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IN BRIEF

A New Indication for Tenecteplase *(TNKase)*

The tissue plasminogen activator (tPA) tenecteplase (*TNKase* – Genentech) has been approved by the FDA for treatment of acute ischemic stroke in adults. It is the second tPA to be approved in the US for this indication; alteplase *(Activase)* was approved in 1996. Tenecteplase was approved in 2000 to reduce the risk of death associated with acute ST-elevation myocardial infarction (STEMI).

STANDARD TREATMENT — Thrombolysis with IV alteplase is the first-line treatment for acute ischemic stroke.[1] Tenecteplase has been used off-label as an alternative. Mechanical thrombectomy is another alternative.

MECHANISM OF ACTION — Tenecteplase is a recombinant tPA that binds to fibrin and converts plasminogen to plasmin, promoting fibrinolysis. It is a modified variant of alteplase that has a longer half-life (22 vs 4 min), is more fibrin-specific, and has increased resistance to plasminogen activator inhibitor-1, an inhibitor of tPA; the clinical significance of these differences is not clear.[2]

CLINICAL STUDIES — FDA approval of tenecteplase for the new indication was based on the results of an open-label trial (AcT) in 1577 adults who had an ischemic stroke causing a disabling neurological deficit and presented within 4-5 hours of symptom onset. Patients were randomized to receive tenecteplase or alteplase. The primary endpoint was the percentage of patients who had a score of 0-1 (no symptoms or no significant disability despite having symptoms) on the modified Rankin Scale (mRS; a 7-point scale that measures disability after stroke, with higher scores indicating greater disability) 90–120 days after treatment. At the time of data cutoff, the percentage of patients who achieved the primary endpoint was noninferior with tenecteplase compared to alteplase (36.9% vs 34.8%). Rates of symptomatic intracerebral hemorrhage were similar in both groups.[3]

ADVERSE EFFECTS — The most common adverse effect of tenecteplase is bleeding. Thromboembolism, cholesterol embolization, and arrhythmias have been reported with thrombolytics.

CONTRAINDICATIONS — Tenecteplase is contraindicated for use in patients with internal bleeding, intracranial hemorrhage, intracranial or intraspinal surgery or trauma within the previous 2 months, known bleeding diathesis, severe uncontrolled hypertension, or an intracranial condition that may increase the risk of bleeding (e.g., intracranial neoplasm, arteriovenous malformation, aneurysm).

DOSAGE, ADMINISTRATION, AND COST — For treatment of ischemic stroke, *TNKase* is supplied in 25-mg single-dose vials containing powder for reconstitution. The drug should be administered as a single IV bolus dose over 5 seconds as soon as possible and within 3 hours of symptom onset. (Alteplase is administered as an initial IV bolus dose, followed by an IV infusion over 1 hour). The recommended dose of tenecteplase for acute ischemic stroke is weight-based: 15 mg (<60 kg), 17.5 mg (≥60 to <70 kg), 20 mg (≥70 to <80 kg), 22.5 mg (≥80 to <90 kg), or 25 mg (≥90 kg). The wholesale acquisition cost for one 25-mg vial of *TNKase* is not yet available; a 50-mg vial costs $8300.[4]

CONCLUSION — In one randomized trial in patients presenting with an acute ischemic stroke, the tissue plasminogen activator (tPA) tenecteplase *(TNKase)* was noninferior to the tPA alteplase *(Activase),* the current standard of care, in preventing disability. Tenecteplase can be administered more rapidly than alteplase. ■

1. WJ Powers 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:e344.
2. H Kobeissi et al. Tenecteplase vs. alteplase for treatment of acute ischemic stroke: a systematic review and meta-analysis of randomized trials. Front Neurol 2023; 14:1102463.
3. BK Menon et al. Intravenous tenecteplase compared with alteplase for acute ischaemic stroke in Canada (AcT): a pragmatic, multicentre, open-label, registry-linked, randomised, controlled, non-inferiority trial. Lancet 2022; 400:161.
4. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. April 5, 2025. Reprinted with permission by First Databank, Inc. All rights reserved. ©2025. www.fdbhealth.com/policies/drug-pricing-policy.

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