| Pharmacy Manual | |
|---|---|
| **AIR-NET Trial: Testing anti-inflammatories for the treatment of bronchiectasis**<br>A randomised, open-label, multifactorial, multicentre, platform trial using a range of repurposed anti-inflammatory treatments to improve outcomes in patients with bronchiectasis within the EMBARC clinical research network. | |
| **IRAS ID:** 1010124 | |
| Sponsor:<br>University of Dundee & NHS Tayside | Chief Investigator:<br>Prof. James Chalmers |

This document describes the process for Investigational Medicinal Product (IMP) and placebo management at site.

Abbreviations / terms used

| | |
|---|---|
| CTP | Clinical Trial Pharmacy |
| IMP | Investigational Medicinal Product |
| IWRS | Interactive Web Response System |
| PIL | Patient Information Leaflet |
| PSF | Pharmacy Site File |
| SOP | Standard Operating Procedure |
| SmPC | Summary of Product Characteristic |
| TM | Trial Manager |
| TRuST | Tayside Randomisation System |

# Contents

## 1. Treatment Overview

Participants will be randomly assigned to receive a 28-day treatment period of either:

- Usual care
- Disulfiram (two 200 mg oral tablets once daily)
- Dipyridamole (one 200 mg oral prolonged/modified release capsule twice daily)
- Doxycycline (one 100 mg oral capsule once daily)

This trial is open label. The trial team, pharmacy team & the trial participants will be aware of the treatment allocation.

## 2. Investigational Medicinal Product (IMP) Description

| Description | Packaging | Storage conditions | Supplier |
|---|---|---|---|
| Disulfiram 200mg tablets<br>Any brand is permitted | To be dispensed by pharmacy & clinical trial label to be applied | As per summary of product characteristics (SmPC) conditions | Generic drug, procured through local site NHS pharmacy |
| Dipyridamole 200 mg capsules<br>Any brand is permitted | To be dispensed by pharmacy & clinical trial label to be applied | As per SmPC conditions | Generic drug, procured through local site NHS pharmacy |
| Doxycycline 100 mg capsules<br>Any brand is permitted | To be dispensed by pharmacy & clinical trial label to be applied | As per SmPC conditions | Generic drug, procured through local site NHS pharmacy |

## 3. IMP Supply

IMP will not be provided and should be procured through local site NHS pharmacy. Clinical Trial Pharmacy (CTP) should ensure that there is a minimum stock of each IMP at site before recruitment begins and is maintained throughout the trial duration. Where a site has difficulty obtaining the supply of medication for any of the treatment arms, the site will continue to recruit and randomise participants between the available treatment arms and usual care at that site.

Suggested minimum stock levels required at site throughout the trial duration:

| IMP | Minimum stock required at site |
|---|---|
| Disulfiram 200 mg tablets | 2 x 50 |
| Dipyridamole 200 mg MR capsules | 2 x 60 |
| Doxycycline 100 mg capsules | 2 x 50 |

## 4. IMP Storage

Each IMP should be stored according to the SmPC conditions. If a temperature excursion occurs, this should be recorded following local pharmacy procedures and reported to the trial manager. The stock should not be issued to participants if the temperature excursion has exceeded allowable conditions.

## 5. Interactive Web-based Randomisation System (IWRS)

Randomisation will be performed by a delegated member of the research team on the IWRS called Tayside Randomisation System (TRuST). The clinical research team will provide clinical trial pharmacy with a Clinical Trial Request & Release Form, which will document the participant ID and the treatment allocation to be prepared & dispensed from pharmacy. CTP will not require access to TRuST. See Appendix 1 for the template Clinical Trial Request & Release Form.

## 6. IMP Preparation

### 6.1. IMP Dispensing

IMP will be dispensed at visit 2, following randomisation. Following randomisation, clinical trial pharmacy will receive a Clinical Trial Request & Release Form (appendix 1) which has been signed by a delegated trial doctor. This will detail the participant ID, treatment allocation and total number of capsules/tablets to be dispensed.

Site pharmacies can use their own prescription form (paper or electronic) provided it collects the same data as the AIR-NET request & release form.

The IMP detailed on the Clinical Trial Request & Release Form must be dispensed to provide only the required number of tablets/capsules for the trial treatment. The IMP may be removed from their original packaging and placed into a box/bottle for clinical trial dispensing. Please see the table below for the required number of tablets/capsules for each treatment allocation.

