From Ischemia to Intervention: Antiplatelets in Action

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Disclosures

The planner(s) and speaker(s) have indicated that there are no relevant financial relationships with any ineligible companies to disclose.

Learning Objectives

At the end of this session, learners should be able to:

1. Compare different antiplatelet agents and how they exert their effects in the context of cerebrovascular events
2. Summarize key recommendations from major guidelines regarding antiplatelet use in TIA and CVA
3. Outline evidence from literature to support clinical decision-making in neuroendovascular antiplatelet management
4. Recall appropriate safety and monitoring parameters for antiplatelet therapy

Abbreviation Key

ACS: Acute coronary syndromes

ADP: Adenosine Diphosphate

AIS: Acute ischemic stroke

ASA: Acetylsalicylic Acid

AVM: Arteriovenous malformation

CAD: Coronary artery disease

cAMP: cyclic Adenosine monophosphate

CAST: Chinese acute stroke trial

COX1: Cyclooxygenase-1

CrCl: Creatinine clearance

CVA: Cerebrovascular accident

DAPT: Dual antiplatelet therapy

DDIs: Drug-drug interactions

GPIIb/IIIa: Glycoprotein IIb/IIIa

HF: Heart failure

ICAD: Intracranial atherosclerotic disease

ICH: Intracranial hemorrhage

IST: Ischemic stroke trial

Abbreviation Key

LD: Loading dose

LOF: Loss of function

MCA: Middle cerebral artery

MD: Maintenance dose

MI: Myocardial infarction

mRS: modified Rankin Scale

NIHSS: National Institutes of Health Stroke Scale

NNH: Number needed to harm

NNT: Number needed to treat

NSAID: Non-steroidal anti-inflammatory drug

P&T: Pharmacy and Therapeutics

PDE: Phosphodiesterase

PO: Oral

RCT: Randomized control trial

TIA: Transient ischemic attack

TTP: Thrombotic thrombocytopenic purpura

TxA2: Thromboxane A2

UFH: Unfractionated heparin

vWF: von Willebrand factor

Platelets in Clot Formation

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Role of Platelets

Clot Formation: When a blood vessel is injured, platelets are the first responders

Adhere	Activate	Aggregate
• To the damaged vessel wall	• By changing shape and releasing chemical signals	• By clumping together to form a temporary plug

Leads to triggering of the **coagulation cascade**, starting formation of a stable fibrin clot that seals the wound

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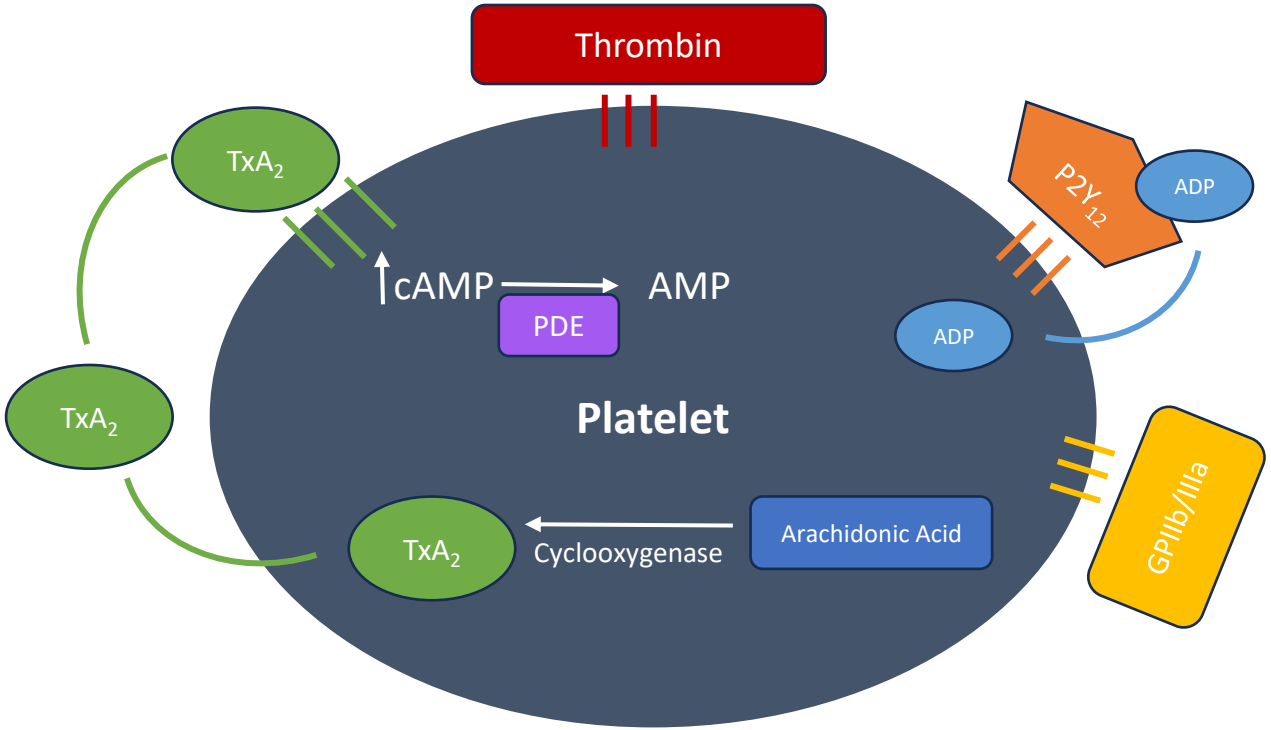
Del Zoppo GJ. Neurology. 1998;51.

