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Simplified IMP-Dossier

Tranexamic Acid

Simplified IMP-D agreed by:

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University of Nottingham

Simplified IMP-D

Tranexamic Acid

Investigational Product Name (S)	Tranexamic Acid
Trade Name(s)	Not applicable
Generic Names (active)	Tranexamic Acid
MA Indication	Fibrinolysis
International Non-proprietary Name	Tranexamic Acid
ATC Code	B02AA02
CAS Number	1197-18-8
IUPAC	*trans*-4-(Aminomethyl)cyclohexanecarboxylic acid

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Introduction

This supplementary IMP-D only details aspects of secondary packaging, labelling and any changes from the reference SmPC. A reference SmPC is available for both the active and placebo products.
This document is to be used in conjunction with the SmPCs which details the primary packaging and shelf life.
Blinded individual treatment packs containing four 5ml glass ampoules of TXA 500mg or sodium chloride 0.9% which will be very similar in appearance. The justification for blinding can be found in the protocol.

Manufacturing Process

2.2.1.S Drug Substance

Tranexamic Acid Injection 500mg/5ml will be used in this trial.

2.1.1.P Test Product

2.2.1.P.3 Manufacture

2.2.1.P.3.1 Manufacturer(s)

Name:	Sharp Clinical Services Ltd
Address:	Unit 28 Heol Klockner Heads of the Valleys Ind Est Rhymney Wales, NP22 5RLUnited Kingdom
Licence:	MIA(IMP) 10284
Responsibility:	Blinding, labelling and secondary packaging, QC testing and release of final clinical trial supplies (UK and non-EU countries)

Name:	Manufacturing Packaging Farmaca (MPF) B.V.
Address:	Neptunus 12 8448 CN Heerenveen The Netherlands
Licence:	108630 F
Responsibility:	Importation into the EU, QP certification and distribution for EU countries

2.2.1.P.3.3 Description of Manufacturing Process and Process Controls

This is the marketed product that is manufactured according to marketing authorisation.

The Tranexamic Acid 500mg/5ml injection will be allocated to participants randomised to active.

The tranexamic acid injection will be purchased and shipped to Sharp Clinical Services Ltd who will prepare the final blinded supplies.

Sharp Clinical Services Ltd will add a heat shrink sleeve to the ampoule neck to cover most identifying marks. They will label all ampoules with the primary black-out label (see appendix 1). A pack number will be assigned to each group of 4 ampoules (i.e. 4 ampoules will have the same pack number and will be packed in the corresponding secondary pack). The secondary pack will be labelled with the secondary label (see appendix 1) according to clinical trial regulations prior to final QP release. Participant Name, and date of randomisation will be added to the secondary label at the time of dispensing. The label will be in English only for the start up phase of the trial when the supplies are to the UK only. The label will be translated for supply to other countries as required by local regulations.

To preserve blinding, the expiry date of a batch of the finished blinded IMP (both tranexamic acid and placebo) will correspond to the IMP with the shortest assigned expiry date.

Final QP release for UK and non-EU countries will be performed by the designated individual at Sharp Clinical Services Ltd.

Importation and Final QP release for EU countries will be performed by the designated individual at Manufacturing Packaging Farmaca (MPF) B.V (part of Sharp Packaging Solutions)

2.2.1.P.7 Container Closure System

The trial design, “double blind randomised placebo controlled” requires that all supplies are de-identified or blinded. Therefore, for the purpose of this trial the packaging and labelling has been changed from the authorised product to ensure that all containers, labels and pack size match for each of the active and placebo ampoules.

The SmPC defines no special precautions for storage. We will label the IMP as avoid freezing or excessive heat.

2.2.1.P.8 Stability

Secondary packaging will not affect stability.

