DOWNSTATE
HEALTH SCIENCES UNIVERSITY

Tenecteplase (TNKase®) for Acute Ischemic Stroke

Sun Hyee Park, PharmD, BCEMP
Manisa Tanprayoon, PharmD, BCPS
Pharmacy Department

Presentation Outline

- Tenecteplase (TNKase) Medication Overview
- Transitioning from Alteplase (tPA) to Tenecteplase (TNKase) for Acute Ischemic Stroke (AIS) at Downstate:
    - Prescribing and Transcribing
    - Storage and Dispensing
    - Preparation and Administering
    - Patient Monitoring

Tenecteplase (TNKase) Medication Overview

Medication Overview: Tenecteplase (TNKase)

Pharmacologic Category

- Thrombolytic agent

Mechanism of Action

- Binds to fibrin, coverts plasminogen to plasmin → fibrinolysis

Available Dosage Forms

- Kit: 50 mg vial for injection

FDA-approved Indications & Dosing

ST-Elevation Myocardial Infarction (STEMI)

- **IV**: bolus over 5 seconds
  - <60 kg: 30 mg
  - ≥60 to <70 kg: 35 mg
  - ≥70 to <80 kg: 40 mg
  - ≥80 to <90 kg: 45 mg
  - ≥90 kg: 50 mg

No renal or hepatic dose adjustments per manufacturer's labeling

Off-Label Indications & Dosing

Acute Ischemic Stroke

- **IV**: 0.25 mg/kg (maximum total dose: 25 mg) bolus over 5 seconds

Acute Pulmonary Embolism

- **IV**: bolus over 5 seconds

  <60 kg: 30 mg
  ≥60 to <70 kg: 35 mg
  ≥70 to <80 kg: 40 mg
  ≥80 to <90 kg: 45 mg
  ≥90 kg: 50 mg

No renal or hepatic dose adjustments per manufacturer's labeling

Medication Safety

Contraindications

- CT demonstrating extensive clear hypoattenuation/obvious hypodensity
- Acute or history of Intra Cranial Hemorrhage (ICH)
- Ischemic stroke ≤3 months
- Acute head trauma
- Intracranial/intraspinal surgery ≤3 months
- Subarachnoid Hemorrhage (SAH)
- GI malignancy/bleed ≤21 days
- Concomitant abciximab
- Concomitant IV aspirin
- Infective endocarditis

Medication Safety *(Cont.)*

Contraindications

- Aortic arch dissection
- Intra-axial intracranial neoplasm
- Active bleeding diathesis, including but not limited to:
    - Platelet count <100,000/mm^3
    - Heparin ≤48 hours, resulting in abnormally elevated aPTT >40 secs
    - Enoxaparin treatment dose ≤24 hours
    - Concurrent use of warfarin with INR >1.7 or PT >15 secs
    - Concurrent use of direct thrombin inhibitors or direct factor Xa inhibitors ≤48 hours (or longer if abnormal renal function)

Medication Safety *(Cont.)*

Warnings & Precautions

- Arrhythmias
- Bleeding (2-3%), including symptomatic intracranial hemorrhage (sICH)
- Cholesterol embolization
- Hypersensitivity reaction (including anaphylaxis and angioedema)
    - Reported frequency 0.4 to 5.1%
    - Risk can be 6x higher in patients taking ACE inhibitors

Adverse Reactions

- Heart failure (12%)
- Cardiogenic shock (6%)
- Antibody development (<1%)

Place in Therapy: Fibrinolysis for AIS

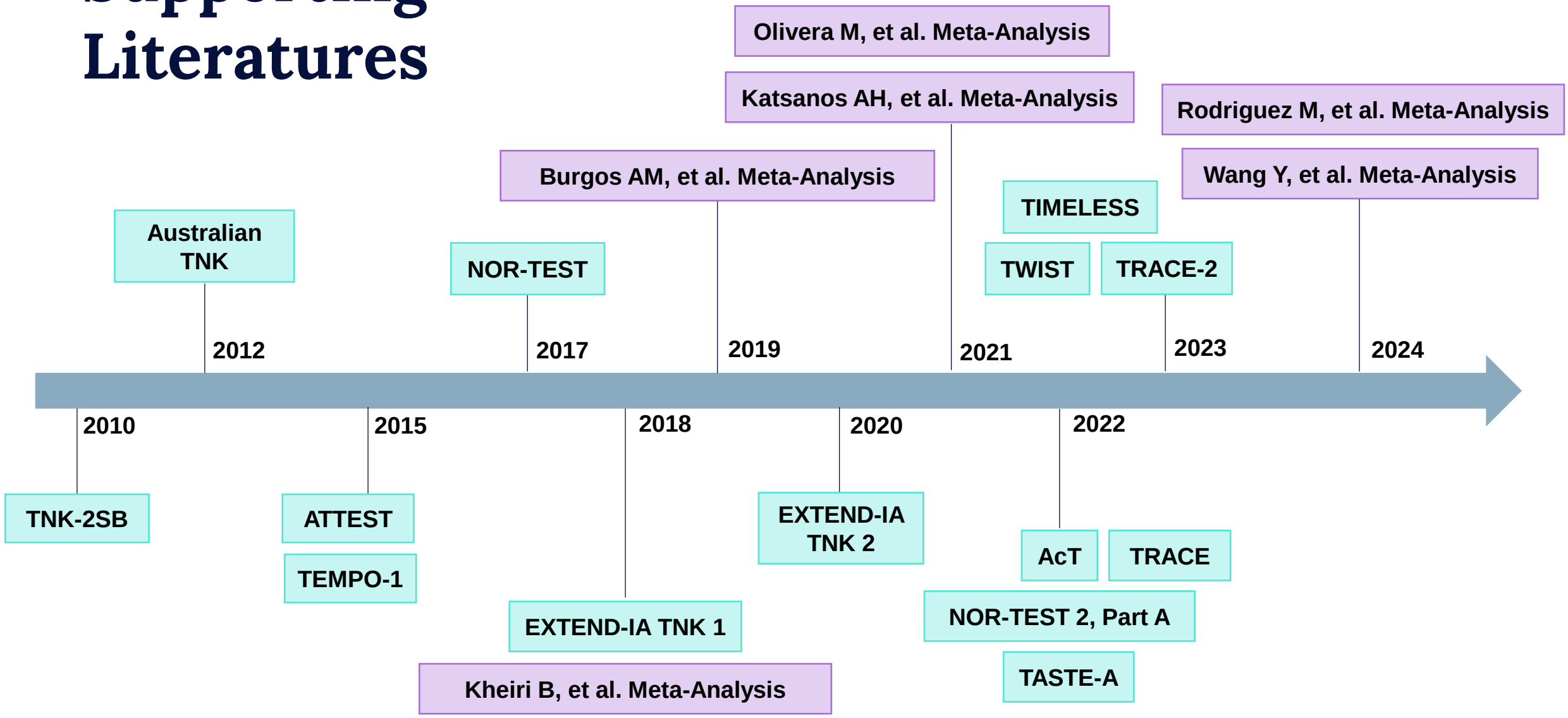
AHA/ASA 2019 Update to the 2018 Guidelines for the Early Management of AIS

