NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

MOST

MOST Pharmacy Training Slides

StrokeNet Central Pharmacy

Christian Unger PharmD.

Noor Sabagha RPh, MPH

Washington University in St. Louis

MUSC Medical University of South Carolina

UTHealth The University of Texas Health Science Center at Houston

Memorial Hermann Texas Medical Center

University of Iowa Health Care

Table of Contents

MOST Overview

MOST is a:

- Three arm, single blinded, acute trial comparing:

  ARGATROBAN vs EPTIFIBATIDE vs PLACEBO

  In patients with an acute ischemic stroke who have already received standard of care thrombolysis (either tPA or tenecteplase (TNK))

- Study drug must be given within 75 minutes of standard care thrombolysis, ideally within 60 minutes.

- MOST will utilize a response adaptive randomization when assigning patients to each study arm. Based on benefit/futility, one or both treatment arms may be stopped during the study.

Shipment of Study Drug

Study drug will be sent to sites in kits using refrigerated shippers.

Each shipment will contain a packing slip that lists the contents of the shipment.

- Each shipment should be checked for any discrepancies between the packing slip and shipment contents.

Each shipment will contain a temperature monitor.

- Upon receipt, the temperature monitor must be checked for temperature excursions.
- Temperature Excursions covered on slide 10

StrokeNet Central Pharmacy will ship kits overnight to sites Mondays-Wednesday.

- No shipments will be made on weekends or holidays unless deemed necessary by StrokeNet Central Pharmacy and MOST Study Team

MOST Packing Slip # 1002

From:	To:
StrokeNet Central Pharmacy University of Cincinnati Holmes Hospital Room 1209 200 Albert Sabin Way ML 0405 Cincinnati, OH 45267-0405 Phone: (513) 584-3166 Fax: (513) 584-0091	**WebDCU Test Site 2, Charleston, SC** 2348 DCU, Medical University of South Carolina 135 Cannon Street, Suite 303, MSC 835 Charleston SC, 29425-8350

#	Drug Kit ID	Drug Name	Kit Expiration Date
1	88077	Argatroban	03-Jul-2021
2	88199	Placebo	03-Jul-2021

Pack List Date: 26-Sep-2019

Checking In Shipments

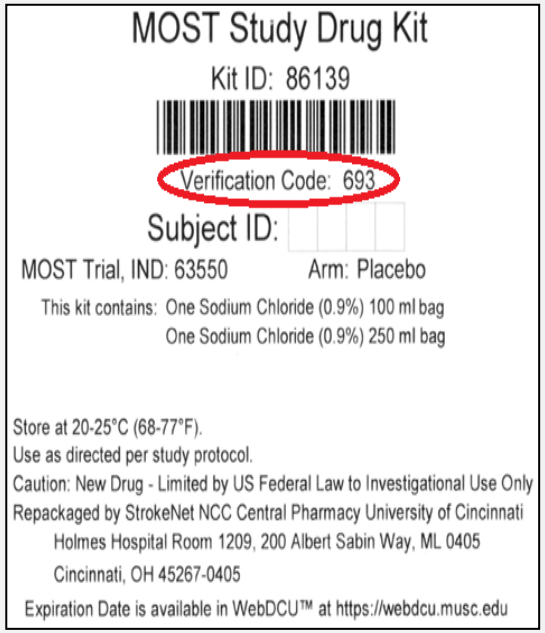
Shipments that do not have a temperature excursion or discrepancies will be received into WebDCU at: https://webdcu.musc.edu/ > MOST > Drug Tracking > Drug Site Receiving > Page Actions > Drug Site Receiving Pending.

Study drug kits are unavailable for dispensing until received into WebDCU™.

Kits should be marked as received in WebDCU within 2 days of shipment.

Kit labels, will have a unique verification code on the kit label that will be used to receive them into WebDCU (circled in red).

Storage areas must have a temperature monitoring system.