Overview of Platelets



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Yun SH et al. *Biomed Res Int*. 2016:9060143.

Impact of Platelets in Stroke

- Platelets are essential for stopping bleeding by forming clots
- Excessive platelet activity or high platelet counts can lead to abnormal clot formation inside blood vessels
- If a clot forms in or travels to the brain's arteries, it can block blood flow, causing an acute ischemic stroke (AIS)

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Del Zoppo GJ. Neurology. 1998;51.

Antiplatelet Medications

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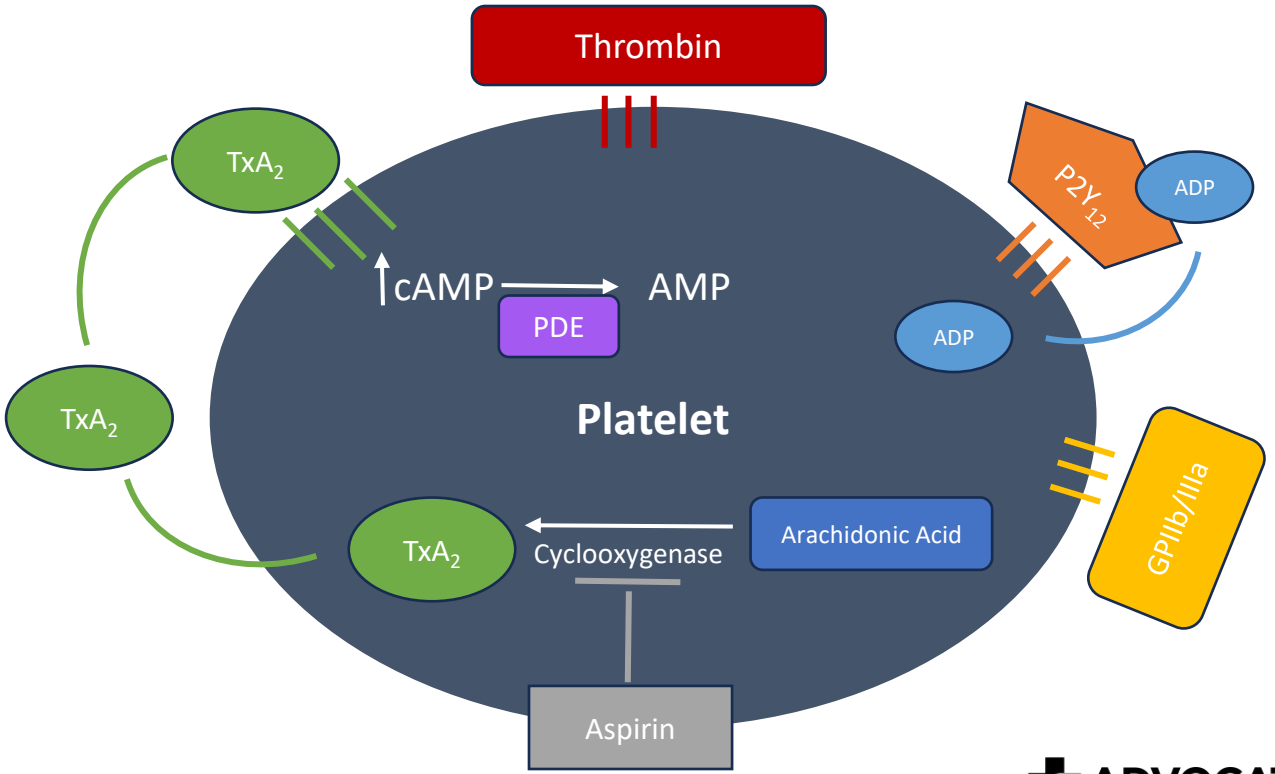
Aspirin



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Kashyap R, Sharma S. StatPearls. StatPearls Publishing; 2023.

Aspirin Overview

	Aspirin
Mechanism of Action	• Nonsteroidal anti-inflammatory drug (NSAID) • Irreversible inactivation of cyclooxygenase 1 (COX1) • Inhibits conversion of arachidonic acid to thromboxane A2 (TXA2)
Dosing	• LD: 160 – 325 mg PO • MD: 75 – 100 mg PO
PK/PD	• Onset: ~1 hour • Duration: ~7 days
Clinical Pearls	• Increased bleeding risk • Fetal toxicity • Renal impairment

Aspirin [package insert]. Houston, TX: PLx Pharma Inc.; 2018.
Powers WJ et al. Stroke. 2019;50(12):e344–e418.

