Emergency Department Pharmacist's Notes

(2019 AIS Guideline p1-2 | 2019 CAP Guideline p3-5) **February 2020**

2019 AHA/ASA Guidelines: Eligibility for IV Alteplase Treatment in Patients with Acute Ischemic Stroke

Alteplase Contraindications:

- Mild **non-disabling** stroke
- Acute head trauma (posttraumatic infarction during acute in-hospital phase)
- Acute intracranial hemorrhage on imaging
- Aortic arch dissection
- Blood pressure > 185/110 mm Hg (must be lowered prior to administration)
- Coagulopathy including Plt < 100,000/mm^3, INR > 1.7, aPTT > 40 s, or PT > 15 s
- Concomitant use of abciximab
- Concomitant administration of IV aspirin
- Extensive regions of clear hypoattenuation on CT brain imaging
- GI malignancy or recent bleeding event within 21 days
- History of intracranial hemorrhage
- Infective endocarditis
- Intra-axial intracranial neoplasm
- Intracranial or intraspinal surgery within 3 mo
- Low-molecular-weight heparin treatment dose within the previous 24 h (DVT prophylaxis dosing is NOT a contraindication)
- Prior ischemic stroke within 3 mo
- Symptoms and signs most consistent with subarachnoid hemorrhage
- Severe head trauma within 3 mo
- Use of direct thrombin inhibitors or direct factor Xa inhibitors unless pertinent laboratory tests such as aPTT, INR, ecarin clotting time, platelet count, thrombin time or direct factor Xa activity assays are normal or patient has not received a dose in > 48 hr (assuming normal clearance)

Additional Recommendations In the 3- to 4.5-hr window:

- Alteplase may be reasonable for patients with mild, disabling stroke
- Benefit of alteplase is uncertain in patients with severe stroke symptoms (NIHSS score > 25)
- Treatment appears to be safe and may be beneficial in: patients > 80, patients with INR ≤ 1.7, and patients with both a prior stroke and diabetes

Alteplase is reasonable in patients with:

- Acute MI or MI within the past 3 mo
- AIS as a complication of cardiac or cerebral angiographic procedures
- AIS known or suspected to be associated with extracranial arterial cervical artery dissection within 4.5 h
- Baseline mRS score ≥ 2 or patients with dementia
- Early improvement, but persisting symptoms causing moderate impairment or disability
- Extra-axial intracranial neoplasm
- GI or genitourinary bleeding > 21 days ago
- History or active menorrhagia without clinically significant anemia or hypotension
- History of hemorrhagic ophthalmic condition
- Hyperdense MCA sign
- Illicit drug use–associated AIS given no other exclusions
- Initial blood glucose concentrations < 50 or > 400 mg/dL that are normalized and patients remain otherwise eligible for treatment
- Low burden of CMBs (1–10) on MRI
- Lumbar dural puncture in the preceding 7 days
- Malignancy and a reasonable life expectancy (> 6 mo) without contraindications
- Sickle cell disease
- Small or moderate (< 10 mm) unruptured and unsecured aneurysm
- Seizure at onset of AIS if impairment appears to be caused by stroke rather than postictal phenomenon
- Severe stroke leading to severe disability and acute pericarditis, left atrial or ventricular thrombus, cardiac myxoma, or papillary fibroelastoma
- Stroke mimics, given the low risk of intracranial hemorrhage
- Wake up stroke, and stroke of unclear time of onset >4.5 h since last known well who have a diffusion-weighted MRI lesion smaller than 1/3 the MCA territory and no visible signal change on FLAIR

Weigh risk-benefit in patients with:

- Arterial puncture at a non-compressible blood vessel in the preceding 7 days
- Bleeding diathesis or coagulopathy
- Pregnancy when treating moderate or severe strokes
- Recent or active vaginal bleeding causing clinically significant anemia; recommend an emergency consultation with a gynecologist
- Recent major trauma or recent major surgery, not involving the head, within 14 days
- Unruptured and untreated intracranial vascular malformation

Safety and efficacy of Alteplase are not well established in patients with:

