Information for Pharmacy

Trial Title:	Tranexamic acid for hyperacute spontaneous IntraCerebral Haemorrhage **(TICH-3)**
EudraCT No:	2021-001050-62
SITE DETAILS	
Participants	Adults within 4.5 h of onset of acute spontaneous ICH (confirmed on brain imaging).
Randomisation and Treatment details	Randomisation will be to TXA vs. placebo in a 1:1 ratio. Intravenous tranexamic acid 2g: 1g loading dose given as 100 mls infusion over 10 minutes, followed by 1g in 250 mls infused over 8 hours. Comparator – matching placebo (normal saline 0.9%) administered by an identical regimen. Due to the emergency situation, a straightforward randomisation process will be used, where sites will simply select the next available treatment pack, which will be a numbered box containing either TXA or placebo according to a computer-defined sequence. Boxes will be identical with the exception of the treatment pack number. Randomisation will be stratified by site with supply to each site balanced for TXA and placebo. A block of 6 treatment packs will be provided together. The block will be sent to the hospital pharmacy prior to being stored in the stroke unit/emergency department. Once the block of 6 treatment packs has arrived on the stroke unit/emergency department, an investigator will need to login to the TICH-3 web site and mark the block as available for randomisation.
Source of IMP	Sharp Clinical Services Ltd will prepare blinded individual treatment packs containing four 5ml glass ampoules of tranexamic acid 500mg or sodium chloride 0.9% which will be very similar in appearance by the addition of a heat shrink sleeving. Ampoules and the secondary carton will be labelled in accordance with Annex 13 of Volume 4 of The Rules Governing Medicinal Products in the EU: Good Manufacturing Practices, assuming that the primary and secondary packaging remain together throughout the trial. To facilitate identification the carton and the ampoules contained within it will be labelled with the same unique pack number. Detailed prescribing and administration instructions will be provided in the treatment pack (available on the TICH-3 trial website). The final product will be QP released by the designated person at Sharp Clinical Services to provide blinded trial treatment packs for this trial. Participant Treatment Packs are delivered to the hospital pharmacy from Sharp Clinical Services Ltd.
Storage of material	The packs will be stored at room temperature and protected from excessive heat and freezing in a restricted access area. Stability data exists which demonstrates that Tranexamic Acid is stable at temperatures between -20°C and 50°C. Temperature monitoring will not be required. The IMP will be clearly labelled for clinical trial use only. The blinding and labelling does not alter the integrity of the primary pack. It is expected that the IMP will be stored in a controlled temperature environment (at or below 25°C) at Sharp Clinical Services prior to dispatch and at Pharmacy Departments prior to delivery to the stroke unit/emergency department. It is expected that Clinical Trials Pharmacists take into account the SmPC (please see below for reference safety information) requirements of the active and placebo products when conducting their assessment of the suitability of the IMP storage area in the stroke unit/emergency department.

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	Reference Safety Information: Example Tranexamic Acid SmPC: https://www.medicines.org.uk/emc/product/1220/smpc Section 4.8 of the SmPC, date of last revision 02 February 2021, will act as the reference safety information. Example Sodium Chloride SmPC: https://www.medicines.org.uk/emc/product/6269/smpc#gref Section 4.8 of the SmPC, date of last revision 01 April 2020, will act as the reference safety information.
Receipt of goods	Pharmacy will acknowledge receipt of IMP and complete an IMP Inventory (download from TICH-3 Trial website http://tich-3.ac.uk/docs/).
Procedure for managing returns	Any unused ampoules are returned to pharmacy. The local site investigator is responsible for ensuring trial treatment accountability, including reconciliation of trial treatment and maintenance of trial treatment records, throughout the course of the trial in accordance with UK regulatory requirements. Responsibility can be delegated to the site pharmacy clinical trials staff in accordance with local process.
Unblinding of treatment code procedure	Clinicians, patients and outcome assessors (clinical, radiological assessors) will be blinded to treatment allocation. In general there should be no need to unblind the allocated treatment. If some contraindication to tranexamic acid develops after randomisation (e.g. clinical evidence of thrombosis), the trial treatment should simply be stopped. Unblinding should be done only in those rare cases when the doctor believes that clinical management depends importantly upon knowledge of whether the patient received TXA or placebo. In those few cases when urgent unblinding is considered necessary, the emergency telephone number (see trial website http://tich-3.ac.uk/docs/) should be telephoned, giving the name of the doctor authorising unblinding and the treatment pack number. The caller will then be told whether the patient received TXA or placebo. The rate of unblinding will be monitored and audited. In the event of breaking the treatment code this will normally be recorded as part of managing a SAE and such actions will be reported in a timely manner. The Chief Investigator (delegated the sponsor's responsibilities) shall be informed immediately (within 24 hours) of any safety events occurring within the first 7 days after randomisation (including SARs/SUSARs/fatal SAEs). Safety events include venous thromboembolism; ischaemic events (arterial thrombosis at any site, ischaemic stroke, transient ischaemic attack peripheral artery embolism, myocardial infarction, acute coronary syndrome); seizures. Serious adverse events that are not safety outcomes do not need reporting unless the investigator believes them to be a SAR or SUSAR. Local investigators shall determine seriousness and causality in conjunction with treating medical practitioners.