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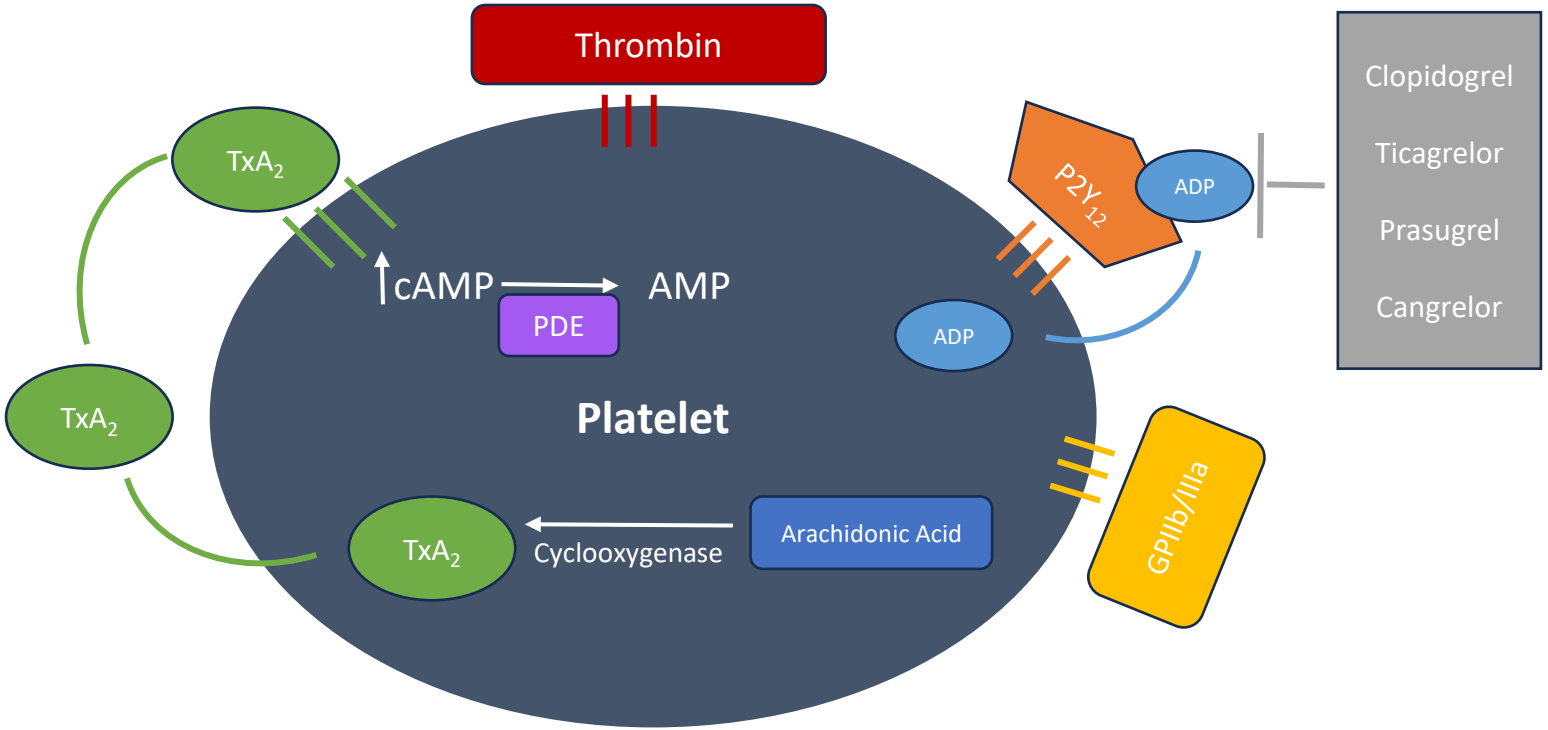
$P2Y_{12}$ Inhibitors



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Oral $P2Y_{12}$ Inhibitors Overview

	Clopidogrel	Ticagrelor	Prasugrel
Mechanism of Action	Irreversible inhibition of P2Y12 receptor	**Reversible** inhibition of P2Y12 receptor	Irreversible inhibition of P2Y12 receptor
Dosing	• LD: 300-600 mg PO x 1 • MD: 75 mg PO once daily	• LD: 180 mg PO x 1 • MD: 90 mg PO twice daily	• LD: 60 mg PO x1 • MD: 10 mg PO daily
PK/PD	• Onset: 2 hours • Time to steady state: 3-7 days • Duration: 5 days	• Onset: 2 hours • Time to steady state: 2-3 days • Duration: 5 days	• Onset: 1 hour • Time to steady state: 3-5 days • Duration: 5-9 days
Considerations	• **CYP2C19** metabolism • TTP	• Decreased effect with ASA doses > 100 mg • Risk of **dyspnea**	• Not recommended in patients ≥ 75 years of age • Increased **bleeding risk** • Dose reduce for < 60 kg

Brilinta [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2016.
Plavix [package insert]. Bridgewater, NJ: Sanofi-Aventis U.S. LLC; 2019.
Effient [package insert]. Indianapolis, IN: Eli Lilly and Company; 2020.