- Acute pericarditis or left atrial or ventricular thrombus and moderate stroke with mild disability
- Concomitant use of tirofiban or eptifibatide
- Current active malignancy
- Giant unruptured and unsecured intracranial aneurysm
- High burden of CMBs (> 10)
- Intracranial arterial dissection
- Recent postpartum status (<14 d after delivery)

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Comparison of the AHA/ASA Acute Ischemic Stroke Guidelines			
	2013 Guideline	**2018 Guideline**	**2019 Guideline**
Door-to-needle times for IV thrombolysis	Goal < 60 min	• Establish internal goals • Primary goal of ≤60 min in 50% of patients, secondary goal of ≤45 min in 50% of patients	• Establish internal goals • Thrombolysis and thrombectomy should be performed as fast as possible* (see below)
Tenecteplase instead of alteplase for AIS	Usefulness is unknown, should only be used in the setting of a clinical trial	May consider in minor neurological impairment without LVO	• May consider in minor neurological impairment without LVO • Reasonable to consider over alteplase in patients who are candidates for thrombectomy with LVO
Alteplase eligibility recommendations	Listed as inclusion, exclusion and relative exclusion criteria	Listed as indications, contraindications and additional recommendations, significantly more inclusive	Listed as indications, contraindications and additional recommendations, slight modifications to recommendations
Alteplase extended 3- to 4.5-hr window	Contraindicated in warfarin use regardless of INR, age >80, history of both stroke and diabetes, or NIHSS >25	• Beneficial in warfarin use with INR <1.7, age >80 or history of both stroke and diabetes • Uncertain benefit in NIHSS >25	• Beneficial in warfarin use with INR <1.7, age >80 or history of both stroke and diabetes • Uncertain benefit in NIHSS >25
Alteplase for mild non-disabling stroke	Reasonable to consider	Reasonable to consider	Contraindicated
Neuroimaging for thrombolysis guidance	No recommendation	No recommendation	MRI to identify diffusion-positive and FLAIR-negative lesions can be used to identify candidates for IV thrombolysis
DAPT (dual antiplatelet therapy)	No recommendation	In patients with mild stroke, not receiving IV fibrinolysis, 21 days of aspirin and clopidogrel started within the first 24 hr may reduce risk of recurrent ischemic stroke	In patients with mild stroke, not receiving IV fibrinolysis, 21 days of aspirin and clopidogrel started within the first 24 hr is effective in reducing the risk of recurrent ischemic stroke
Thrombectomy	No recommendation	Extended time window to 24 hr in patients meeting eligibility criteria	Extended time window to 24 hr in patients meeting eligibility criteria

*Target: Stroke is a national quality improvement initiative developed and implemented by the AHA/ASA to improve AIS treatment by reducing DTN (AHA 2019). Phase III of Target: Stroke has recently proposed more aggressive national goals, including more stringent targets for DTN: 50% within 30 minutes, 75% within 45 minutes, and 85% within 60 minutes.

References: Jauch EC, Saver JL, Adams HP, et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2013;44:870-947; Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2018;49:e46-e110; 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:e344-e418.

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2019 Community Acquired Pneumonia (CAP) Guideline by ATS/IDSA

Reference: Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America https://www.atsjournals.org/doi/full/10.1164/rccm.201908-1581ST

Comparisons between the 2019 and 2007 CAP guidelines

Recommendation	2007 Guideline	2019 Guideline
Sputum culture	In pts with severe dz	▪ In pts with severe dz ▪ In all inpts empirically treated for MRSA or Pseudomonas
Blood culture	In pts with severe dz	▪ In pts with severe dz ▪ In all inpts empirically treated for MRSA or Pseudomonas
Macrolide monotherapy	Strong recommendation for outpts	Conditional recommendation for outpts based on resistance levels
Use of procalcitonin	Not covered	Not recommended to determine need for initial abx therapy
Use of corticosteroids	Not covered	▪ Recommended not to use ▪ May be considered in pts w/ refractory septic shock
Use of HCAP category (healthcare-associated)	Accepted as introduced in 2005 HCAP and VAP guidelines	▪ Recommended abandoning this category ▪ Evaluate local epidemiology and risk factors to determine need for MRSA or Pseudomonas. Deescalate of tx if cultures are negative
Standard empiric tx for severe CAP	Combo of Beta-lactam/macrolide and Beta-lactam/FQ given equal weighing	▪ Both combo tx accepted but ▪ Beta-lactam/macrolide favored
Routine use of follow-up chest imaging	Not addressed	▪ Recommended not to obtain ▪ Pts may be eligible for lung cancer screening if clinically indicated