3.6. Other IV Fibrinolytics and Sonothrombolysis	COR	LOE	New, Revised, or Unchanged
1. It may be reasonable to choose tenecteplase (single IV bolus of 0.25-mg/kg, maximum 25 mg) over IV alteplase in patients without contraindications for IV fibrinolysis who are also eligible to undergo mechanical thrombectomy.	IIb	B-R	New recommendation.

Drug	Alteplase	Tenecteplase
Dosing & Administration	0.09 mg/kg IV bolus over 1 min, followed by 0.81 mg/kg IV continuous infusion over 60 mins (maximum dose: 90 mg)	0.25 mg/kg (maximum dose: 25 mg) IV once over 5 secs
Fibrin Selectivity	+	+++
Resistance to PAI-1	+	++
Pharmacokinetics	t ½: <5 mins	Initial t ½: 20-24 mins, Terminal t ½: 90-130 mins

AHA = American Heart Association; AIS = acute ischemic stroke; ASA = American Stroke Association; PAI-1 = plasminogen activator inhibitor-1

Supporting Literatures



Major Clinical Trials

	Methods	Results	Conclusion
EXTEND-IA TNK Campbell BCV, et al. *N Engl J Med*. 2018; 378(17):1573-1582	Multicenter, prospective, randomized, open-label, blinded outcome • Patients (n=202) with LVO prior to thrombectomy, treated <4.5 hours after symptom onset • TNK 0.25 mg/kg vs ALT 0.9 mg/kg	Primary outcome: • Reperfusion >50% (mTICI 2b/3); 22% TNK vs 10% ALT (p=0.002 for non-inferiority; p=0.03 for superiority) Secondary outcome: • Median mRS at 90 days; 2 TNK vs 3 ALT (p=0.04) Safety: • sICH at 24-48 hours: 1% TNK vs 1% ALT (p=0.99) • 90-day morality: 10% TNK vs 18% ALT (p=0.08)	TNK prior to thrombectomy was associated with higher incidence of reperfusion and better functional outcome compared to ALT; no significant difference in sICH at 24-48 hours between TNK vs ALT

DOWNSTATE
HEALTH SCIENCES UNIVERSITY

ALT = alteplase; LVO = large vessel occlusion; mRS = modified Rankin score; mTICI: modified thrombolysis in cerebral infarction; sICH = symptomatic intracranial hemorrhage; TNK = tenecteplase

Major Clinical Trials *(Cont.)*

	Methods	Results	Conclusion
TRACE-2 Wang, Y, et al. *Lancet*. 2023; 401(10377):645-654	Multicenter, prospective, randomized, open-label, blinded outcome • Patients (n=1,430) eligible for IV fibrinolytics and ineligible for or refused EVT, treated ≤4.5 hours after symptom onset • TNK 0.25 mg/kg vs ALT 0.9 mg/kg	Primary outcome: • mRS 0-1 at 90 days; 62% TNK vs 58% ALT Safety: • sICH at 36 hours; 2% TNK vs 2% ALT (*p*=0.72) • Mortality at 90 days; 7% TNK vs %5 ALT (*p*=0.22)	TNK was non-inferior to ALT in patients eligible for standard IV fibrinolytics and ineligible for EVT; no significant difference in sICH within 36 hours or mortality at 90 days between TNK vs ALT

ALT = alteplase; EVT = endovascular thrombectomy; mRS = modified Rankin score; sICH = symptomatic intracranial hemorrhage; TNK = tenecteplase

Transitioning from Alteplase (tPA) to Tenecteplase (TNKase) for Acute Ischemic Stroke (AIS) at Downstate

What is the Change?

- Changing IV thrombolytic for the treatment of **Acute Ischemic Stroke (AIS)** from Alteplase (tPA) to **Tenecteplase (TNKase)**
- Alteplase (tPA) will remain on formulary for other indications (non-AIS) or when TNKase is not available (for AIS)

Why Tenecteplase over Alteplase?