Oral $P2Y_{12}$ Inhibitors Overview

	Clopidogrel	Ticagrelor	Prasugrel
Mechanism of Action	Irreversible inhibition of P2Y12 receptor	**Reversible** inhibition of P2Y12 receptor	Contraindicated in stroke/TIA
Dosing	• LD: 300-600 mg PO x 1 • MD: 75 mg PO once daily	• LD: 180 mg PO x 1 • MD: 90 mg PO twice daily	
PK/PD	• Onset: 2 hours • Time to steady state: 3-7 days • Duration: 5 days	• Onset: 2 hours • Time to steady state: 2-3 days • Duration: 5 days	
Considerations	• **CYP2C19** metabolism • TTP	• Decreased effect with ASA doses > 100 mg • Risk of **dyspnea**	

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Effient [package insert]. Indianapolis, IN: Eli Lilly and Company; 2020.

Intravenous $P2Y_{12}$ Inhibitor Overview

	Cangrelor
Mechanism of Action	Reversible inhibition of P2Y12 receptor
Dosing	• Bolus: 15–30 µg/kg IV • MD: 2–4 µg/kg/minute IV
PK/PD	• Onset: 2 minutes • Duration: 1 hour
Clinical Pearls	• Not used in chronic platelet inhibition • Transition to oral therapy

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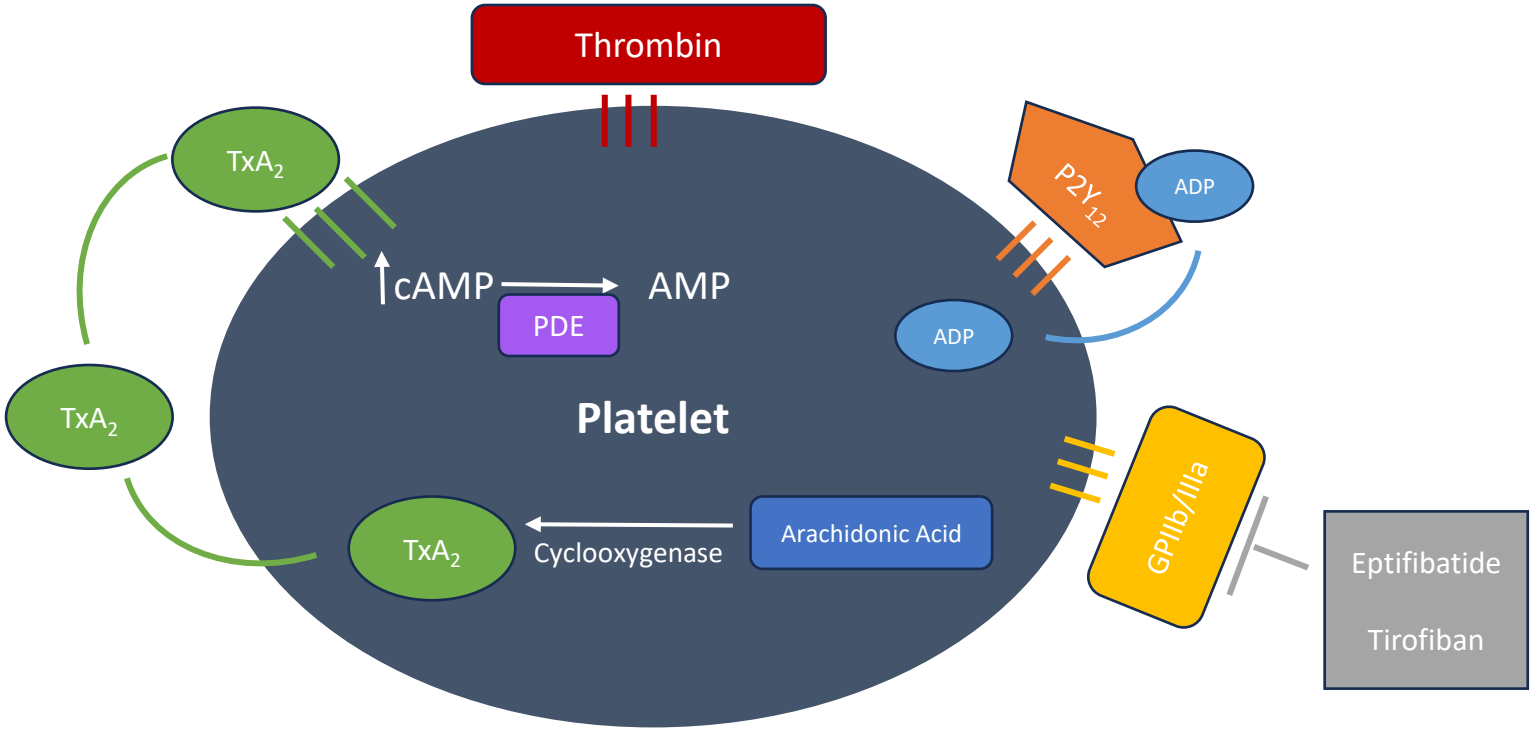
Kashyap R, Sharma S. StatPearls. StatPearls Publishing; 2023.
Kengreal [package insert]. Cary, NC: Chiesi USA, Inc.; 2023.