The manufacturer patient information leaflet (PIL) must be issued with the trial medication. The PIL can be provided from the original medication pack, photocopied from the original pack or downloaded and printed from the electronic medicines compendium. https://www.medicines.org.uk/emc

| IMP | Total dose | Duration of dose | Total number required |
|---|---|---|---|
| Disulfiram 200 mg tablets | 2 tablets, once daily | 28 days | 60 |
| Dipyridamole 200 mg MR capsules | 1 capsule, twice daily | 28 days | 60 |
| Doxycycline 100 mg capsules | 1 capsule, once daily | 28 days | 30 |

Once the required number of tablets/capsules have been dispensed and packaged, the outer packaging must be labelled with a clinical trial label. Please see Appendix 2 for the labelling requirements. A delegated member of the pharmacy team to check the IMP and sign the Clinical Trial Request & Release Form. All completed Clinical Trial Request & Release Forms should be filed in the PSF.

### 6.3. IMP Accountability

CTP must record full accountability for the trial IMPs. A paper IMP Accountability Log will be provided in the pharmacy site file (PSF) (see Appendix 3). The IMP accountability log can be held on paper or electronically, according to local procedures. Local IMP accountability log may be used provided it collects the same data as the AIR-NET IMP accountability log.

The participant ID, treatment allocation, batch number, expiry date, date of dispensing, number of tablets/capsules released and who performed the IMP release, as well as any IMP returns & disposal, will be documented on the accountability log.

If an error occurs in completing the Clinical Trial Request & Release Form prior to the release of the IMP a file note should be completed and a copy of incorrect document(s) filed in the PSF.

Where an error is noticed after dispensing the appropriate action to recall the IMP should be made. The Principal Investigator and TM should be informed, and a Protocol Breach Report completed. The Breach Reporting Form can be found under TASC SOP 59 here: https://www.dundee.ac.uk/tasc/policies-sops-templates/study-progress

### 6.4. Recording IMP Returns

Participants will be requested to return their IMP box/bottle after they have completed the trial treatment. IMP returns will be recorded at visit 5. The number of tablets/capsules returned should be documented on the IMP accountability log held in the PSF. Pharmacy should dispose of any remaining IMP as per local policy and document the disposal on the IMP Accountability Log.

At the end of the trial, CTP will be requested to sign the final IMP Accountability Log, file in the PSF and email a copy to the TM.

Signed Shona Carson Date 18 Nov 2024

Shona Carson

Clinical Trials Pharmacist, Clinical Trial Pharmacy, Ninewells Hospital, Dundee

| | | |
|---|---|---|
| Clinical Trial Manager | airnet-tm@dundee.ac.uk | 01382 383097 |
| Chief Investigator | j.chalmers@dundee.ac.uk | 01382 386131 |
| Lead Clinical Trial Pharmacist (Tayside) | shona.carson@nhs.scot | 01382 632969 |

**Appendices**

## Appendices

## Appendix 1 Template Clinical Trial Request & Release Form

AIR-NET

AIR-NET Trial: Testing anti-inflammatories for the treatment of bronchiectasis

### CLINICAL TRIAL REQUEST & RELEASE FORM

| | | | |
|---|---|---|---|
| Sponsor: | **University of Dundee and NHS Tayside** | | |
| IRAS | **1010124** | CTP No. | |
| Chief Investigator: | **Prof James Chalmers** | Tel No: **01382 386131** | |
| Principal Investigator: | | Tel No: | |
| Participant ID: | | | |
| Participant Name: | | | |
| Date of Birth: | | Hospital Number/CHI Number | |
| Visit Number: | | Visit Date: | |

Participant has been randomised to the following:

☐ **Disulfiram 200mg tablets 2 tablets 1 daily for 28 days**

☐ **Dipyridamole 200mg capsules 1 capsule twice daily for 28 days**

☐ **Doxycycline 100mg capsules 1 capsule once daily for 28 days**

| | | |
|---|---|---|
| Investigator or delegate Signature: | | Date: |

Clinical Trial Pharmacy: Please supply the following:

☐ **Disulfiram 200mg x 60 tablets**

☐ **Dipyridamole 200mg x 60 MR capsules.**

☐ **Doxycycline 100mg x 30 capsules**

☐ **PIL issued with trial medication**

| | | |
|---|---|---|
| Dispensed By: | | Date: |
| Checked By: | | Date: |
| Collected by: | | Date: |