- Higher fibrin specificity = Targeted specificity and Reduced risk of bleeding complications
- Greater resistant to PAI-1 = Higher efficacy in clot lysis
- Longer serum half-life = Single bolus IV administration (tPA requires bolus and infusion doses)
- Non-inferior to Alteplase and potentially superior in patients who receive thrombectomy
- Easier to dose, prepare and administer = Reduce complications of care or potential medication errors. Potentially improve door-to-needle time.

PAI-1 = plasminogen activator inhibitor-1

Why Tenecteplase over Alteplase? *(Cont.)*

- Easier to dose – tPA has 2 different dosing for IV bolus and infusion
- Less time to prepare (Simple reconstitution) – tPA requires multiple steps
- No infusion, No pump: Single IV bolus over 5 seconds – tPA requires IV bolus then IV infusion given via smart pump
- 0.9% Normal Saline (NS)* flush instead of IV infusion of 0.9% NS
- More cost effective

*Not compatible with Dextrose

Tenecteplase (TNKase®) for Acute Ischemic Stroke

Focus on Prescribing and Transcribing

Order Entry – HealthBridge Order Set

Tenecteplase (TNKase) for Acute Ischemic Stroke can be order using the following:

- Ischemic Stroke Tenecteplase IV Administration Order Set OR
- Stroke Tenecteplase IV Administration Order Set

Dosing Instructions:

- Tenecteplase IV push 0.25 mg/kg actual body weight (Max dose 25 mg/5 mL), round to the nearest 1 mg (2 mL) – Refer to dosing table
- Ensure 0.9% Sodium Chloride Flush is ordered

Tenecteplase (TNKase) Dosing

ACUTE ISCHEMIC STROKE

Dose: 0.25 mg/kg Actual Body Weight

Final Concentration 5 mg/mL **MAXIMUM DOSE 25 mg (5 mL)**

Weight (kg)	Dose (mg)	Volume (mL)
40 to <42	10	2
42 to <46	11	2.2
46 to <50	12	2.4
50 to<54	13	2.6
54 to <57	14	2.8
57 to <62	15	3
62 to <66	16	3.2
66 to <70	17	3.4
70 to<74	18	3.6
74 to <78	19	3.8
78 to <82	20	4
82 to <86	21	4.2
86 to <90	22	4.4
90 to<94	23	4.6
94 to <98	24	4.8
≥98 kg	25	5

DOWNTIME Order Entry

Ischemic Stroke TENECTEPLASE Intravenous Administration Orders

- ❑ **Admit to:** ❑ Stroke Unit/Neuro Step-down Unit ❑ MICU Attending: _____ **Diagnosis:** _____
  Secondary diagnoses: _____ **Allergies:** _____ **Weight:** _____
- ❑ Patient/family informed of benefits and risks of TENECTEPLASE - About 1 in 3 patients will have some improvement and symptomatic intracranial hemorrhage rate of 2-3%.
- ❑ **Symptom onset between 3 to 4.5 hours: Informed Consent obtained from patient/family**

CONTRAINDICATIONS to TENECTEPLASE: (Check box if applicable)		WARNINGS
❑ ICH on pre-treatment CT or history of prior ❑ CT exhibiting extensive regions of clear hypoattenuation ❑ SBP >185 or DBP >110 mmHg ❑ Suspicion of subarachnoid hemorrhage ❑ Active bleeding diathesis, including but not limited to: platelets <100,000/mm^3; heparin use within 48 hours resulting in aPTT >40 sec; enoxaparin treatment dose within 24 hours; current warfarin use with PT >15 or INR >1.7; current use of direct thrombin inhibitor or factor Xa inhibitor within 48 hours (or longer if abnormal renal function)	❑ Active internal bleeding ❑ Intra-axial intracranial neoplasm ❑ Gastrointestinal malignancy or gastrointestinal bleed (<21 days) ❑ Recent intracranial or spinal surgery, severe head trauma, or ischemic stroke (<3 months) ❑ Aortic arch dissection ❑ Infective endocarditis ❑ Concomitant abciximab or IV aspirin within 90 mins	❑ Glucose <50 or >400 mg/dL ❑ Seizure at onset of stroke symptoms ❑ Rapid improvement or mild nondisabling stroke (NIHSS 0-5) ❑ Pregnancy ❑ Sickle cell disease ❑ Recent lumbar puncture or arterial puncture at non-compressible site (<7 days) ❑ Recent trauma (not involving head) or major surgery (< 15 days) ❑ Cerebral microbleeds (>10) ❑ Recent or active vaginal bleeding causing clinically significant anemia ❑ Unruptured intracranial aneurysm (<10 mm) or intracranial vascular malformations

TENECTEPLASE (TNKase®) Initiation Order	For suspected bleeding complication/ deterioration of neuro status:
Standard concentration of 5 mg/mL in sterile water ❑ Total Dose: 0.25 mg/kg x _____ kg = _____ mg x 1 dose IV over 5 seconds (maximum dose: 25 mg) ❑ Flush: 0.9% NaCl 10 mL after bolus dose	• Notify MD Stat • Emergent nonenhanced head CT to rule-out intracranial hemorrhage • Obtain CBC, PT (INR), aPTT, fibrinogen level, and type and cross-match • Plan for blood products and/or blood transfusion: Cryoprecipitate 10 units infused over 10-30 minutes; administer additional dose for fibrinogen level <150 mg/dL
WARNINGS *Do NOT use cardiac dosing* **Do NOT exceed a TOTAL dose of 25 mg**	

Vital Signs Assessment Every:	BP Parameter Goal	Notify MD (917) 219-1705 for:
Q 15 minutes x 2 hours Q 30 minutes x 6 hours Q 1 hour x 16 hours	Pre-TENECTEPLASE: <185/110 mmHg Post-TENECTEPLASE: <180/105 mmHg	BP >185/110 mmHg during TNK infusion AND SBP <100 mmHg

