

STROKE

Pharmacologic Agents for Management

Audience: APRN | **Contact hrs:** 1.5 hrs | **Pharmacology hrs:** 1.25 hrs

Expected revision: October 3, 2028

Pharmacology hours are included in the total contact hours.

Clinical purpose and learning outcomes

Acute ischemic stroke pharmacotherapy is no longer centered on a single thrombolytic. Current practice integrates rapid reperfusion, early antiplatelet decisions, cause-specific anticoagulation, physiologic support, medication safety, and long-term vascular risk reduction. For APRNs, the critical task is to connect the drug to the treatment window, mechanism, imaging findings, bleeding risk, stroke mechanism, renal and hepatic function, and the patient's competing indications.

After completing this article, the learner should be able to: compare alteplase and tenecteplase for intravenous thrombolysis; identify medication checks that protect patients before and after thrombolysis; select evidence-based antiplatelet strategies after noncardioembolic stroke or high-risk TIA; explain when and how oral anticoagulation is used after atrial-fibrillation-associated stroke; recognize drug strategies for blood pressure, cerebral edema, seizures, glucose, fever, and secondary prevention; and distinguish established pharmacotherapy from investigational neuroprotection.

Audience and scope. This activity is written for APRNs caring for adults with acute ischemic stroke and patients transitioning to secondary prevention. It emphasizes U.S. practice, including the 2026 American Heart Association/American Stroke Association (AHA/ASA) acute ischemic stroke guideline and current U.S.

labeling where relevant. Local protocols, formulary restrictions, stroke-center pathways, and prescriptive authority remain controlling.

What changed from older pharmacologic stroke care

Several concepts in older stroke pharmacology reviews are now obsolete or incomplete. Intravenous alteplase is no longer the only accepted thrombolytic option: the 2026 AHA/ASA guideline recommends either tenecteplase 0.25 mg/kg or alteplase 0.9 mg/kg for eligible adults treated within 4.5 hours. Tenecteplase has operational advantages because it is given as a single bolus. In February 2025 the U.S. Food and Drug Administration expanded the TNKase indication to acute ischemic stroke, although the U.S. label specifies initiation within 3 hours; guideline-supported use through 4.5 hours therefore requires clinicians to understand the difference between product labeling and professional-society guidance (Prabhakaran et al., 2026; Genentech, 2025).

Routine urgent anticoagulation with unfractionated heparin, low-molecular-weight heparin, argatroban, or other agents is not an established method to improve acute neurologic outcome in unselected ischemic stroke. Similarly, glycoprotein IIb/IIIa inhibitors and experimental neuroprotective drugs are not routine substitutes or add-ons to evidence-based reperfusion. Modern pharmacotherapy prioritizes treatments with demonstrated clinical benefit and reserves investigational strategies for trials (Prabhakaran et al., 2026).