GPIIb/IIIa Inhibitors



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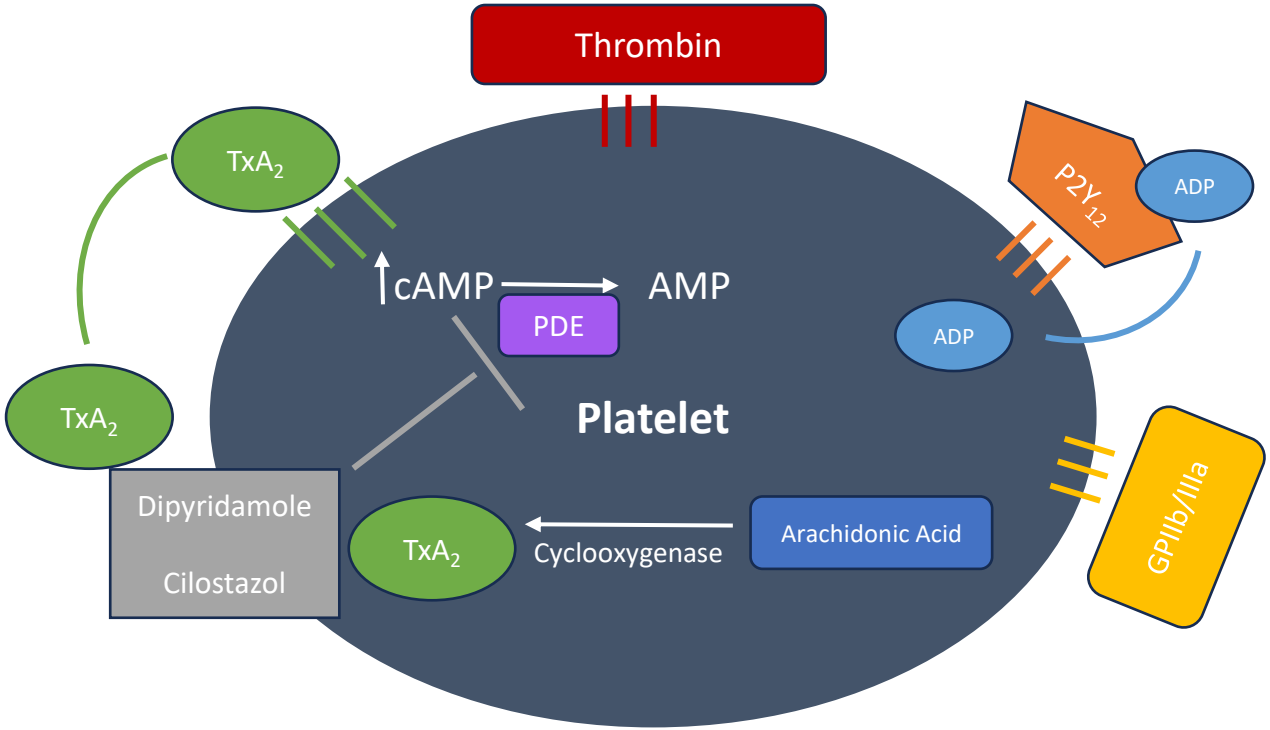
GPIIb/IIIa Inhibitors Overview

	Eptifibatide	Tirofiban
Mechanism of Action	Competitive inhibition of von Wildebrand Factor (vWF) and fibrinogen	
Dosing	Bolus: 180–200 mcg/kg IV MD: 0.5–2 mcg/kg/min IV	Bolus: 25 mcg/kg IV MD: 0.10-0.15 mcg/kg/min IV
PK/PD	Onset: Immediate Half-life: ~2.5 hours	Onset: Within 10 minutes Half-life: ~ 2 hours
Clinical Pearls	• Increased risk of hemorrhage • Renal adjustment for **CrCl < 50 ml/min**: ~ 50% dose reduction	• Increased risk of hemorrhage • Renal adjustment for **CrCl < 60 ml/min**: ~ 50% dose reduction

Integrilin (eptifibatide) injection [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; Revised 2013.
Aggrastat (tirofiban hydrochloride) injection [package insert]. Somerset, NJ: Medicure Pharma, Inc.; Revised 2021.