MUST include patient location, height, weight, and allergy information

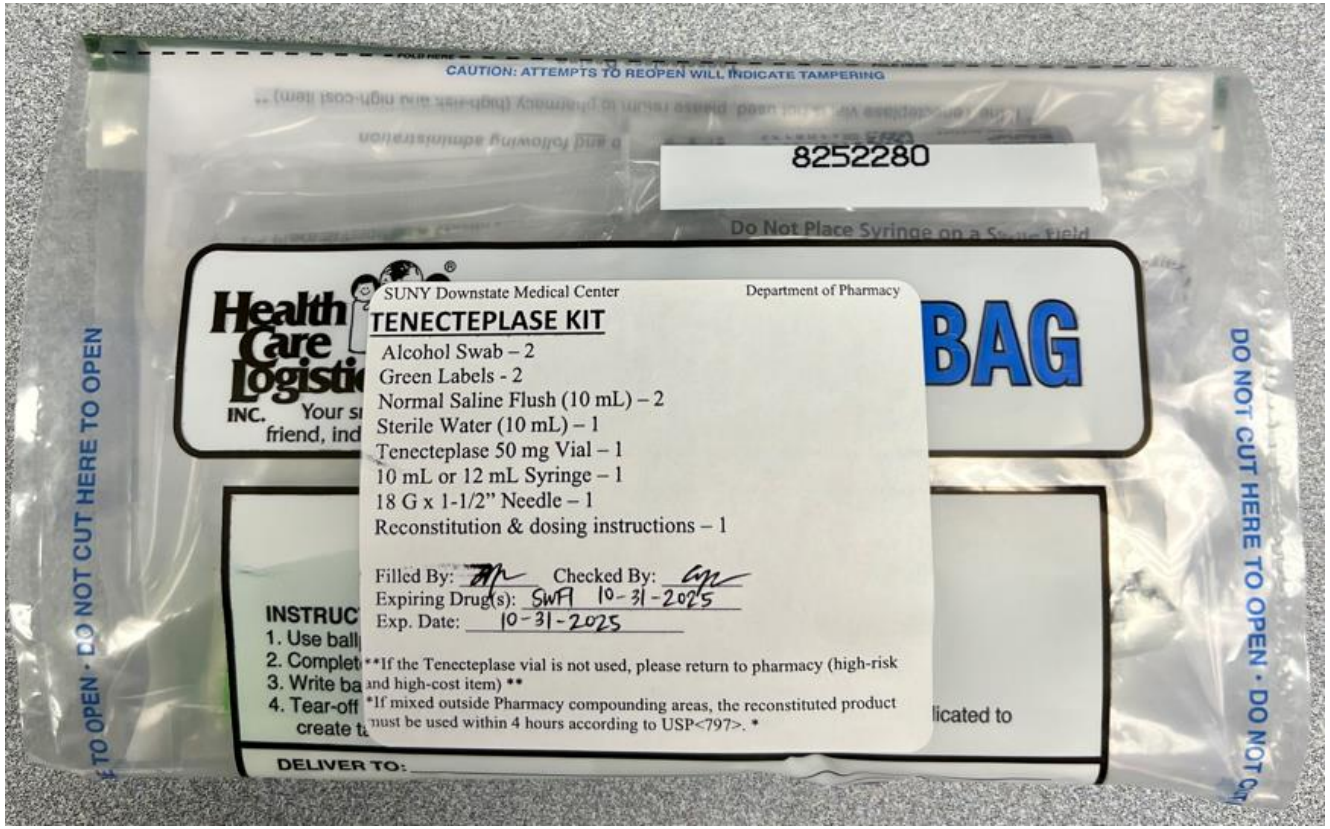
Fax order to Pharmacy's "STAT" fax machine (**x2855**) & call to confirm receipt

