SUMMARY OF DRUG ARRANGEMENTS

R-CODOX-M/IVAC
United Kingdom

CONTACT DETAILS

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VERSION HISTORY

Version number	Date	Summary of changes from previous version	Changes made by	Released to sites on
2.0	05/07/2011	Template adapted to be trial specific	Humra Shah	29/07/2011
2.1	10/08/2011	Section 6 – Pegfilgrastim listed in error on 'Hospital Commercial Stock' list. It is supplied for the trial.	Humra Shah	16/08/2011

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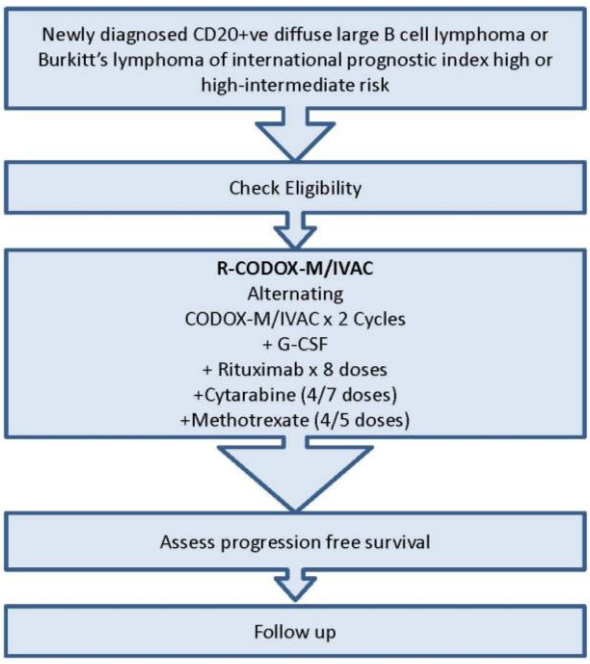
1. OVERVIEW

1.1 APPLICABILITY

This Summary of Drug Arrangements is applicable to the Pharmacy Lead and all other members of site staff who have responsibilities in conducting the R-CODOX-M/IVAC trial.

2. TRIAL INFORMATION



For detailed information on the R-CODOX-M/IVAC – A phase II Single Arm Study of the use of CODOX-M/IVAC with Rituximab (R-CODOX-M/IVAC) in the treatment of patients with Diffuse Large B-Cell Lymphoma (DLBCL) or Burkitt's Lymphoma (BL) of International Prognostic Index (IPI) High or High Intermediate Risk please refer to the current version of the protocol.

3. PHARMACY REGISTRATION & SET-UP

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

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

The Pharmacy Lead is responsible for ensuring all members of staff undertaking trial related activities have completed the Delegation Log or a separate Signature Log held in the Pharmacy Site File.

The Pharmacy Lead (or appropriate delegate) must be present at the site initiation teleconference, which will take place prior to site activation. If the Pharmacy Lead (or appropriate delegate) is not available for the general site initiation, a separate teleconference conducted by UCL CTC trial staff must be held.

Prior to site initiation, Pharmacy Site File documentation for a file to be prepared at site will be sent to the Pharmacy Lead from UCL CTC.

The contents of the file will include copies of forms for drug ordering and accountability logs for R-CODOX-M/IVAC. All trial related documentation should be retained in the Pharmacy Site File (or a statement of its location).

3.1 PHARMACY ACTIVATION

The following must be completed and/or in place prior to site activation;

- Clinical Trial Authorisation
- REC Approval
- R&D and other local approvals as applicable
- Signed Clinical Trial Site Agreement
- Site (Principal Investigator & Research Team) & Pharmacy Initiation
- Completed and signed Declaration of Participation and Delegation log

Once the above are completed and/or are in place a Site Activation letter will be sent from UCL CTC, confirming site is open to recruit patients

4. REGISTRATION

Once the site is activated, patients may be recruited into the trial. Once an eligible patient has been identified, the site research team will fax a completed registration form to UCL CTC to register the patient. UCL CTC will provide confirmation of registration by fax to the research team.

5. TRIAL DRUGS

In accordance with the Clinical Trial Authorisation (CTA) granted by the MHRA on the 09/12/2005, the following are classed as Investigational Medicinal Products (IMPs):

- Pegfilgrastim
- Rituximab
- Cyclophosphamide
- Cytarabine
- Methotrexate
- Ifosfamide
- Etoposide
- Doxorubicin
- Vincristine

6. SUPPLY OF TRIAL DRUGS

For R-CODOX-M/IVAC the following drugs will be provided free of charge to site pharmacies for the duration of the trial:

- Pegfilgrastim (IMP) – provided by Amgen

The following drugs **will not** be provided for the trial therefore hospital commercial stock should be used. Pharmacies must ensure they have adequate supplies for the trial.