Study Drug Kits

Each study drug kit box will be 8”x 8”x 3” by size containing the following kit components:

Argatroban Kit

2-argatroban 250mg/2.5mL vial

1-sodium chloride 0.9% 100mL bag

1-sodium chloride 0.9% 250mL bag

1- argatroban compounding card

Eptifibatide Kit

1- eptifibatide 75mg/100mL with attached vial hanger

1- sodium chloride 0.9% 250mL bag

Placebo Kit

1- sodium chloride 0.9% 100mL bag

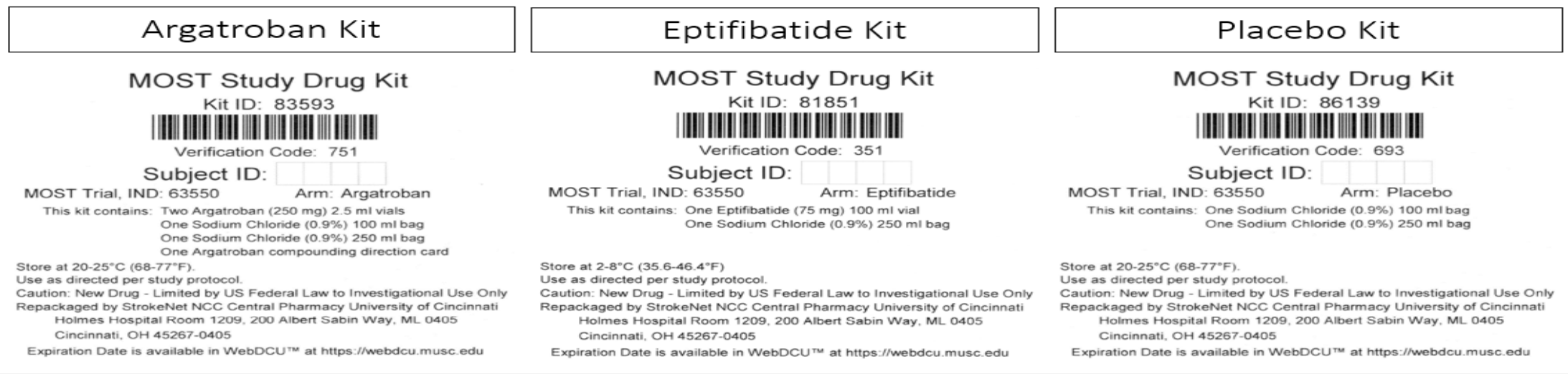
1- sodium chloride 0.9% 250mL bag

Study Drug Kits

Kits will arrive unblinded to the site pharmacy.

MOST is a single blinded study, the pharmacy and the study team know what the patient is receiving, but the patient does not know what they are receiving.

Each kit label will identify the treatment arm and components of the kit:



Argatroban Kit

MOST Study Drug Kit
Kit ID: 83593
Verification Code: 751
Subject ID:
MOST Trial, IND: 63550 Arm: Argatroban
This kit contains: Two Argatroban (250 mg) 2.5 ml vials
One Sodium Chloride (0.9%) 100 ml bag
One Sodium Chloride (0.9%) 250 ml bag
One Argatroban compounding direction card
Store at 20-25°C (68-77°F).
Use as directed per study protocol.
Caution: New Drug - Limited by US Federal Law to Investigational Use Only
Repackaged by StrokeNet NCC Central Pharmacy University of Cincinnati
Holmes Hospital Room 1209, 200 Albert Sabin Way, ML 0405
Cincinnati, OH 45267-0405
Expiration Date is available in WebDCU™ at https://webdcu.musc.edu

Eptifibatide Kit

MOST Study Drug Kit
Kit ID: 81851
Verification Code: 351
Subject ID:
MOST Trial, IND: 63550 Arm: Eptifibatide
This kit contains: One Eptifibatide (75 mg) 100 ml vial
One Sodium Chloride (0.9%) 250 ml bag
Store at 2-8°C (35.6-46.4°F)
Use as directed per study protocol.
Caution: New Drug - Limited by US Federal Law to Investigational Use Only
Repackaged by StrokeNet NCC Central Pharmacy University of Cincinnati
Holmes Hospital Room 1209, 200 Albert Sabin Way, ML 0405
Cincinnati, OH 45267-0405
Expiration Date is available in WebDCU™ at https://webdcu.musc.edu

Placebo Kit

MOST Study Drug Kit
Kit ID: 86139
Verification Code: 693
Subject ID:
MOST Trial, IND: 63550 Arm: Placebo
This kit contains: One Sodium Chloride (0.9%) 100 ml bag
One Sodium Chloride (0.9%) 250 ml bag
Store at 20-25°C (68-77°F).
Use as directed per study protocol.
Caution: New Drug - Limited by US Federal Law to Investigational Use Only
Repackaged by StrokeNet NCC Central Pharmacy University of Cincinnati
Holmes Hospital Room 1209, 200 Albert Sabin Way, ML 0405
Cincinnati, OH 45267-0405
Expiration Date is available in WebDCU™ at https://webdcu.musc.edu

Storage of Study Drug

Eptifibatide kits should be stored refrigerated between 2-8°C (36-46°F).

Argatroban and Placebo kits should be stored at room temperature 20-25°C (68-77°F).

- Argatroban will precipitate if it is stored under refrigeration

Study drug should be protected from excessive exposure to light.

Storage areas must have a temperature monitoring system.

- Sites may use their own institution-specific temperature monitoring log to document temperature or our study specific MOST Temperature Accountability Log, as long as drug storage temperatures are recorded on a regular basis.
- Sample temperature monitoring logs will be provided and available in WebDCU™ at: WebDCU>Most>Toolbox>Project Documents>Most Study Drug Temperature Log (Ambient) or (Refrigerated).

Temperature Excursions

A temperature excursion can occur during **daily monitoring** of the study drug storage area or during **transit** of the study drug.

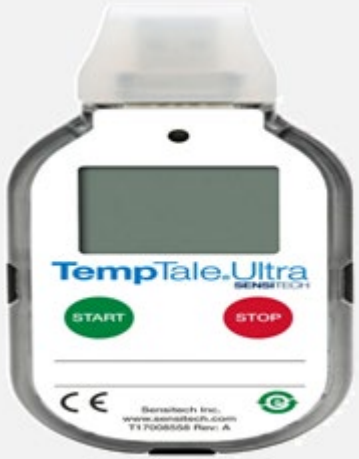
Any study drug exposed to a temperature excursion should be quarantined in the appropriate storage temperature.

Any known temperature excursions should be reported to:

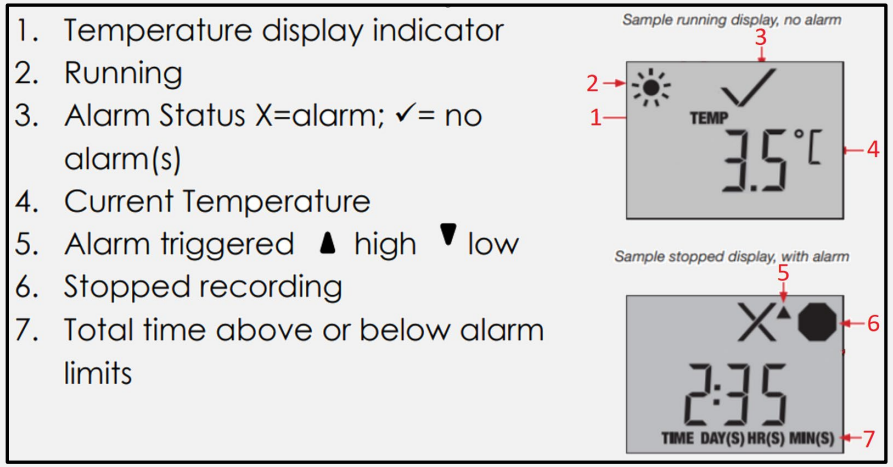
- Iris Deeds: irisdeeds@wustl.edu
- StrokeNet Central Pharmacy: strokenetcpharm@ucmail.uc.edu

Submit the following documents for temperature excursions

- Temperature Excursion Report Form (TERF) - available in WebDCU™
  - WebDCU>Most>Toolbox>Project Documents – **submit for both storage and in transit excursions**.
- Temperature data log from USB logger for excursions **in transit only.**



Data Logger Display



Shipment Requests

Study drug shipment requests will automatically be sent to the StrokeNet Central Pharmacy when sites are released to enroll, subjects are randomized, or study drug is damaged/expired.

- Drug Request will be sent to the Central Pharmacy 3 days prior to kit expiration.

Sites will have 2-3 study drug kits in stock initially.

- The maximum number of kits a site is expected to keep in inventory will be adjusted as the trial progresses according to individual site dispensing volume.

Sites can still enroll patients if they have only 1 or 2 kits in stock

Study Drug Kit Components

The MOST study will use marketed product commercially available in the United States.

Manufacturers of all drug kit components will change throughout the trial based on market availability.

Regardless of the manufacturer the following will remain the same:

- Drug Concentration
- Vial and Bag Volumes

Study Drug Compounding Pearls

No matter which arm you are preparing, you are always making 3 final products that will be administered to the patient. Dosing is weight-based and will always be **patient-specific**.

1. A bolus dose, **drawn up into a syringe** taken from the 100ml vial/bag.
2. 0-2 hour dose, a volume to be infused (VTBI) administered from the 100ml vial/bag run, over 2 hours at a specific rate.
3. 2-12 hour dose, administered from the 250ml bag as an infusion that will run over 10 hours at a specific rate.

It is important to prepare the bolus dose and infusion 1 first so that they can be administered as soon as possible.

Since dosing is weight-based patients will not receive the total volume in the 100ml vial/bag or the 250ml bag.

Upon Randomization, a Randomization Verification Form will be generated by WebDCU for the study team. This form must be provided to the pharmacy by the study team before compounding of study drug.

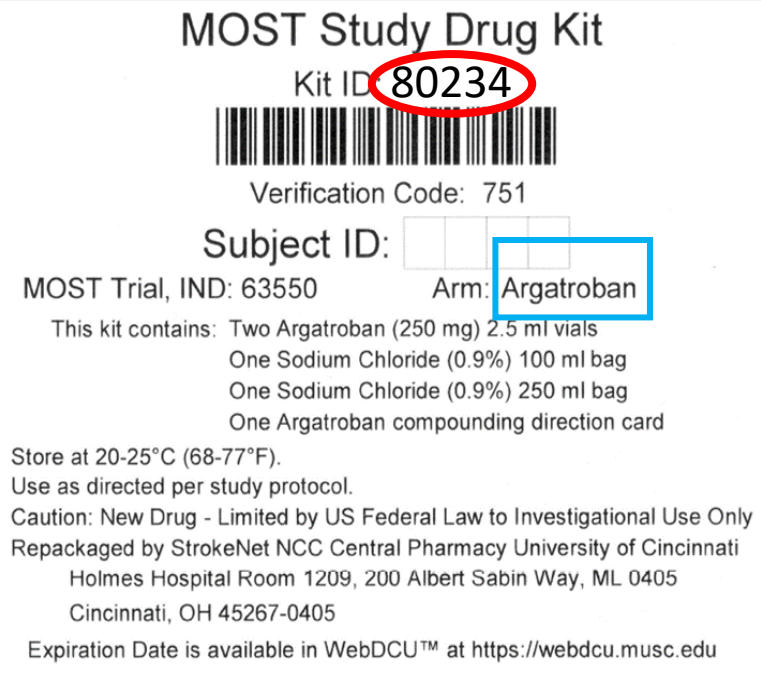
Organization of study drug and communication between the study team and pharmacy are essential to meet this window.

Randomization Verification Form

The Randomization Verification Form contains important information including:

1. Treatment Arm (Blue)
2. Assigned Kit Number (Red)
3. Bolus Dose Volume that should be drawn up into a syringe (Pink)
4. Infusion rate for 0-2 hour and 12-12 hour doses (Pink)

The Kit ID and Treatment arm from the Verification form should be matched with the MOST Kit Label:


MOST Study Drug Kit

Kit ID: 80234

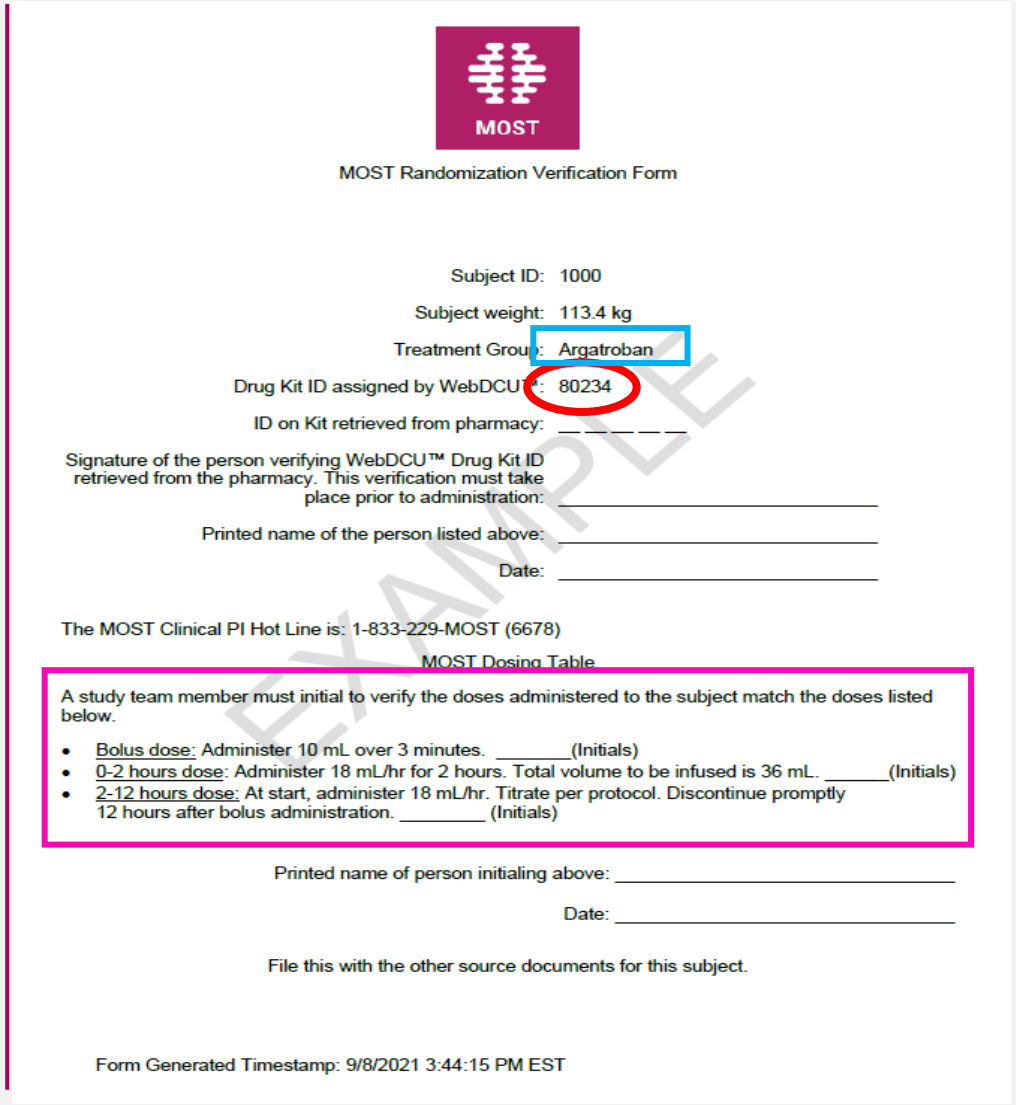
Verification Code: 751

Subject ID:

MOST Trial, IND: 63550 Arm: Argatroban

This kit contains: Two Argatroban (250 mg) 2.5 ml vials
One Sodium Chloride (0.9%) 100 ml bag
One Sodium Chloride (0.9%) 250 ml bag
One Argatroban compounding direction card

Store at 20-25°C (68-77°F).
Use as directed per study protocol.
Caution: New Drug - Limited by US Federal Law to Investigational Use Only
Repackaged by StrokeNet NCC Central Pharmacy University of Cincinnati
Holmes Hospital Room 1209, 200 Albert Sabin Way, ML 0405
Cincinnati, OH 45267-0405
Expiration Date is available in WebDCU™ at https://webdcu.musc.edu


MOST

MOST Randomization Verification Form

Subject ID: 1000

Subject weight: 113.4 kg

Treatment Group: Argatroban

Drug Kit ID assigned by WebDCU™: 80234

ID on Kit retrieved from pharmacy: _ _ _ _ _

Signature of the person verifying WebDCU™ Drug Kit ID retrieved from the pharmacy. This verification must take place prior to administration: _____

Printed name of the person listed above: _____

Date: _____

The MOST Clinical PI Hot Line is: 1-833-229-MOST (6678)

MOST Dosing Table

A study team member must initial to verify the doses administered to the subject match the doses listed below.

- Bolus dose: Administer 10 mL over 3 minutes. _____(Initials)
- 0-2 hours dose: Administer 18 mL/hr for 2 hours. Total volume to be infused is 36 mL. _____(Initials)
- 2-12 hours dose: At start, administer 18 mL/hr. Titrate per protocol. Discontinue promptly 12 hours after bolus administration. _____ (Initials)

Printed name of person initialing above: _____

Date: _____

File this with the other source documents for this subject.

Form Generated Timestamp: 9/8/2021 3:44:15 PM EST

EXAMPLE

Argatroban Compounding Procedures

1. Obtain the MOST Randomization Verification Form from the study team (shown on previous slide). If your institution requires pharmacy receiving informed consent before compounding study drug, obtain informed consent from study team.

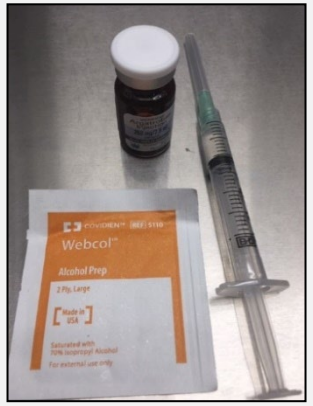
2. Retrieve the appropriate MOST kit from your pharmacy's inventory by matching the treatment group and kit ID on the verification form with the kit label.

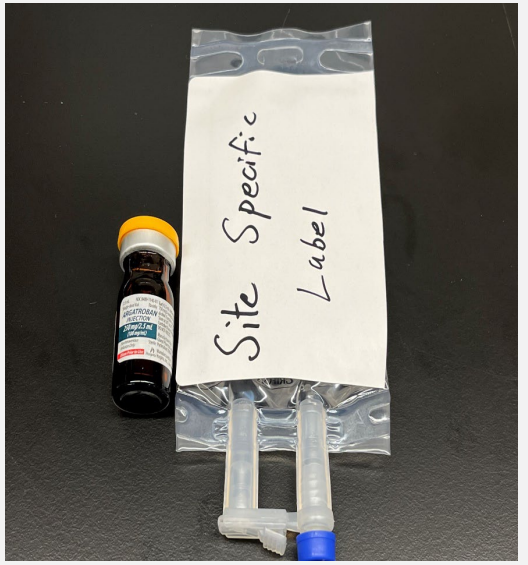
<u>Argatroban</u> kits will contain the following:

- 2- argatroban 250mg/2.5mL vials
- 1- sodium chloride 0.9% 100mL bag
- 1- sodium chloride 0.9% 250mL bag
- 1- argatroban compounding direction card

Argatroban Compounding Procedures: Bolus and 0-2 Hour Dose

3. Following all hospital specific protocols and applicable laws, aseptically prepare argatroban bolus and 0-2 hour dose (infusion 1).
    a. Retrieve 1 vial of 250mg/2.5 mL argatroban and the 100 mL normal saline bag from MOST Study Kit.
    b. Remove the cap from each vial and swab septum with an isopropyl alcohol swab.
    c. Withdraw 1 mL (100 mg) from the 250mg/2.5mL argatroban and inject it into the 100mL normal saline bag.
    d. The bolus dose should be drawn from the resultant bag into a syringe and labeled with patient specific label.
    e. Label the resultant bag with a subject-specific study label that follows your sites local standards and practices for labeling.





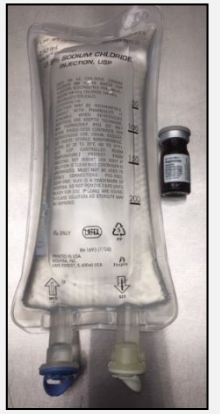
Argatroban Compounding Procedures: Bolus and 0-2 Hour Dose

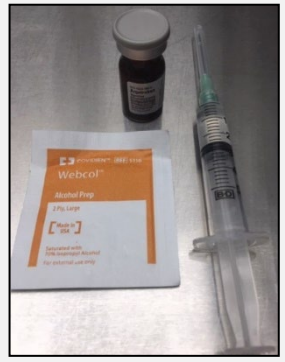
4) Verify product and label then dispense immediately.
   a) Check 0-2 hour dose for argatroban precipitation.
      If precipitation occurs shake the vial gently until completely dissolved.
   b) This bag (Infusion 1) will be used for the 0-2 hour dose and the drawn syringe will be used for the bolus.
      Study drug bolus should be administered within 60 minutes but no later than 75 minutes from tPA or TNK bolus dose.
   c) You can now start to prepare the 2-12 hour dose.

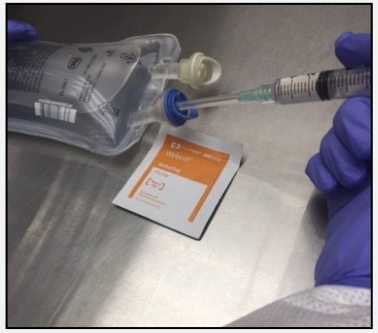
5) Within 1 hour of dispensing the bolus dose and 0-2 hour dose, please prepare and dispense the 2-12 hour dose.
   a) If time allows, the 0-2 hour and 2-12 hour doses can be compounded and dispensed simultaneously, but priority should always be given to preparing the 0-2 hour and the bolus dose first.

Argatroban Compounding Procedures: 2-12 Hour Dose

6) Following all hospital specific protocols and applicable laws aseptically prepare argatroban 2-12 hour dose (infusion 2).
   a) Retrieve the second 250mg/2.5mL argatroban vial and 250 mL 0.9% sodium chloride bag.
   b) Remove the cap from the argatroban vial and swab septum with an isopropyl alcohol swab.
   c) Swab the 250 mL 0.9% sodium chloride bag port using an isopropyl alcohol swab.
   d) Aseptically withdraw 2.5 mL (250 mg) from the 250mg/2.5mL argatroban vial and inject it into the 250mL normal saline bag.
   e) Label 2-12 hour dose with a subject-specific study label (example on next slide).
      - The label for 2-12 hour dose does not have to cover the entire manufacturer's label.
      - All arms of the study will use a 250mL normal saline bag as a base for 2-12 hour dose.