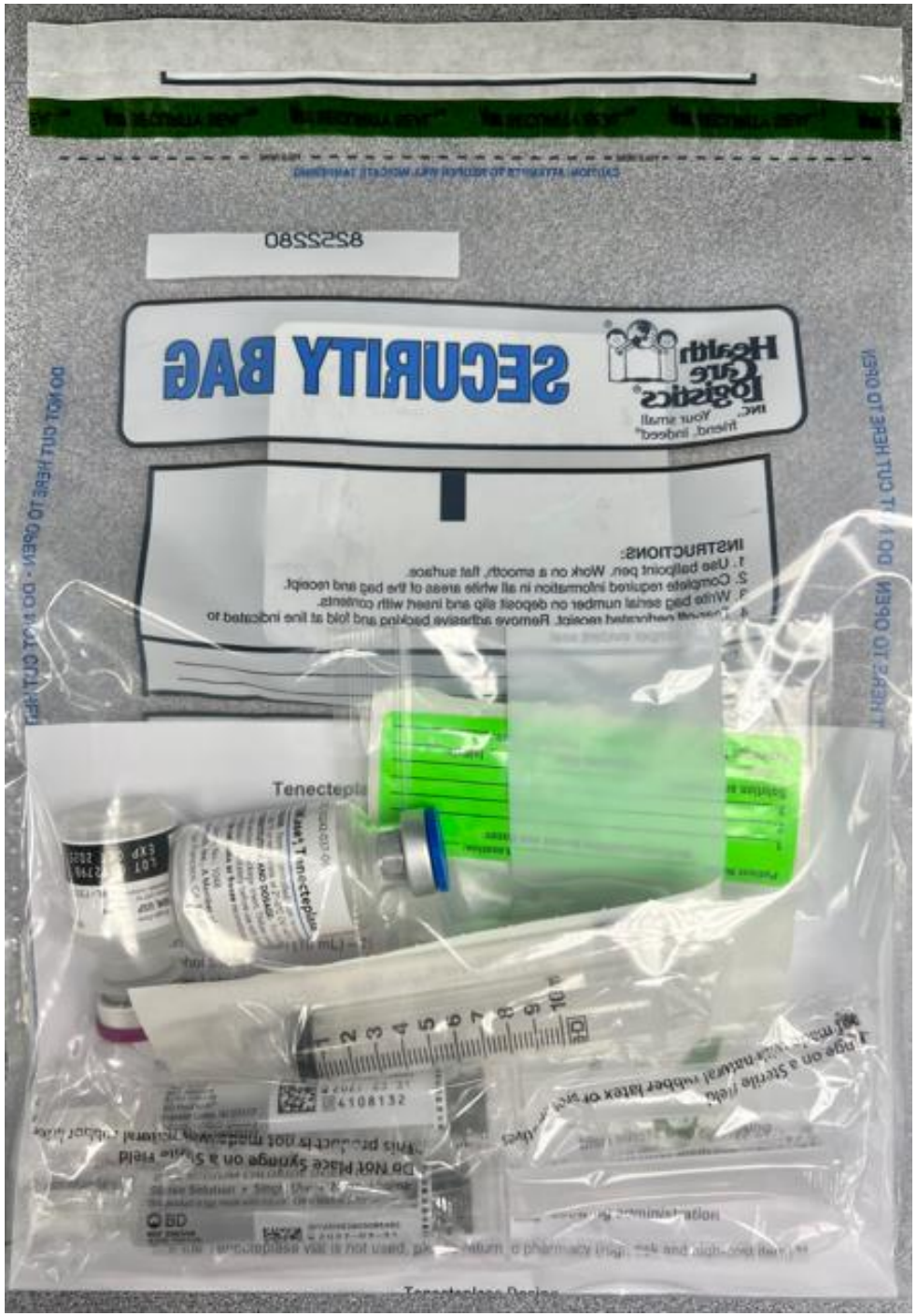
Refer to STK-03 Policy Attachment

Tenecteplase (TNKase®) for Acute Ischemic Stroke

Focus on Storage and Dispensing

Tenecteplase (TNKase) Kit





** If the Tenecteplase vial is not used, please return to main pharmacy (high-risk and high-cost item) **

DOWNSTATE
HEALTH SCIENCES UNIVERSITY

Kit Content & Storage

TENECTEPLASE KIT

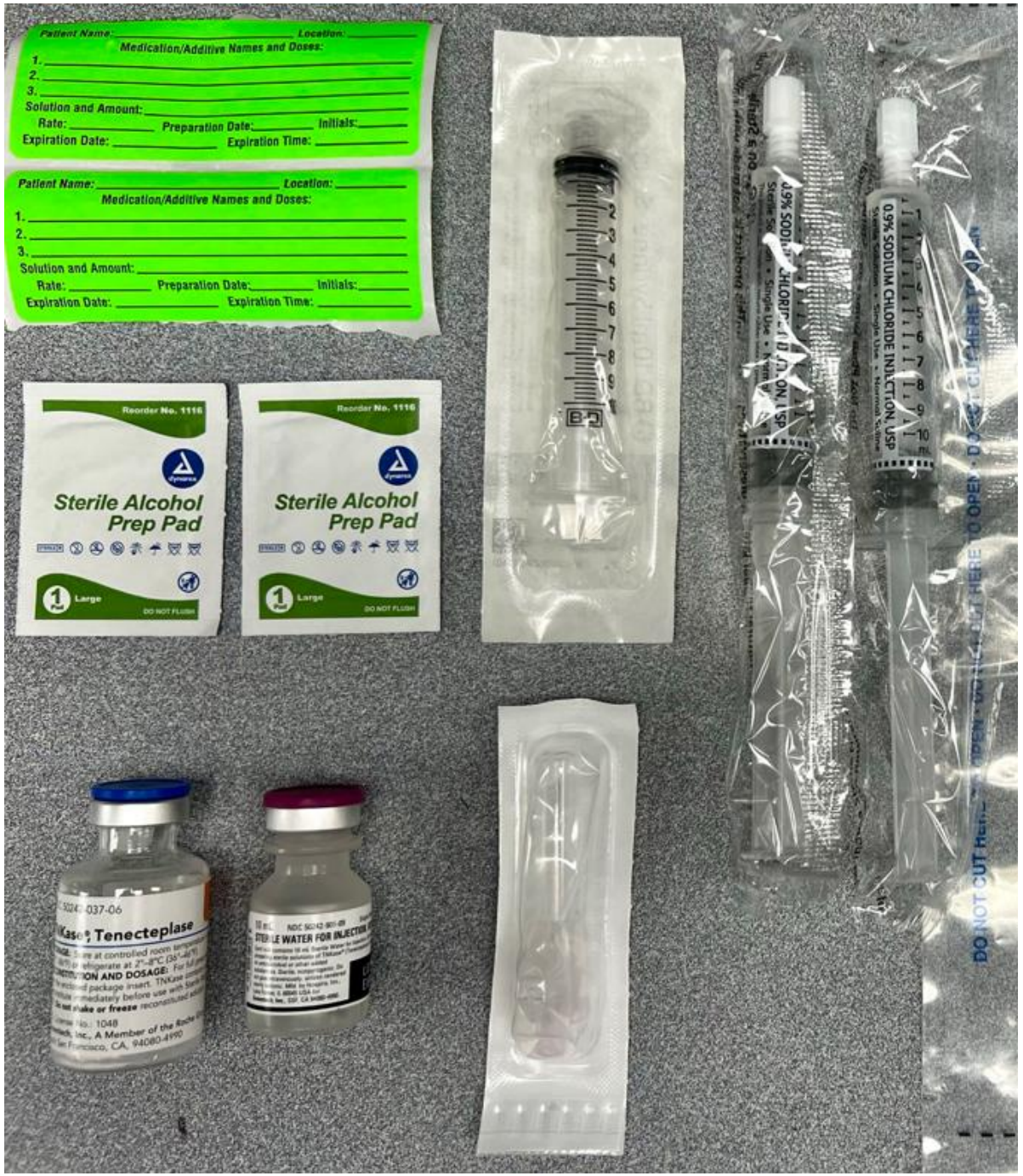
Alcohol Swab – 2
Green Labels - 2
Normal Saline Flush (10 mL) – 2
Sterile Water (10 mL) – 1
Tenecteplase 50 mg Vial – 1
10 mL or 12 mL Syringe – 1
18 G x 1-1/2" Needle – 1
Reconstitution & dosing instructions – 1