- Rituximab (IMP)
- Cyclophosphamide (IMP)
- Cytarabine (IMP)
- Methotrexate (IMP)
- Ifosfamide (IMP)
- Etoposide (IMP)
- Doxorubicin (IMP)
- Vincristine (IMP)

6.1. INITIAL SUPPLY OF Pegfilgrastim

Amgen are providing Pegfilgrastim free of charge for the trial. Pegfilgrastim should be ordered directly from Amgen. This should be ordered on a strictly per-patient basis. A Pegfilgrastim Drug Order form is provided in the PSF. Please complete the form with patient's trial number, name of the PI, the Pharmacist's name, telephone and fax numbers and the address for delivery. The number of syringes of Pegfilgrastim must also be entered.
The completed form should be faxed to Amgen Customer Services on 0203 024 0073. Please allow 5 working days for delivery. Completed Drug Order forms must be retained in the relevant section of Pharmacy Site File.
Patients have Pegfilgrastim on day 13 of the CODOX-M cycles (1 & 3) and day 7 of the M-IVAC cycles (2 & 4), and the supplier will not permit sites to order stock in advance of entering a patient into the trial.

6.2 RECEIPT OF Pegfilgrastim

It is important to log receipt of each batch of Pegfilgrastim on the **Accountability Log** in a timely manner and store the drug appropriately (see section 6.4). Sites are permitted to use in-house records but they must include all the information requested in the trial-specific logs.

Drug receipts and all subsequent drug movements should be recorded in the accountability logs. These must be filed in the pharmacy site file, and must be sent to UCL CTC on request.
Following delivery of Pegfilgrastim, please inspect and verify the contents and conditions of the shipment.

If the Pegfilgrastim has not arrived by the expected date and time, pharmacy must contact Amgen.

6.3 LABELLING OF Pegfilgrastim

Pegfilgrastim will be supplied on a per patient basis by Amgen Ltd. Pharmacy must add the label information below upon receipt. All other Annex 13 information required should be adhered to and will be on the commercial packs.

Primary Label - Syringe (can be attached on protective packaging)

For Clinical Trial Use ONLY
EudraCT no: 2005-003479-19
Sponsor: University College London W1T 4TJ

Trial Number: _____
Site: _____
Cycle no: _____

Secondary Label - Box

For Clinical Trial Use ONLY
EudraCT no: 2005-003479-49
Sponsor: University College London CTC, London W1T 4TJ

Principal Investigator: _____
Trial Number: _____
Site: _____

Store in a refrigerator (2°C - 8°C)
Keep out of reach of children

Principal Investigator Information, Site name and Patient trial number are blank and are to be added by the site.

6.3.1 Labelling of Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide, Doxorubicin and Vincristine

An exemption from IMP labelling was granted for Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide, Doxorubicin and Vincristine on 09.06.2011 by the MHRA as its use falls under the remit of Regulation 46(2) of the medicines for human use (clinical trials) regulations.
3) The IMPs will be labelled in accordance with the requirements of Schedule 5 to the Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994 that apply in relation to dispensed relevant medicinal products

6.4 IMP STORAGE AND HANDLING OF Pegfilgrastim, Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide, Doxorubicin and Vincristine

6.4.1 Pegfilgrastim

For details of IMP handling and incompatibilities please refer to the current version of the supplied Summary of Product Characteristics.

6.4.2 Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide, Doxorubicin and Vincristine

For details of IMP handling and incompatibilities please refer to the current version of the Summary of Product Characteristics for the brand used at site

6.5 STORAGE CONDITIONS FOR Pegfilgrastim, Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide and Doxorubicin

6.5.1 Pegfilgrastim

Pegfilgrastim should be stored in accordance with the current Summary of Product Characteristics. The supplied drug must be kept segregated from hospital stock in a designated area. Pharmacies must keep a record of temperature in the drug storage area(s) using their own logs. Pharmacies should insert a file note in the Pharmacy Site File with details of temperature monitor systems and location of temperature logs if held elsewhere.