Phosphodiesterase Inhibitors



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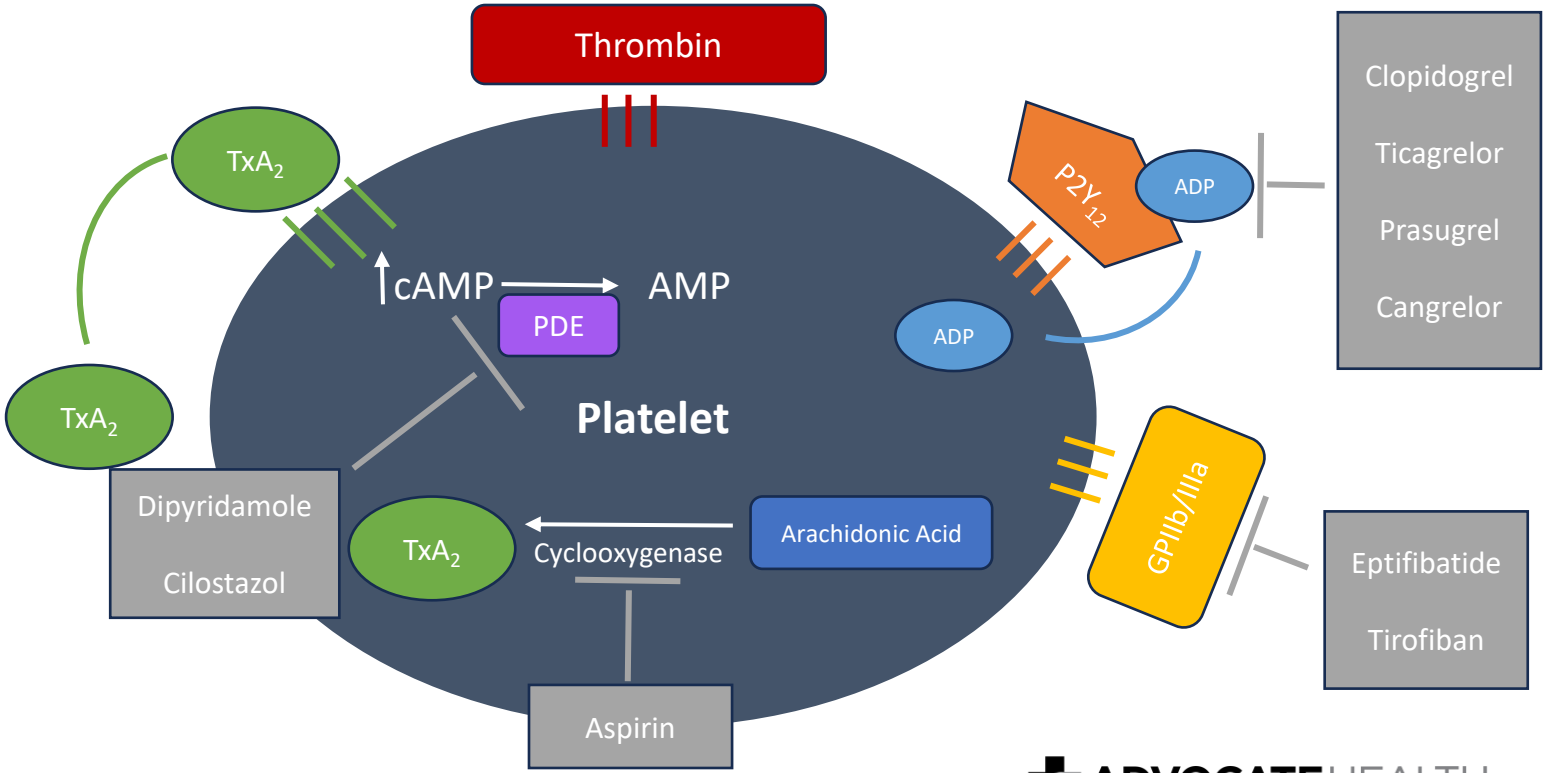
Phosphodiesterase Inhibitors Overview

	Dipyridamole	Cilostazol
Mechanism of Action	• Inhibition of phosphodiesterase 3 • Decreases cAMP concentration	
Dosing	• 75-100 mg PO four times daily • Often combined w/ ASA	• 100 mg PO twice daily
PK/PD	• Onset: 75 minutes • Duration: 10 hours	• Onset: 3 hours • Duration: 96 hours
Clinical Pearls	• Caution in CAD or hypotension • Hepatic metabolism • DDIs: Adenosine, Cholinesterase inhibitors	• Contraindicated in HF • Risk of tachyarrhythmias • DDIs: reduce dose w/ strong CYP3A4 and CYP2C19 inhibitors

Persantine (dipyridamole) tablets and injection [package insert]. Ridgefield, CT; Revised 2009.
Pletal (cilostazol) tablets [package insert]. Rockville, MD; Revised 2007.

Antiplatelet Medication Summary



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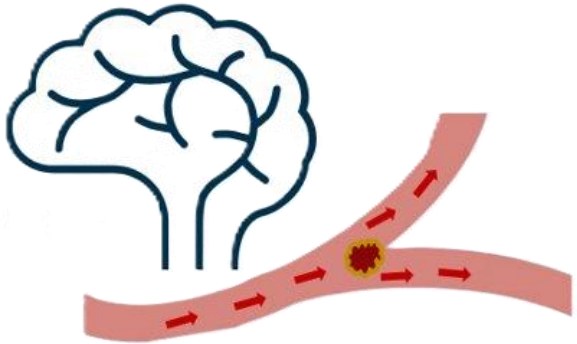
Assessment Question #1

A 78-year-old female presents to the ED with sudden onset of left-sided weakness and facial droop lasting 15 minutes. CT negative for hemorrhage. MRI confirms small infarct in right MCA territory. The team is considering dual antiplatelet therapy for secondary stroke prevention, **which of the following if initiated in this patient exhibits reversible platelet inhibition at the P2Y12 receptor?**

A. Clopidogrel
B. Aspirin
C. Ticagrelor
D. Cilostazol

Ischemic Cerebrovascular Syndromes

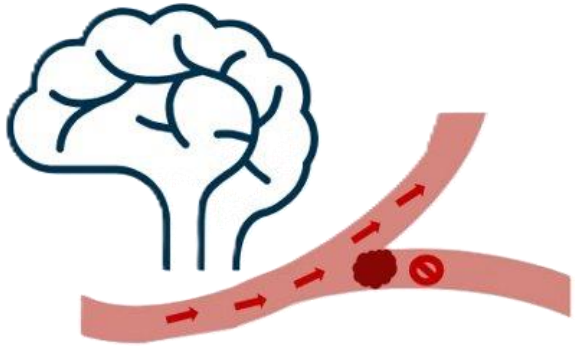
TIA



- Temporary neurologic dysfunction
- Short duration
- No infarct on imaging

VS

CVA



- Permanent neurologic deficit
- Duration > 24 hours
- Requires urgent medical attention

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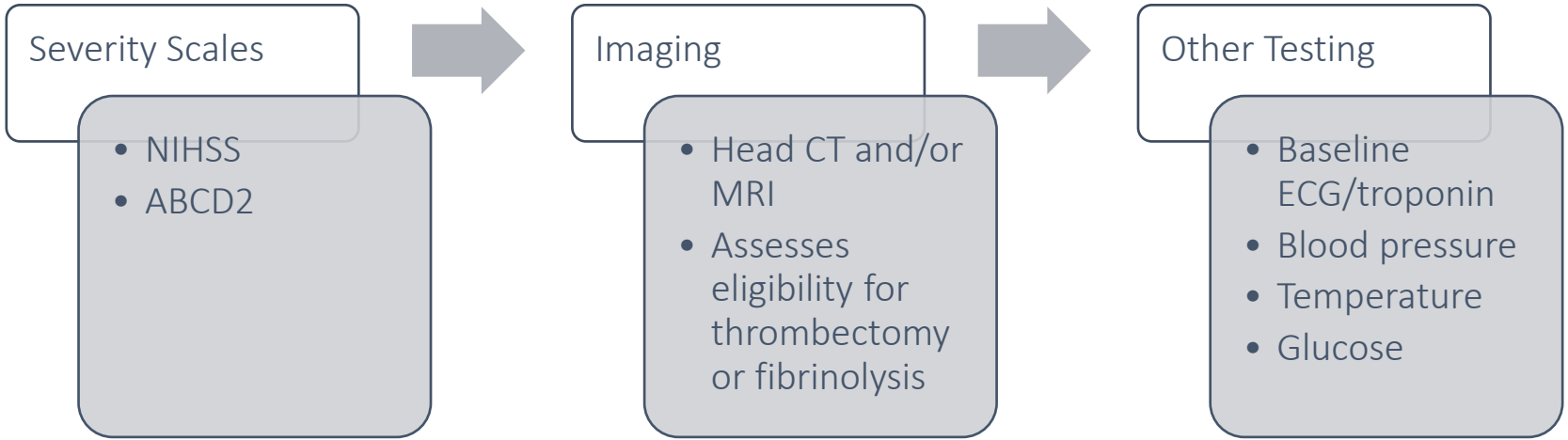
Powers WJ et al. *Stroke*. 2019;50(12):e344–e418.

Assessment of Injury



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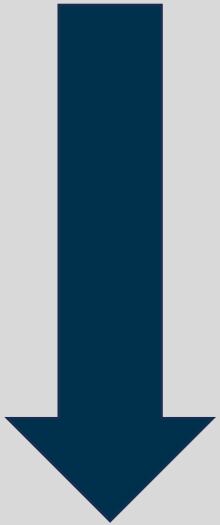
Powers WJ et al. *Stroke*. 2019;50(12):e344–e418.

NIHSS

NIHSS Score	Stroke Severity	Impacted Brain Density
0	No stroke	
1 – 4	Minor stroke	
5 – 15	Moderate stroke	
16 - 20	Moderate to severe stroke	
21 – 42	Severe stroke	

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Cohan R. The National Institutes of Health Stroke Scale (NIHSS). StrokeSciences.

NIHSS

NIHSS Score	Stroke Severity	Impacted Brain Density
21 – 42	Severe stroke	

Scores ≤ 4 = Minor Stroke

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Cohan R. The National Institutes of Health Stroke Scale (NIHSS). StrokeSciences.

ABCD^2

	ABCD2 score item	Points
A	Age ≥ 60 years	1
B	Blood pressure ≥ 140/90 mm Hg	1
C	Clinical features: • Unilateral weakness or • Speech impairment without weakness	 2 1
D	Duration of Symptoms: • ≥ 60 minutes • 10 – 59 minutes	 2 1
D	Diabetes	1

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Wardlaw J, Brazzelli M, Miranda H, et al. Health Technol Assess. 2014;18(27):Ch 4.

ABCD^2

	ABCD2 score item	Points
A	Age ≥ 60 years	1
D	Diabetes	1

Scores ≥ 4 = Increased risk of AIS

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Wardlaw J, Brazzelli M, Miranda H, et al. Health Technol Assess. 2014;18(27):Ch 4.

Secondary Prevention

Why it matters

- Risk of recurrence for AIS is ~25%
- Mortality rate for patients with recurrent stroke ~50%

Goals of secondary prevention

- Reduce risk of future TIA/CVA
- Address modifiable risk factors

Strategies

- Antiplatelet therapy
- Blood pressure control
- Lipid-lowering therapy
- Lifestyle management

Khan M et al. Cureus. 2023;15(6):e40283.
Kleindorfer DO et al. Stroke. 2021;52(7):e364–e467.