Emergency Department <u>ONLY</u>:

- Main ER Pyxis: **#2 kits** (overridable)
  - Store <u>outside</u> the refrigerator
  - Restocked by pharmacy

All Other Patient Care Areas/Floors:

- Dose to be delivered by pharmacy
  - RN to call Pharmacy (x2854/x2856) in 15 minutes to confirm receipt of Tenecteplase order



Stroke Alert Pharmacy Pathway

Overhead Notification:
Telecommunication overhead announcement
"Medical Alert Stroke Code" followed by location.
Pharmacy on standby for thrombolytic IV to be ordered

Non-HealthBridge Areas/Downtime	HealthBridge Areas
Paper Stroke Order Set in non-HealthBridge Areas **(MUST include pt. location, height, weight, and allergy info on order)**	Electronic order in HealthBridge (inpatient areas)
↓	↓
RN faxes the order to the Pharmacy's "STAT" fax machine (x2855) and calls to confirm receipt.	RN acknowledges the order In HealthBridge.
↓	↓
Pharmacy receives thrombolytic IV order & profiles order	Pharmacist reviews order (Enters appropriate total bolus dose, in Pharmacy notes) and verifies thrombolytic IV order
↓	↓
RN calls Pharmacy (x2856/x2854) in 15 minutes to confirm receipt of thrombolytic IV order.	

Thrombolytic IV Preparation & Dispensing

The admixing of thrombolytic IV will occur in the IV lab / Main Pharmacy.

Exception: Emergency Department – RN or ED Pharmacist will prepare IV thrombolytic

- Order for thrombolytic IV is verified/profiled
- IV lab receives a label for thrombolytic IV, prepares medication to provide the exact dose
- IV lab labels final product in syringe with patient-specific HealthBridge label
- Pharmacy sends technician to hand deliver thrombolytic IV to RN or MD for patient **for IMMEDIATE administration**