Acute ischemic stroke: medication decision sequence

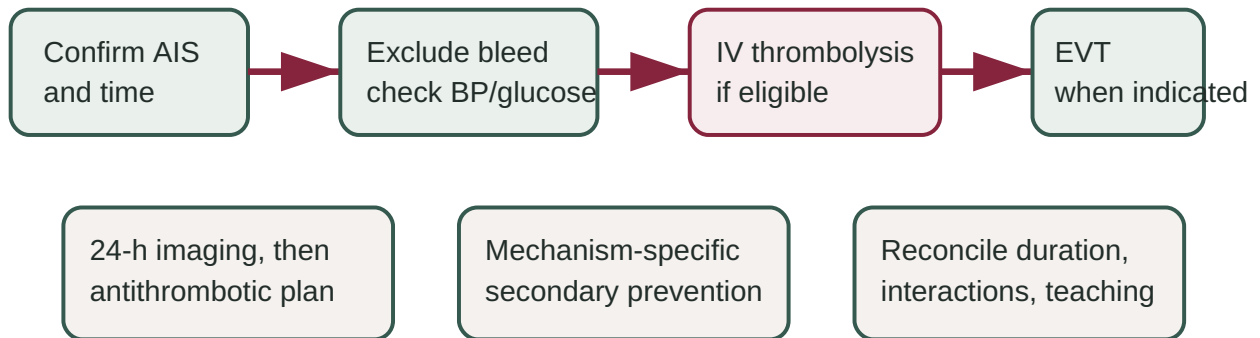


Figure 1. Medication decisions are sequenced around eligibility, timing, mechanism, and safety.
Evidence basis: Prabhakaran et al., 2026.

Intravenous thrombolysis: tenecteplase and alteplase

Intravenous thrombolysis remains time-dependent. For adults who are otherwise eligible within 4.5 hours of symptom onset or last known well, the 2026 AHA/ASA guideline recommends tenecteplase 0.25 mg/kg (maximum 25 mg) or alteplase 0.9 mg/kg. Alteplase is given as 10% of the total dose as an initial intravenous bolus and the remainder over 60 minutes. Tenecteplase is administered as a single intravenous bolus. A tenecteplase dose of 0.40 mg/kg should not be substituted; trials have not shown added benefit and have raised safety concerns at the higher dose (Prabhakaran et al., 2026).

The medication decision is inseparable from eligibility assessment. Before thrombolysis, clinicians verify a disabling neurologic deficit, time last known well, noncontrast brain imaging excluding hemorrhage, blood pressure that can be safely controlled, glucose, medication history, recent procedures or bleeding, platelet count and coagulation results when clinically indicated, and the timing of any anticoagulant exposure. Treatment should not be delayed for additional multimodal imaging when a patient is otherwise eligible within the standard 4.5-hour window (Prabhakaran et al., 2026).

Blood pressure management is a medication-safety step rather than an independent reason to delay all reperfusion. Trial protocols used a pre-thrombolysis threshold below 185/110 mm Hg, followed by maintenance at or below 180/105 mm Hg during the first 24 hours. Commonly used intravenous agents include labetalol, nicardipine, and clevidipine; selection depends on heart rate, ventricular function, infusion resources, and local protocol. Overly intensive systolic pressure reduction to below 140 mm Hg after thrombolysis does not improve functional outcome and is not recommended as a routine target (Prabhakaran et al., 2026).

After thrombolysis, frequent neurologic and blood-pressure checks are essential. New severe headache, vomiting, acute hypertension, or neurologic worsening should trigger immediate evaluation for intracranial hemorrhage; if alteplase is still infusing, the infusion is stopped. Antiplatelet and anticoagulant therapy is generally deferred until follow-up CT or MRI at about 24 hours excludes hemorrhage. Avoiding unnecessary nasogastric tubes, urinary catheters, arterial punctures, and other invasive procedures during the high-risk period also reduces bleeding exposure (Prabhakaran et al., 2026).

Alteplase vs tenecteplase for eligible AIS within 4.5 hours

Alteplase

0.9 mg/kg (max 90 mg)
10% bolus, remainder over 60 min
Established thrombolytic pathway
Requires infusion management

Tenecteplase

0.25 mg/kg (max 25 mg)
Single IV bolus
AHA/ASA: option through 4.5 h
U.S. label: initiate within 3 h

Do not use tenecteplase 0.40 mg/kg as a routine stroke dose.

Figure 2. Current thrombolytic options and dosing for eligible adult AIS.
Evidence basis: Prabhakaran et al., 2026; Genentech, 2025.

Extended-window thrombolysis and wake-up stroke

Time remains central, but selected patients can receive thrombolysis beyond a simple clock cutoff. The 2026 guideline states that intravenous thrombolysis may be reasonable for selected patients 4.5 to 9 hours from last known well, or for some wake-up strokes, when advanced imaging demonstrates salvageable tissue. These pathways are imaging-dependent and should be executed through a stroke protocol with validated perfusion or MRI selection. The drug is not chosen in isolation from imaging eligibility, and patients who are candidates for thrombectomy should not have endovascular therapy delayed to observe whether thrombolysis works (Prabhakaran et al., 2026).

Antiplatelet therapy in acute noncardioembolic stroke

Aspirin remains foundational after ischemic stroke when hemorrhage has been excluded and thrombolysis-related restrictions are satisfied. Historical trials established benefit when aspirin was started within 48 hours, primarily by reducing early recurrent ischemic events. Aspirin is not a substitute for thrombolysis or thrombectomy in an otherwise eligible patient, and intravenous aspirin given during alteplase treatment increased symptomatic intracranial hemorrhage in the ARTIS trial without improving outcome (Prabhakaran et al., 2026).

Short-term dual antiplatelet therapy (DAPT) is now a targeted strategy rather than a general rule. For early-arriving minor noncardioembolic stroke or high-risk

TIA, clopidogrel plus aspirin reduces early recurrence when initiated promptly and used for a limited course. The 2026 guideline summarizes evidence supporting 21 days of clopidogrel plus aspirin followed by single antiplatelet therapy in appropriate patients; longer-term DAPT increases bleeding and is not routinely beneficial. In selected patients with NIHSS 4 to 5 and presumed symptomatic large-artery atherosclerosis, a short course may also be reasonable when thrombolysis was not given (Prabhakaran et al., 2026).

Ticagrelor plus aspirin for 30 days is another evidence-based option in selected mild-to-moderate noncardioembolic stroke or high-risk TIA populations, but the benefit is accompanied by increased severe bleeding. Ticagrelor can be particularly relevant when clopidogrel effectiveness is uncertain, including CYP2C19 loss-of-function settings, but genotype-guided decisions should follow local protocols and the population studied. Prasugrel is generally avoided in patients with prior stroke or TIA because of bleeding risk and is not a stroke-prevention substitute for clopidogrel or ticagrelor.

Long-term antiplatelet selection after noncardioembolic ischemic stroke commonly includes aspirin, clopidogrel, or aspirin plus extended-release dipyridamole. The choice is individualized by tolerance, adherence, bleeding history, cost, prior therapy, drug interactions, and stroke mechanism. Combining antiplatelet therapy with full-dose oral anticoagulation is usually avoided unless another compelling vascular indication exists (Kleindorfer et al., 2021).

Anticoagulation after atrial-fibrillation-associated stroke

For ischemic stroke caused by atrial fibrillation, oral anticoagulation is generally more effective than antiplatelet therapy for preventing recurrent cardioembolic events. Direct oral anticoagulants (DOACs) are preferred over warfarin for most patients with atrial fibrillation who do not have a mechanical heart valve or moderate-to-severe rheumatic mitral stenosis. Warfarin remains the standard in those exceptions. Renal function, age, body weight, interacting drugs, adherence, cost, and bleeding risk determine the specific agent and dose (Joglar et al., 2024).

The timing of anticoagulation after an acute infarct must balance recurrent embolism against hemorrhagic transformation. The ELAN trial compared imaging-guided early DOAC initiation with later initiation and found a low rate of symptomatic intracranial hemorrhage in both strategies, with no signal of excess harm from the early strategy in selected patients.

Reflecting these data, the 2026 AHA/ASA acute stroke guideline considers early oral anticoagulation reasonable in carefully selected patients, especially those with milder stroke, while recognizing that the exact timing should account for infarct size, hemorrhagic transformation, reperfusion treatment, renal function, and overall bleeding risk (Fischer et al., 2023; Prabhakaran et al., 2026).

Urgent therapeutic heparin or low-molecular-weight heparin is not routinely used as a bridge to prevent early recurrent stroke in unselected atrial-fibrillation-related ischemic stroke. Bridging can increase bleeding without proven improvement in neurologic outcome. When anticoagulation is started, medication reconciliation should identify antiplatelets, NSAIDs, strong P-glycoprotein or CYP3A4 modulators, and other drugs that amplify bleeding or alter DOAC exposure. Aspirin should not be used as an alternative to anticoagulation solely for AF stroke prevention when the patient is an appropriate anticoagulation candidate (Joglar et al., 2024).

Antithrombotic choice follows stroke mechanism and timing

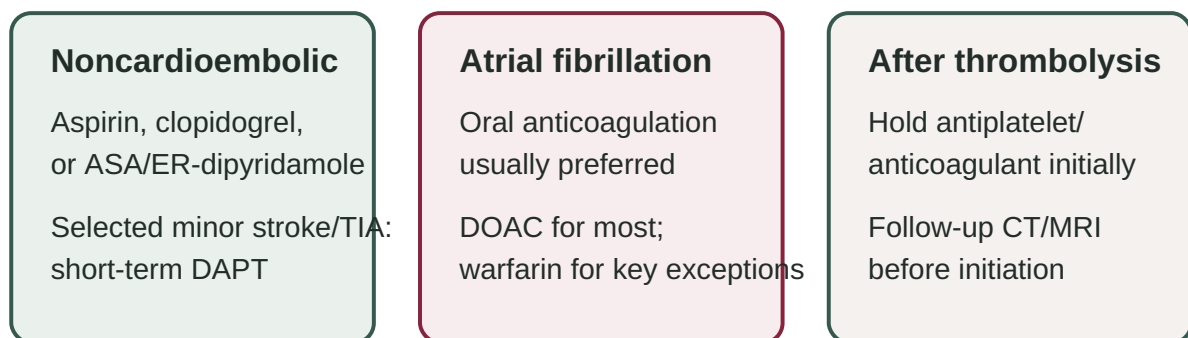


Figure 3. Antiplatelet and anticoagulant strategies answer different stroke mechanisms.
Evidence basis: Kleindorfer et al., 2021; Prabhakaran et al., 2026.

Lipid-lowering therapy and vascular risk reduction

High-intensity statin therapy is a core medication strategy after many atherosclerotic ischemic strokes. The 2021 AHA/ASA secondary-prevention guideline recommends intensive lipid lowering, commonly targeting LDL cholesterol below 70 mg/dL for patients with atherosclerotic disease, using maximally tolerated

statin therapy and adding ezetimibe when needed. A PCSK9 inhibitor may be considered in very-high-risk patients whose LDL remains above target despite maximally tolerated statin plus ezetimibe (Kleindorfer et al., 2021).

Medication counseling should cover myalgias, the uncommon risk of severe muscle injury, potential liver-enzyme abnormalities, pregnancy considerations, and the importance of persistence when side effects are

manageable. Stopping a statin reflexively after a stroke because of nonspecific muscle symptoms can remove a therapy with substantial vascular benefit; evaluation should instead consider temporal relationship, creatine

kinase when indicated, drug interactions, thyroid disease, and rechallenge or alternative dosing when appropriate.