6.5.2 Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide, Doxorubicin and Vincristine

Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide, Doxorubicin and Vincristine should be stored in accordance with the current Summary of Product Characteristics for the brand used at site. **Note:** Pharmacies are responsible for ensuring that Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide, Doxorubicin and Vincristine has been stored appropriately **prior to use**, and has not been the subject of a prior temperature excursion.

6.6 TEMPERATURE EXCURSIONS

6.6.1 Pegfilgrastim

Temperature excursions outside of the acceptable ranges as specified in the current Summary of Product Characteristics must be reported to UCL CTC as soon as possible. Affected trial stock must be quarantined until notice from UCL CTC as to whether it can be used for the trial.
Procedures 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 document.

Sites will be notified by UCL CTC whether quarantined drug should be destroyed or can be used for the trial.

6.7 PRESCRIBING IMPs

The Investigator is responsible for ensuring all Trial Drugs are prescribed appropriately for a patient on the trial. Please refer to the trial protocol for dosing schedules of Pegfilgrastim, Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide, Doxorubicin and Vincristine.

Sites should develop their own trial specific prescriptions. New sites must be forward a copy to UCL CTC prior to the first patient being registered.

Prescriptions must be signed by the PI or appropriate member of staff (as identified on the site delegation log) and a copy must be retained in the Pharmacy Site File.

6.8 DISPENSING & RECORDING OF Pegfilgrastim, Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide, Doxorubicin and Vincristine

The Pegfilgrastim, Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide, Doxorubicin and Vincristine **Drug Accountability Log** must be completed to record each dose of Pegfilgrastim, Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide, Doxorubicin and Vincristine dispensed for each trial participant. This must be retained in the relevant section of the Pharmacy Site File, and a copy must be submitted to UCL CTC upon request.

Trial specific Pegfilgrastim must not be dispensed to patients who are not enrolled in the R-CODOX-M/IVAC trial.

When a prescription of Pegfilgrastim, Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide, Doxorubicin and Vincristine is made, Pharmacy must label the reconstituted solution with the following details in addition to the standard dispensing label:

- For Clinical Trial Use Only
- Name of the Trial /Trial Acronym (not required if
- EudraCT Number used) EudraCT number (not required if Name of the Trial used)
- Name of the Sponsor (not mandatory)
- Name of the Local Investigator (not mandatory)

6.9 ACCOUNTABILITY LOGS FOR Pegfilgrastim, Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide, Doxorubicin and Vincristine

During the course of the trial UCL CTC will request copies of the following for central monitoring purposes:

- Pegfilgrastim Drug Order form
- Pegfilgrastim Drug Receipt form
- Pegfilgrastim, Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide, Doxorubicin and Vincristine Accountability logs.

Accountability Logs will be provided for the trial; however, 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.

Accountability Logs must be retained in the relevant section of the Pharmacy Site File.

It is the responsibility of the Pharmacy Lead to maintain drug accountability records for Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide, Doxorubicin and Vincristine. The Pharmacy Lead (or appropriate delegate) must record the receipt and dispensing of Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide, Doxorubicin and Vincristine the appropriate **Accountability Log** found in the Pharmacy Site File.

6.10 DISPOSAL/DESTRUCTION OF Pegfilgrastim, Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide, Doxorubicin and Vincristine Details

Any dispensed and subsequently unused Trial Drugs (i.e not administered) will be processed according to local policy. Details of the local drug destruction policy should be filed in the pharmacy site file.

6.11 RECALL OF Pegfilgrastim, Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide and Doxorubicin

Pegfilgrastim
In the event of Pegfilgrastim recall, UCL CTC will notify the Pharmacy Lead with arrangements for recall and liaise with Amgen to ensure replacement product is supplied where necessary.

Rituximab, Cyclophosphamide, Cytarabine, Methotrexate, Ifosfamide, Etoposide and Doxorubicin
In the event of a recall initiated by the manufacturer or RA site will follow hospital procedure and must notify UCL CTC if a patient has received IMP from affected batches.

7. NON INVESTIGATIONAL MEDICINAL PRODUCTS (NIMPS)

The following drugs **will not** be provided for the trial and so hospital commercial stock should be used. Pharmacies must ensure they have adequate supplies for the trial.

- Mesna (NIMP)
- Leucovorin (NIMP)

7.1 RECALL

Mesna and Leucovorin

In the event of a national recall by the manufacturer site should follow hospital procedure and must notify UCL CTC if a patient has received IMP from affected batches.