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Outpatient CAP Initial ABX

	Standard Regimen
No comorbidities or **risk factors*** for MRSA or Pseudomonas	▪ Amoxicillin OR ▪ Doxycycline OR ▪ Macrolide (if local Strep pneumonia resistance is <25%)
With **comorbidities****	▪ Combo tx (augmentin or cephalosporin **AND** macrolide or doxycycline) OR ▪ Mono tx with respiratory FQ

***Risk factors** include prior respiratory isolation of MRSA or P. aeruginosa or recent hospitalization AND receipt of parenteral antibiotics (in the last 90 d).

Antibiotic dosing

- Amoxicillin 1 g three times daily
- Doxycycline 100 mg twice daily
- Azithromycin 500 mg on first day then 250 mg daily
- Clarithromycin 500 mg twice daily, or clarithromycin ER 1,000 mg daily.
- Amoxicillin/clavulanate 500 mg/125 mg three times daily
- Amoxicillin/clavulanate 875 mg/125 mg twice daily
- Amoxicillin/clavulanate 2,000 mg/125 mg twice daily
- Cefpodoxime 200 mg twice daily
- Cefuroxime 500 mg twice daily
- Levofloxacin 750 mg daily
- Moxifloxacin 400 mg daily
- Gemifloxacin 320 mg daily

****Comorbidities** include chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancy; or asplenia.

Duration of therapy: Usually 5-7 days (minimum 5 days)

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Inpatient CAP Initial ABX

	Standard regimen	Prior respiratory MRSA hx	Prior respiratory Pseudomonas hx	Recent hospitalization and IV abxs and locally validated risk factors for MRSA	Recent hospitalization and IV abx and locally validated risk factors for Pseudomonas
Nonsevere	Betalactam + macrolide OR Respiratory FQ	Add MRSA coverage and obtain cultures/nasal PCR for de-escalation or confirmation for tx	Add Pseudomonas coverage and obtain cultures for de-escalation or confirmation of tx	Obtain cultures but withhold MRSA coverage unless cultures are positive. If rapid nasal PCR is positive, add MRSA coverage and obtain cultures	Obtain cx but initiate Pseudomonas coverage if culture is positive
Severe*	Betalactam + macrolide OR Betalactam + FQ	Add MRSA coverage and obtain cultures/nasal PCR for de-escalation or confirmation of tx	Add Pseudomonas coverage and obtain cultures for de-escalation or confirmation of tx	Add MRSA coverage and obtain nasal PCR and Cx for de-escalation or confirmation of tx	Add Pseudomonas coverage and obtain cx for de-escalation or confirmation of tx

Definition of *severe CAP: one major or ≥ 3 minor criteria

Minor criteria	Major criteria
▪ RR ≥ 30 bpm ▪ PaO2/FiO2 ≤ 250 ▪ Multilobar infiltrates ▪ Confusion/disorientation ▪ BUN ≥ 20 mg/dL ▪ WBC < 2000 cells/uL ▪ PLT <100000 ▪ T <36 C ▪ Hypotension requiring fluids	▪ Septic shock requiring pressors ▪ Respiratory failure requiring mechanical ventilation

ABXs

Betalactam
- Ampicillin1sulbactam 1.5–3 g every 6 hours
- Ceftriaxone 1–2 g daily

Macrolides
- Azithromycin 500 mg daily
- Clarithromycin 500 mg twice daily

Respiratory FQ
- Levofloxacin 750 mg daily

MRSA coverage: IV vancomycin; linezolid

Betalactam covering *Psedomonas*: piperacillin-tazobactam; cefepime; ceftazidime; meropenem, aztreonam