AF-associated stroke: timing oral anticoagulation

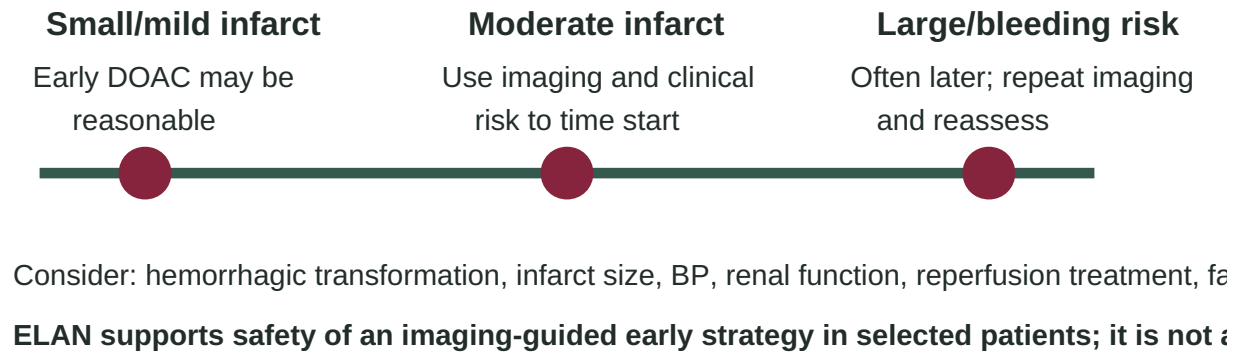


Figure 4. Anticoagulation timing after AF-associated stroke is individualized by imaging and bleeding risk. Evidence basis: Fischer et al., 2023; Prabhakaran et al., 2026.

Blood pressure pharmacotherapy after the hyperacute phase

Blood-pressure treatment goals change across the stroke timeline. In the first hours, aggressive lowering can worsen cerebral perfusion in some patients, while uncontrolled hypertension increases hemorrhagic risk when thrombolysis is used. Beyond the hyperacute phase, long-term antihypertensive therapy is central to recurrent-stroke prevention. The 2021 secondary-prevention guideline supports a blood-pressure goal below 130/80 mm Hg for most patients after stroke or TIA, individualized for tolerability and comorbidity (Kleindorfer et al., 2021).

No single antihypertensive class is mandatory for every survivor. Thiazide-type diuretics, ACE inhibitors, angiotensin receptor blockers, calcium-channel blockers, and other agents are chosen according to renal function, potassium, heart failure, coronary disease, diabetes, orthostasis, and adherence. APRNs should explicitly separate the permissive or protocol-driven targets used during acute reperfusion from the chronic prevention target used after stabilization.

Cerebral edema, seizures, fever, and glucose

Large hemispheric or cerebellar infarction can produce life-threatening edema. Hyperosmolar therapy with hypertonic saline or mannitol may temporarily reduce intracranial pressure and can be used while definitive neurocritical-care and neurosurgical decisions are made. These agents do not reverse the infarction, and routine prophylactic use is not justified. Mannitol requires attention to volume status, serum osmolality, kidney function, and hypotension; hypertonic saline requires sodium, chloride, volume, and access monitoring. Malignant swelling should prompt early decompressive-surgery evaluation rather than repeated osmotherapy as a substitute for definitive care.

Seizures after ischemic stroke are treated when they occur, but routine prophylactic antiseizure medication is not recommended for patients who have never seized. Agent selection should account for mental-status effects, cardiac conduction, renal or hepatic function, and interactions with anticoagulants and antiplatelet drugs. Levetiracetam is commonly used because of relatively few pharmacokinetic interactions, although behavioral adverse effects and renal dosing still matter.

Fever should trigger a search for infection or another cause and is generally treated with antipyretics and supportive measures when clinically indicated.

Hyperglycemia is associated with worse outcomes, but intensive intravenous insulin targeting 80 to 130 mg/dL is not recommended because it does not improve functional outcome and increases severe hypoglycemia. A practical inpatient target should follow the stroke unit and diabetes protocol while avoiding both marked hyperglycemia and hypoglycemia (Prabhakaran et al., 2026).

Hemorrhagic complications and reversal planning

The most feared medication complication of thrombolysis or antithrombotic therapy is intracranial hemorrhage. Management begins with immediate cessation of the causative infusion or anticoagulant when applicable, urgent neuroimaging, laboratory assessment, airway and blood-pressure stabilization, and rapid activation of stroke, neurocritical-care, hematology, transfusion, and neurosurgical pathways as appropriate. A reversal plan should be known before high-risk therapy is administered.