3.2.1.P Placebo Product in Clinical Trials

3.2.1.P.3 Manufacture

3.2.1.P.3.1 Manufacturer(s)

Name:	Sharp Clinical Services Ltd
Address:	Unit 28 Heol Klockner Heads of the Valleys Ind Est Rhymney Wales, NP22 5RL United Kingdom
Licence:	MIA(IMP) 10284
Responsibility:	Labelling and secondary packaging, QC testing and release of final clinical trial supplies

Name:	Manufacturing Packaging Farmaca (MPF) B.V.
Address:	Neptunus 12 8448 CN Heerenveen The Netherlands
Licence:	108630 F
Responsibility:	Importation into the EU, QP certification and distribution for EU countries

3.2.1.P.3.3 Description of Manufacturing Process and Process Controls

Sodium Chloride 0.9% Injection will be used in this trial.

This is the marketed product that is manufactured according to Marketing Authorisation.

The sodium chloride 0.9% injection will be allocated to participants randomised to placebo.

The Sodium Chloride 0.9% Injection will be purchased and shipped to Sharp Clinical Services Ltd who will prepare the final blinded supplies.

Sharp Clinical Services Ltd will add a heat shrink sleeve to the ampoule neck to cover most identifying marks. They will label all ampoules with the primary black-out label (see appendix 1). A pack number will be assigned to each group of 4 ampoules (i.e. 4 ampoules will have the same pack number and will be packed in the corresponding secondary pack). The secondary pack will be labelled with the secondary label (see appendix 1) according to clinical trial regulations prior to final QP release. Participant Name and date of randomisation will be added to the secondary label at the time of dispensing. The label will be in English only for the start up phase of the trial when the supplies are to the UK only. The label will be translated for supply to other countries as required by local regulations.

To preserve blinding, the expiry date of a batch of the finished blinded IMP (both tranexamic acid and placebo) will correspond to the IMP with the shortest assigned expiry date.

Final QP release for UK and non-EU countries will be performed by the designated individual at Sharp Clinical Services Ltd.

Importation and Final QP release for EU countries will be performed by the designated individual at Manufacturing Packaging Farmaca (MPF) B.V (part of Sharp Packaging Solutions)

3.2.1.P.7 Container Closure System

The trial design, “double blind randomised placebo controlled” requires that all supplies are de-identified or blinded. Therefore, for the purpose of this trial the packaging and labelling has been changed from the authorised product to ensure that all containers, labels and pack size match for each of the active and placebo ampoules.

The SmPC defines storage at room temperature and protected from excessive heat and freezing. We will label the IMP as avoid freezing or excessive heat.

3.2.1.P.8 Stability

Secondary packaging will not affect stability.

Appendix 1

Sample study label for blinded clinical supplies:

Primary (ampoule) label:

TICH-3 Study **Eudract Number 2021-001050-62**
Injection for Intravenous Use
Tranexamic Acid 500mg in 5mls OR Sodium Chloride 0.9%
Pack Number: xxxx
BN xxxx Expiry Date xx/xx/xx
Chief Investigator: Prof N Sprigg
Deputy Chief Investigator: Prof P Bath
Sponsor: University of Nottingham

Secondary (outer box) label:

For Clinical Trial Use Only Avoid freezing or excessive heat.
Tranexamic Acid in Intracerebral Haemorrhage (TICH-3)
EudraCT Number 2021-001050-62
(4) 5ml ampoules for intravenous injection.
Tranexamic Acid 500mg in 5ml or Sodium Chloride 0.9%
Administer in accordance with the protocol

Participant Name _____

Date of randomisation _____Pack Number: xxxx
Batch Number: xxxx Expiry Date: xx/xx/xx
Chief Investigator Prof Nikola Sprigg, University of Nottingham, QMC Campus, Nottingham NG7 2UH Tel xxxxxx
Deputy Chief Investigator Prof Philip Bath, University of Nottingham, QMC Campus, Nottingham NG7 2UH Tel xxxxxx
Sponsor: University of Nottingham.

Label content as shown, formatting of final versions may vary.