AIR-NET IMP Request Release Form V1 18-11-2024

**Appendix 2 IMP Label Requirements**

Outer package label requirements:

- Trial name & IRAS ID
- Pharmaceutical dosage form, route of administration, quantity of dosage units, the name and strength of IMP
- Directions for use
- Storage conditions
- Participant ID number
- Participant name
- Expiry date
- Batch number
- Date of dispensing
- Chief Investigator details
- “Keep out of reach of children”
- “For clinical trial use only”

Where IMP is supplied in original pack – storage conditions, batch number and expiry date do not need to be duplicated on the dispensing label

<table>
<tr><td>Example template label for Disulfiram</td><td>AIR-NET Trial<br>Contains: Disulfiram 200 mg, 60 tablets<br>Directions for use: Take 2 tablets, once daily for a total of 28 days.<br>For oral use only. Store below 25°C.<br><br><table><tr><td>Participant ID</td><td></td></tr><tr><td>Participant name</td><td></td></tr><tr><td>Date of dispensing</td><td></td></tr><tr><td>Expiry date</td><td></td></tr><tr><td>Batch number</td><td></td></tr></table><br>Chief Investigator: Prof James Chalmers, Ninewells Hospital, Dundee DD1 9SY. Tel: 01382 383642<br>IRAS number: 1010124<br><br>Keep out of the sight and reach of children<br>For clinical trial use only</td></tr>
</table>

<table>
<tr><td>Example template label for Dipyridamole</td><td colspan="2">AIR-NET Trial<br>Contains: Dipyridamole 200 mg, 60 MR capsules<br>Directions for use: Take 1 capsule, twice daily for a total of 28 days.<br>For oral use only.</td></tr>
<tr><td></td><td>Participant ID</td><td></td></tr>
<tr><td></td><td>Participant name</td><td></td></tr>
<tr><td></td><td>Date of dispensing</td><td></td></tr>
<tr><td></td><td>Expiry date</td><td></td></tr>
<tr><td></td><td>Batch number</td><td></td></tr>
<tr><td></td><td colspan="2">Chief Investigator: Prof James Chalmers, Ninewells Hospital, Dundee DD1 9SY. Tel: 01382 383642<br>IRAS number: 1010124<br><br>Keep out of the sight and reach of children<br>For clinical trial use only</td></tr>
</table>

<table>
<tr><td>Example template label for Doxycycline</td><td colspan="2">AIR-NET Trial<br>Contains: Doxycycline 100 mg, 30 capsules<br>Directions for use: Take 1 capsule, once daily for a total of 28 days.<br>For oral use only. Store below 25°C.</td></tr>
<tr><td></td><td>Participant ID</td><td></td></tr>
<tr><td></td><td>Participant name</td><td></td></tr>
<tr><td></td><td>Date of dispensing</td><td></td></tr>
<tr><td></td><td>Expiry date</td><td></td></tr>
<tr><td></td><td>Batch number</td><td></td></tr>
<tr><td></td><td colspan="2">Chief Investigator: Prof James Chalmers, Ninewells Hospital, Dundee DD1 9SY. Tel: 01382 383642<br>IRAS number: 1010124<br><br>Keep out of the sight and reach of children<br>For clinical trial use only</td></tr>
</table>

Appendix 3. IMP Accountability Log

**AIR-NET Trial: Testing anti-inflammatories for the treatment of bronchiectasis**

A randomised, open-label, multifactorial, multicentre, platform trial using a range of repurposed anti-inflammatory treatments to improve outcomes in patients with bronchiectasis within the EMBARC clinical research network.

**IMP ACCOUNTABILITY FORM FOR PHARMACY**

| | | | | | |
|---|---|---|---|---|---|
| **IRAS** | 1010124 | | **Chief Investigator** | Prof James Chalmers | |
| **Local CTP ID** | | **Principal Investigator** | | **Tel No** | |

| | |
|---|---|
| **IMP** | |

| **FROM HOSPITAL SUPPLY** | | | | **ISSUED** | | | | STOCK BALANCE | **RETURNED** | | | **DISPOSED OF** | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Date received | Quantity | Batch Number | Expiry | Participant ID | Date | Quantity (capsules/ tablets) | Signature | | Date | Quantity (capsules/ tablets) | Signature | Date | Signature |
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Please complete a separate accountability log for each IMP for AIR-NET.

**Comments:**

Signed for Pharmacy: Date: