given earlier than D29 of induction phase 2
- If patient has grade 2 or more Central Nervous System (CNS) toxicity at the end of phase 2 induction, nelarabine must not be given. Patient should proceed to next scheduled phase of treatment

The Nelarabine **Accountability Log** must be completed to record each dose of Nelarabine dispensed for each trial participant. This must be retained in the relevant section of the Pharmacy Site File, and a copy must be returned to UCL CTC upon request.

**Nelarabine supplied for UKALL14 must not be dispensed for non-trial patients or 'registration only' patients and trial patients must not receive hospital stock of nelarabine.**

### 8.6 Accountability of Nelarabine

It is the responsibility of the pharmacist to maintain drug accountability records for Nelarabine. Sites can use their own logs providing they capture the same information as the UCL CTC supplied logs and a copy is sent to UCL CTC for approval prior to site activation.

The pharmacist must record the receipt, dispensing, return and destruction of Nelarabine on the appropriate **Stock Balance Log** and **Accountability Log** found in section 4.6 of the Pharmacy Site File.

The UCL CTC will request copies of the accountability logs as necessary during the course of the trial, in accordance with the trial monitoring plan.

### 8.7 Recall of Nelarabine

In the event of Nelarabine recall, UCL CTC will notify pharmacies of actions required, and liaise with Novartis to ensure replacement product is supplied.

### 8.8 Reconciliation of Nelarabine

Nelarabine reconciliation will be performed by UCL CTC, in accordance with the trial monitoring plan. To facilitate this, pharmacists must provide the following documents to UCL CTC upon request:

- **Nelarabine Drug Order form** (section 4.3 of the Pharmacy Site File)
- **Drug delivery** documentation (section 4.3 of the Pharmacy Site File)
- **Stock Balance Log** for nelarabine (section 4.6 of the Pharmacy Site File)
- **Accountability Log** for nelarabine (section 4.6 of the Pharmacy Site File)

### 8.9 Destruction of Nelarabine

Once reconciliation is complete, UCL CTC will give Pharmacy authorisation to destroy any remaining nelarabine supplied for UKALL14, in accordance with approved local pharmacy policy. Ensure the relevant documentation is completed and copies are sent to the CTC:

- Complete a **Destruction Log**, found in section 4.6 of the Pharmacy Site File, and file a copy
- Record the destruction on the **Stock Balance Log**, found in section 4.6
  *N.B Do not return trial drug to Novartis*

Expired trial specific Nelarabine must be quarantined. Notify UCL CTC who will liaise with Novartis for advice on its use. CTC will communicate destruction confirmation back to sites. Expired vials should be destroyed in accordance with approved local pharmacy policy, and ensure relevant documentation is completed and filed as listed above.

Please include a copy of the local Drug Destruction Procedure/Policy in section 4.6 of the Pharmacy Site File.

## 9. PALIFERMIN

### 9.1 Ordering of Palifermin

Palifermin trial arm closed April 2016. No further drug ordering can take place.

Copies of all Drug Order forms should be located in section 4.3 of Pharmacy Site File.

### 9.2 Receipt of Palifermin

No further supplies of palifermin expected.

All correspondence relating to delivery should be located in section 4.3 of the Pharmacy Site File.

### 9.3 Labelling of Palifermin

No further supplies of palifermin expected.

Approved wording for labels used when palifermin arm was open is located in section 4.2 of the Pharmacy Site File.

### 9.4 Handling & Storage of Palifermin

Palifermin which has been previously supplied for the trial should be appropriately segregated from hospital stock drug and stock for other trials. Details of storage location should be recorded in the Pharmacy Site File.Please refer to the current SmPC for Palifermin for details of storage, handling and incompatibilities.

Details of excursions within permitted range must be documented in Pharmacy Site File. **For temperature excursions see section 10 for full reporting details.**

Details of temperature monitoring systems for the area where the trial specific Palifermin is stored should be retained in the Pharmacy Site File.

### 9.5 Dispensing & Recording of Palifermin

No further dispensing of palifermin to take place.

Copies of completed prescriptions can be located in section 4.5 of the Pharmacy Site File. Completed Palifermin Accountability Logs should be located in section 4.6 of the Pharmacy Site File.

### 9.6 Accountability of Palifermin

No further dispensing of palifermin to trial patients will take place, however destruction accountability is still applicable.

It is the responsibility of the pharmacist to maintain drug accountability records for Palifermin. Sites can use their own logs providing they capture the same information as the UCL CTC supplied logs and a copy is sent to UCL CTC for approval prior to site activation.

The pharmacist must record the receipt, dispensing, return and destruction of Palifermin on the appropriate **Stock Balance Log** and **Accountability Log** found in section 4.6 of the Pharmacy Site File. UCL CTC will request copies of the accountability logs as necessary during the course of the trial.

### 9.7 Recall of Palifermin

Palifermin trial arm closed April 2016. No further drug ordering to take place.

### 9.8 Reconciliation of Palifermin

Palifermin reconciliation will be performed by UCL CTC. To facilitate this, pharmacists must return the following documents to UCL CTC upon request:

- **Palifermin Drug Order form** (section 4.3 of the Pharmacy Site File)
- **Delivery confirmation** documents (section 4.3 of the Pharmacy Site File)
- **Stock Balance Log** for Palifermin (section 4.6 of the Pharmacy Site File)
- **Accountability Log** for Palifermin (section 4.6 of the Pharmacy Site File)

### 9.9 Destruction of Palifermin

Once reconciliation is complete, UCL CTC will give Pharmacy the authorisation to destroy remaining Palifermin supplied for UKALL14 in accordance with approved local pharmacy policy.

Ensure the relevant documentation is completed and copies are sent to the CTC:

- Complete a **destruction log**, found in section 4.6 of the Pharmacy Site File, and file a copy
- Recrord the destruction on the **Stock Balance Log**, found in section 4.6
  *N.B Do not return trial drug to Swedish Orphan Biovotrium*

Expired trial specific Palifermin must be quarantined. Notify UCL CTC who will liaise with Swedish Orphan Biovitrum for advice on its use. Upon authorisation of destruction sites should destroy expired vials in accordance with approved local pharmacy policy, and ensure relevant documentation is completed as listed above.

Please include a copy of the local Drug Destruction Procedure/Policy in section 4.6 of the Pharmacy Site File.

## 10. TEMPERATURE EXCURSIONS FOR SUPPLED IMPs

Temperature excursions outside of the acceptable ranges (as listed in the SPCs for each of the IMPs listed within this document) must be reported to UCL CTC as soon as possible prior to continued use of the IMP. Refer to the relevant Summary of Product Characteristics to check the appropriate temperature ranges.

Affected trial stock must be quarantined until notice from UCL CTC as to whether it can be used for the trial.

Procedures for reporting excursions are outlined in the **'UCL CTC Procedures for Reporting Temperature Excursions**' document, which is held in the Pharmacy Site File. UCL CTC should be notified of temperature excursions using the **Notification of Temperature Excursions form**, and sent to the email address indicated on form.

UCL CTC will contact the relevant drug company for authorisation for continued use or whether quarantined drug should be destroyed, returned, or can be used for the trial.

## 11. NON INVESTIGATIONAL MEDICINAL PRODUCTS (NIMPS)

### 11.1 Traceability

Sites should ensure that appropriate systems are implemented that will allow adequate reconstruction of movement and administration of all NIMPs identified in the Protocol.

### 11.2 Recall

In the event of a national recall by the manufacturer, site will follow hospital procedure and must notify UCL CTC if a randomised trial patient has received NIMP from an affected batch.