For thrombolysis-associated symptomatic intracranial hemorrhage, many institutional protocols use cryoprecipitate to restore fibrinogen and consider antifibrinolytic therapy such as tranexamic acid or aminocaproic acid when cryoprecipitate is delayed or contraindicated; exact thresholds and dosing should follow the institution's current reversal pathway. For dabigatran, idarucizumab is a specific reversal agent. For factor Xa inhibitors, andexanet alfa can reverse apixaban or rivaroxaban in selected life-threatening bleeding, while four-factor prothrombin complex concentrate is used in many protocols when andexanet is unavailable or unsuitable. Warfarin-associated major bleeding is commonly reversed with four-factor prothrombin complex concentrate plus intravenous vitamin K. These reversal decisions require local protocol, timing of the last dose, renal function, drug level information when available, thrombosis risk, and the urgency of hemostasis.

Investigational neuroprotection: what not to present as routine care

Older stroke pharmacology literature devoted substantial attention to melatonin, minocycline, erythropoietin, NMDA antagonists, anti-inflammatory agents, caspase inhibitors, and other neuroprotective compounds. Many showed biological effects in cell culture or animal models but did not establish a routine clinical role. The absence of an approved neuroprotective drug should be taught explicitly so that mechanistic plausibility is not mistaken for patient-

centered efficacy. The practical neuroprotection available today is rapid reperfusion when eligible, avoidance of hypoxia and hypotension, treatment of fever and severe glucose abnormalities, prevention of recurrent thrombosis when appropriate, and organized stroke-unit care (Prabhakaran et al., 2026).

Case 1 - Tenecteplase at the bedside

A 68-year-old patient develops sudden aphasia and right arm weakness 74 minutes before arrival. Noncontrast CT shows no hemorrhage. Blood pressure is 178/98 mm Hg, glucose is 132 mg/dL, there is no recent anticoagulant exposure, and the deficit is disabling. Under the stroke protocol, tenecteplase 0.25 mg/kg up to 25 mg or alteplase 0.9 mg/kg are guideline-supported options. Because tenecteplase is a single bolus, it may simplify transfer for thrombectomy evaluation. The APRN verifies actual or protocol-accepted weight, contraindications, blood pressure, drug dose, and last-known-well time, then ensures post-thrombolysis monitoring and no antiplatelet or anticoagulant until follow-up imaging clears hemorrhage.

Case 2 - Minor stroke and short-term DAPT

A 59-year-old patient presents 8 hours after transient left hand weakness and dysarthria. MRI shows a small acute infarct; NIHSS is 2, there is no atrial fibrillation, and thrombolysis was not given. Vascular imaging shows symptomatic atherosclerotic disease. A short course of aspirin plus clopidogrel is considered to reduce early recurrence, followed by single antiplatelet therapy. The clinician documents the intended duration at the time of prescribing. Leaving both drugs on the medication list indefinitely without a stop plan converts an evidence-based short-term strategy into avoidable long-term bleeding risk.

Case 3 - AF stroke and timing the DOAC

A 76-year-old patient with newly detected atrial fibrillation has a small cortical ischemic infarct without hemorrhagic transformation. The key question is not whether long-term anticoagulation is indicated, but when it can be started safely and which agent fits renal function, weight, interacting medications, valve status, cost, and adherence. In a mild infarct with reassuring imaging, an early DOAC strategy may be reasonable. A large infarct, uncontrolled hypertension, parenchymal hematoma, recent procedure, or other bleeding concern would push the plan toward individualized delay and repeat imaging.

Medication safety checkpoints across the stroke pathway

BEFORE REPERFUSION

Last-known-well • BP • glucose • bleed/procedure history • anticoagulant exposure • dose and weight

FIRST 24 HOURS

Neuro/BP checks • watch for ICH • avoid unnecessary invasive procedures • follow-up CT/MRI

SECONDARY PREVENTION

Define mechanism • antiplatelet vs anticoagulant • statin/BP therapy • interaction review

DISCHARGE

Indication • duration/stop date • missed-dose plan • bleeding warnings • access and adherence

Figure 5. Medication reconciliation should make timing, duration, monitoring, and stop conditions explicit.
Evidence basis: Prabhakaran et al., 2026; Joglar et al., 2024.