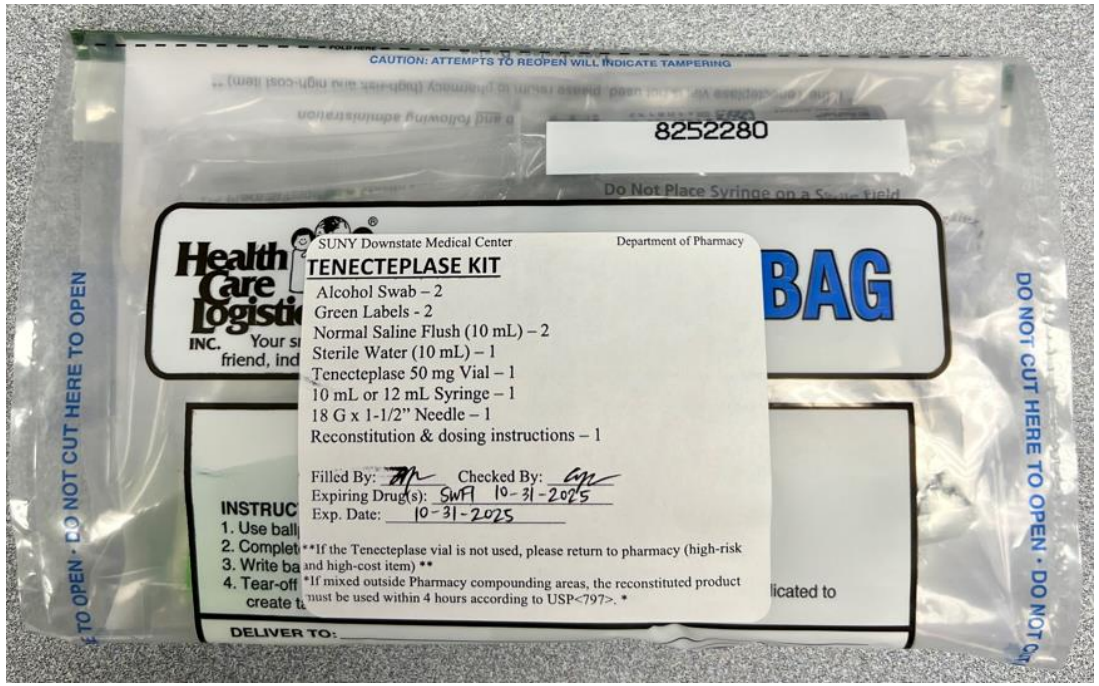
Refer to STK-03 Policy Attachment B

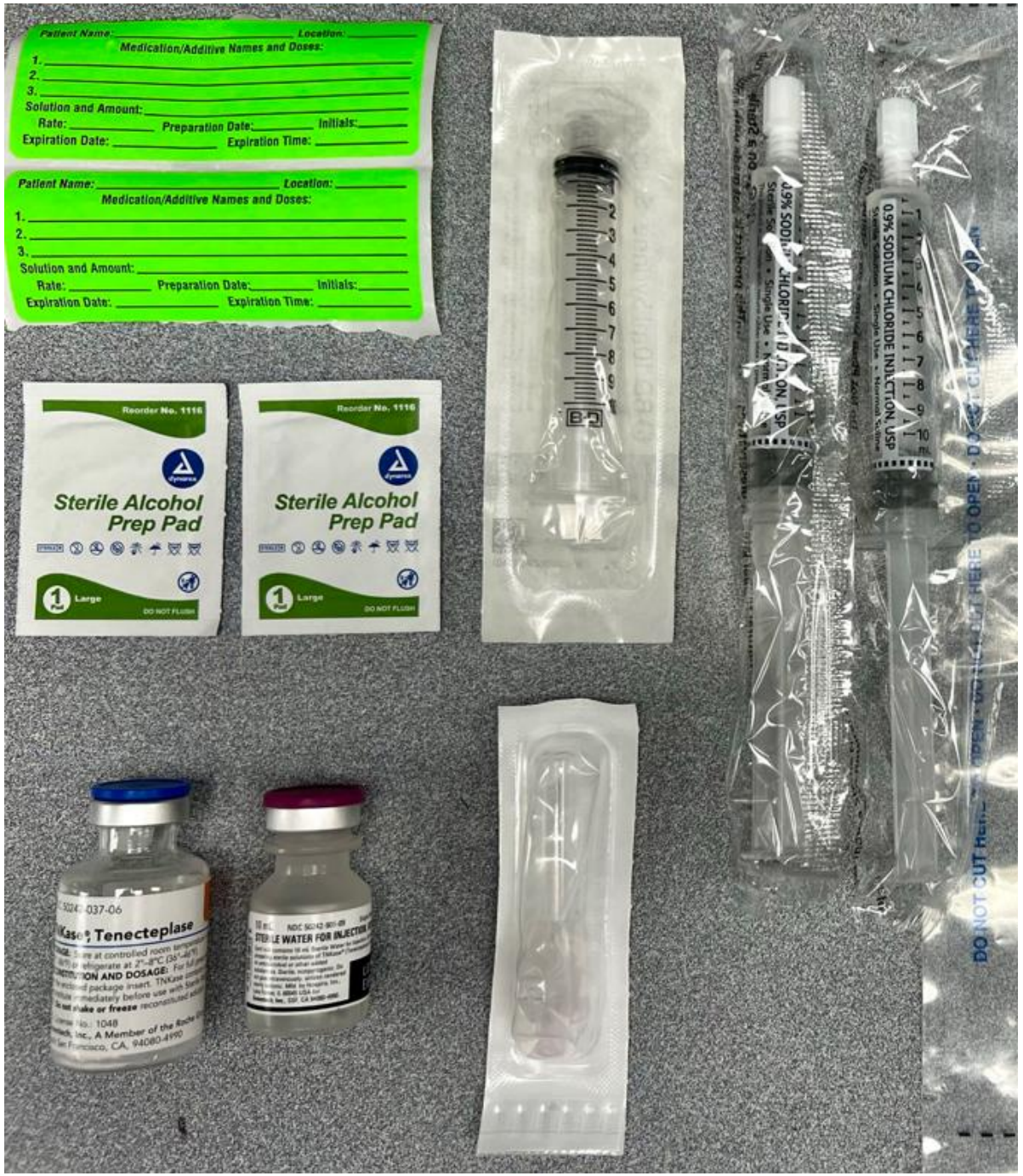
Tenecteplase (TNKase®) for Acute Ischemic Stroke

Focus on Preparation and Administering

TENECTEPLASE KIT

Alcohol Swab – 2
Green Labels - 2
Normal Saline Flush (10 mL) – 2
Sterile Water (10 mL) – 1
Tenecteplase 50 mg Vial – 1
10 mL or 12 mL Syringe – 1
18 G x 1-1/2" Needle – 1
Reconstitution & dosing instructions – 1





Reconstitution and Administering Instructions:

Step 1: Withdraw 10 mL of SWFI using the 10 mL syringe

Step 2: Inject entire contents of SWFI (10 mL) into the Tenecteplase vial, directing the diluent into the powder. Gently swirl until the contents are completely dissolved.
DO NOT SHAKE VIAL.

Step 3: Determine the dose/volume of Tenecteplase based on patient weight
(Refer to dosing chart). Concentration of reconstituted solution is 5 mg/mL.

Step 4: Withdraw appropriate dose of Tenecteplase and administer as an ***IV bolus*** over 5 seconds

Step 5: Flush a line with 10 mL Normal Saline ***prior to and following administration***

** If the Tenecteplase vial is not used, please return to pharmacy (high-risk and high-cost item) **

Tenecteplase Dosing

ACUTE ISCHEMIC STROKE

Dose: 0.25 mg/kg Actual Body Weight

Final Concentration 5 mg/mL **MAXIMUM DOSE 25 mg (5 mL)**

Weight (kg)	Dose (mg)	Volume (mL)
40 to <42	10	2
42 to <46	11	2.2
46 to <50	12	2.4
50 to<54	13	2.6
54 to <57	14	2.8
57 to <62	15	3
62 to <66	16	3.2
66 to <70	17	3.4
70 to<74	18	3.6
74 to <78	19	3.8
78 to <82	20	4
82 to <86	21	4.2
86 to <90	22	4.4
90 to<94	23	4.6
94 to <98	24	4.8
≥98 kg	25	5

Beyond-use Date: If the reconstituted tenecteplase is not used immediately, refrigerate the tenecteplase vial at 36-46 °F and use within 4 hours.