Argatroban Compounding Procedures

7) Verify product and label then dispense 2-12 hour dose immediately.
   a) Check 2-12 hour dose for argatroban precipitation.
   If precipitation occurs shake the bag gently until completely dissolved.

8) The 2-12 hour dose must be at the subject's bedside within 2 hours from the time study drug bolus is administered to avoid treatment gaps.

Front

Back

Eptifibatide and Placebo Kit Compounding

Eptifibatide kits will contain the following:

- 1- eptifibatide 75mg/100mL (manufacturers supplied vial hanger)
- 1- sodium chloride 0.9% 250mL bag

Placebo kits will contain the following:

- 1- sodium chloride 0.9% 100mL bag
- 1- sodium chloride 0.9% 250mL bag

Eptifibatide and Placebo Kit Compounding

1) Confirm proper kit selection using the Study Drug Kit ID on the MOST Randomization Verification Form.
2) Please follow individual site standard operating procedures for sterile compounding and dispensing.
3) Obtain either the 75 mg/100 mL eptifibatide for patients assigned to eptifibatide or 0.9% sodium chloride 100 mL bag for patients assigned to placebo.
4) Withdraw the patient specific bolus dose from the eptifibatide vial for patients assigned to the eptifibatide arm or from the 100ml normal saline bag for patients assigned to the placebo arm.
5) Label the resulting syringe with a patient specific label. This is the bolus dose.
6) The remaining 100ml normal saline bag or eptifibatide vial that the bolus dose was drawn from will be the 0-2 hour dose (infusion 1).
7) Label the eptifibatide vial or 100ml normal saline bag with a patient specific label.
    a) <u>For the eptifibatide vial, the manufacturer's label must be completely covered.</u>

Eptifibatide and Placebo Kit Compounding

3) Verify product and label then dispense immediately.
   a) Study Drug bolus should be administered within 60 minutes but no later than 75 minutes from tPA or TNK bolus dose.

4) Within 1 hour obtain the normal saline 250mL bag for 2-12 hour dose and label it with a subject-specific study label.
   a) The label for 2-12 hour dose does not have to cover the entire manufacturer's label.

5) Verify product and label then dispense the normal saline bag.
   a) The 2-12 hour dose must be at the subject's bedside within 2 hours of study drug bolus administration to avoid treatment gaps.

Study Drug Kit Expiration

Study drug kit expiration is determined by the individual kit components.

- WebDCU™ automatically generates the kit expiration to correspond to the earliest expiration of the kit components.

Study drug kit expiration dates are available in 2 locations:

- MOST study drug packing slip
- WebDCU™ > Drug Tracking >Drug Site Removing

Sites will receive an email notification from WebDCU 3 days before kits in their local inventory will expire.

The StrokeNet Central Pharmacy will receive a notification 14 days before kits are due to expire at each site and will send out replacement kits to each site.

Study Drug Destruction & Return

Sites should follow their institutional policy regarding drug destruction protocol.

The StrokeNet Central pharmacy can accept returns for destruction if a site's institutional policy requires returning the damage or expired drug kits.

Follow the steps below to return study drug to the StrokeNet Central Pharmacy

Study Drug Return Form must be completed and returned with the shipment.
Returns should be addressed and shipped to the StrokeNet Central Pharmacy via the site's preferred postal carrier.

Return cost will be at the expense of the CPS.
Package tracking information must be provided to StrokeNet Central Pharmacy via email.
Temperature monitoring is NOT required for returns.
Subject identifiers must be removed from returns.

Resources:

Pharmacy specific manual is available on WebDCU > MOST > Toolbox > Project Documents > MOST CPS Study Drug Procedures

StrokeNet Central Pharmacy is available for MOST related pharmacy question at:

Telephone: 513-584-3166

Email: strokenetcpharm@ucmail.uc.edu