Case 4 - When medication targets compete

A 71-year-old patient receives thrombolysis and successful thrombectomy. The postprocedure systolic pressure is 152 mm Hg. A reflex order to drive systolic pressure below 120 or 130 mm Hg is not evidence-based and may be harmful after successful reperfusion. The medication plan should instead follow the stroke-center protocol, avoid hypotension and excessive variability, and treat other compelling indications. Later, once neurologically stable, the chronic prevention regimen can target a substantially lower outpatient blood pressure.

Practical medication reconciliation and patient teaching

Stroke medication reconciliation should identify the indication, dose, start date, planned duration, stop date when relevant, renal and hepatic constraints, interactions, and monitoring plan for every antithrombotic. High-risk errors include accidental continuation of DAPT beyond the intended course, combining a DOAC with aspirin without a current indication, restarting anticoagulation before post-thrombolysis imaging, duplicating anticoagulants during transitions, and using the wrong tenecteplase dose.

Patients and caregivers should leave with a plain-language explanation of which medication prevents clot formation, which lowers cholesterol or blood pressure, which drugs should not be stopped abruptly without advice, and which bleeding or neurologic symptoms require urgent evaluation. Teach patients to report melena, hematemesis, hematuria, persistent epistaxis, severe headache, new weakness, falls with head trauma, and medication-access problems. For anticoagulants, missed-dose instructions must be specific to the prescribed drug rather than generalized across the class.

Medication strategy	Key administration point	Priority monitoring / safety check
Alteplase / tenecteplase	Use verified stroke dose and treatment window; do not interchange MI dosing.	BP, neurologic status, bleeding; 24-h imaging before routine antithrombotics.
Short-term aspirin + clopidogrel	Use only for an eligible noncardioembolic minor stroke/TIA pathway and document planned duration.	Bleeding, adherence, interacting NSAIDs; ensure conversion to single therapy.
DOAC after AF-associated stroke	Start timing from infarct size/imaging and bleeding risk; dose by drug-specific renal/age/weight criteria.	Renal function, interacting P-gp/CYP3A4 drugs, bleeding, adherence and access.
High-intensity statin ± ezetimibe	Use maximally tolerated therapy to reach the secondary-prevention LDL goal.	Symptoms, interactions, liver tests when clinically indicated, adherence.
Mannitol / hypertonic saline	Temporizing therapy for dangerous edema, not a replacement for definitive neurosurgical evaluation.	Volume status, sodium/osmolality, kidney function, BP and neurologic trajectory.

Table 1. High-yield medication administration and monitoring checkpoints. Evidence basis: Prabhakaran et al., 2026; Kleindorfer et al., 2021; Joglar et al., 2024.

Clinical synthesis

Contemporary stroke pharmacology is a sequence of time-sensitive decisions. In eligible acute ischemic stroke, alteplase or tenecteplase can provide reperfusion; tenecteplase 0.25 mg/kg is now guideline-endorsed within 4.5 hours, while current U.S. labeling specifies initiation within 3 hours. Aspirin and carefully selected short-term DAPT reduce early noncardioembolic recurrence but should not be used as substitutes for reperfusion. Atrial-fibrillation-associated stroke usually requires oral anticoagulation, with DOACs preferred over warfarin for most patients without mechanical valves or moderate-to-severe rheumatic mitral stenosis. Long-term statin and blood-pressure therapy reduce recurrent vascular risk.

Hyperosmolar agents, antiseizure therapy, glucose management, and reversal drugs address complications and medication safety rather than replacing reperfusion or secondary prevention. The safest regimen is the one in which indication, timing, dose, duration, monitoring, and stop conditions are all explicit.

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