**Use the most up-to-date objective patient's weight, obtained via weighted stretcher **

Notable Changes with Tenecteplase (TNKase)

Emergency Department <u>ONLY</u>:

- **ED RN** or **ED Pharmacist** will prepare TNKase at bedside
- **ED RN** will administer TNKase

All Other Patient Care Areas/Floors:

- RN will acknowledge order of TNKase on HealthBridge
- **Main Pharmacy** will prepare TNKase
- Pharmacy technician will deliver TNKase to patient bedside
- **Neurology Attending/Fellow/Resident** will administer TNKase

****Do not prepare TNK until decision is made to give****

- Tenecteplase is off-label for acute ischemic stroke
- NO replacement program for unused medication

Tenecteplase (TNKase®) for Acute Ischemic Stroke

Focus on Patient Monitoring

Patient Monitoring

** Same inclusion & exclusion criteria *and* post-medication administration monitoring as Alteplase (tPA)**

Patients treated with IV Thrombolytic: Assessment and Reassessment parameters

- Neuro checks are defined as NIH Stoke Scale Score (NIHSS) and Glasgow Coma Scale (GCS) not indicated.
- VS are assessed immediately prior to administration of IV Thrombolytic and reassessed:
  - Q 15 minutes x 2 hours
  - Q 30 minutes x 6 hours
  - Q 1-hour x 16 hours then Q 4 hours x 4 days
  - NIHSS q 4 hours for 24 hours post IV thrombolytic; after 24 hours, assess NIHSS q 4 hours for 4 days
  - Document VS in Flowsheets
  - Document NIHSS in Flowsheets

Refer to STK-04 Policy

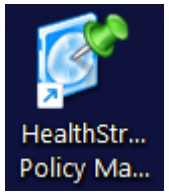
References and Policies

Stroke Policies at Downstate

HealthStream Policy Manager

Stroke Center

- STK-01 Admission / Transfer of Acute Stroke Patients
- STK-02 Admission Transfer of Acute Ischemic Stroke Patients Receiving IV Thrombolytic
- STK-03 Medical Alert Stroke Code Neurology Stroke Program
- STK-04 Documentation Guidelines Acute Stroke Care
- STK-05 Transfer Admission and Initial Management of Patients with Acute Non-traumatic Intracerebral Hemorrhage



https://downstate.healthstreampolicy.com/portal/

DOWNSTATE
HEALTH SCIENCES UNIVERSITY

References

1. TNKase (tenecteplase) [prescribing information]. South San Francisco, CA: Genentech; January 2024.
2. Activase (alteplase) [prescribing information] South San Francisco, CA: Genentech Inc; September 2022.
3. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2019;50(12):e344-e418.
4. Campbell BCV, Mitchell PJ, Churilov L, et al; EXTEND-IA TNK Investigators. Tenecteplase versus alteplase before thrombectomy for ischemic stroke. *N Engl J Med*. 2018;378(17):1573-1582.
5. Meyer G, Vicaut E, Danays T, Agnelli G, Becattini C, et al. PEITHO Investigators. Fibrinolysis for patients with intermediate-risk pulmonary embolism. *N Engl J Med*. 2014;370(15):1402-11.
6. Kline JA, Nordenholz KE, Courtney DM, et al. Treatment of submassive pulmonary embolism with tenecteplase or placebo: cardiopulmonary outcomes at 3 months: multicenter double-blind, placebo-controlled randomized trial. *J Thromb Haemost*. 2014;12(4):459-68.
7. Tanswell P, Modi N, Combs D, Danays T. Pharmacokinetics and pharmacodynamics of tenecteplase in fibrinolytic therapy of acute myocardial infarction. *Clin Pharmacokinet*. 2002;41(15):1229-45.12452736.
8. Wang Y, Li S, Pan Y, Li H, et al. TRACE-2 Investigators. Tenecteplase versus alteplase in acute ischaemic cerebrovascular events (TRACE-2): a phase 3, multicentre, open-label, randomised controlled, non-inferiority trial. *Lancet*. 2023;401(10377):645-654. Epub 2023. Erratum in: *Lancet*. 2023 Apr 1;401(10382):1078.
9. Huang J, Zheng H, Zhu X, Zhang K, Ping X. Tenecteplase versus alteplase for the treatment of acute ischemic stroke: a meta-analysis of randomized controlled trials. *Ann Med*. 2024 Dec;56(1):2320285.
10. Abuelazm M, Seri AR, Awad AK, et al. Th efficacy and safety of tenecteplase versus alteplase for acute ischemic stroke: an updated systematic review, pairwise, and network meta-analysis of randomized controlled trials. *J Thromb Thrombolysis*. 2023 Feb;55(2):322-338.
11. Foster-Goldman A, McCarthy D. Angioedema from recombinant TPA administration: case report and pathophysiology review. *Am J Ther.* 2013 Nov-Dec;20(6):691-3.
12. Dellabella A, May A, Sofio B. Angioedema Following Tenecteplase for Acute Ischemic Stroke. *Stroke*. 2024 Aug;55(8):e242-e244.

Questions?

Email: sunhyee.park@downstate.edu

or Call Main Pharmacy x 2854/x 2856

This presentation is available via Pharmacy Intranet Page via the link below:
https://www.downstate.edu/education-training/fellowship-residency-programs/pharmacy/resources.html

DOWNSTATE
HEALTH SCIENCES UNIVERSITY

Tenecteplase (TNKase®) for Acute Ischemic Stroke

Sun Hyee Park, PharmD, BCEMP
Manisa Tanprayoon, PharmD, BCPS
Pharmacy Department