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Literature

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Landmark Trials

	IST (1997) N = 19,435	CAST (1997) N = 21,106	SOCRATES (2016) N = 13,199
Population	AIS within 48 hours	AIS within 48 hours	TIA or minor stroke not treated w/ fibrinolysis within 24 hours
Intervention	ASA vs. SubQ Heparin	ASA vs. Placebo	ASA vs. Ticagrelor
Outcomes	Death at 14 days / death or dependency at 6 months	All-cause mortality during admission	Composite outcome of stroke, MI, or death within 90 days
Results	ASA > UFH	ASA > placebo	No significant differences
Conclusion	• **ASA modestly reduced recurrent ischemic stroke and death** • UFH increased bleeding risk without overall mortality benefit	• **ASA reduced early death and recurrent ischemic stroke** • Slight increase in minor bleeding, but net clinical benefit favored aspirin	• Ticagrelor was not superior to ASA • **Slight reduction in AIS** with ticagrelor • Trend toward benefit in large artery atherosclerosis • Similar bleeding rates between groups

IST Collaborative Group. Lancet. 1997;349(9065):1569–1581.
CAST Collaborative Group. Lancet. 1997;349(9066):1641–1649.
Johnston SC et al. N Engl J Med. 2016;375(1):35–43.

Key Literature

	CHANCE (2013) *N = 5,170*		POINT (2018) *N = 4,881*		THALES (2020) *N = 11,016*	
Population	Adults ≥ 40 with NIHSS ≤ 3 or ABCD^2 ≥ 4 and symptom onset with 24 hours		Adults ≥ 18 with NIHSS ≤ 3 or ABCD^2 ≥ 4 and enrolled ≤ 12 hours from AIS/TIA		Adults ≥ 40 with NIHSS ≤ 5 or ABCD^2 ≥ 6 and symptom onset with 24 hours	
Intervention	Clopidogrel + ASA x 21 days	ASA Monotherapy	Clopidogrel + ASA x 90 days	ASA Monotherapy	Ticagrelor + ASA x 30 days	ASA Monotherapy
	Clopidogrel 300 mg x1, then 75 mg daily - PLUS - ASA 75-300 mg x1 then 75 mg daily	ASA 75-300mg x1 then 75mg daily plus placebo	Clopidogrel 600 mg x1, then 75 mg daily - PLUS - ASA 50-325 mg daily	ASA 50-325 mg daily plus placebo	Ticagrelor 180 mg x1, then 90 mg BID - PLUS - ASA 300-325 mg x1, then 75-100 mg daily	ASA 300-325 mg x1, then 75-100 mg daily plus placebo
Outcomes	• Incidence of stroke within 90 days • Bleeding events		• Stroke, MI, death within 90 days • Bleeding event		• Stroke or death within 30 days • Severe bleeding	
Results	• Stroke: 11.7% (ASA) vs. 8.2% (DAPT) [P<0.001; NNT=29] • Bleeding: 1.6% (ASA) vs. 2.3% (DAPT) [P=0.09]		• Stroke, MI, death: 5.0% (DAPT) vs. 6.5% (ASA) [P = 0.02; NNT=6] • Bleeding: 0.9% (DAPT) vs. 0.4% (ASA) [P=0.02; NNH=200]		• Stroke or death: 5.5% (DAPT) vs. 6.6% (ASA) [P=0.02; NNT=90] • Bleeding: 0.5% (DAPT) vs. 0.1% (ASA) [P=0.001; NNH=250]	
Conclusion	DAPT = More effective than ASA alone		DAPT = More effective; higher bleed risk		DAPT = More effective; higher bleed risk	

Wang Y et al. N Engl J Med. 2013;369(1):11–19.
Johnston SC, et al. N Engl J Med. 2018;379(3):215–225.
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Takeaways

CHANCE	POINT	THALES
• Supported starting DAPT (clopidogrel + ASA) within 24 hours of symptom onset • Reduced 90-day stroke incidence without increasing bleeding rates	• Validated CHANCE findings • Led to guideline updates recommending 21-day DAPT for patients with minor stroke (NIHSS < 3) or high-risk TIA (ABCD2 > 4)	• Provided alternative to clopidogrel-based DAPT • Added ticagrelor as option in guidelines for early secondary prevention

Meta-Analysis (2021): Short-term DAPT (≤30 days) with ASA + clopidogrel showed a favorable risk-benefit profile

Wang Y et al. N Engl J Med. 2013;369(1):11–19.
Johnston SC, et al. N Engl J Med. 2018;379(3):215–225.
Johnston SC et al. N Engl J Med. 2020;383(3):207-217.
Wang Y et al. JAMA. 2021;326(3):231–239.
Trifan G et al. Circulation. 2021;143(25):2441-2453.

Guideline Recommendations

ADVOCATE HEALTH

American Heart Association/American Stroke Association 2021

Secondary Prevention

- Antiplatelet therapy recommended for non-cardioembolic CVA or TIA for reduction of recurrence

Monotherapy

- **First-line**: ASA 50-325mg daily
  - Alternative: Clopidogrel 75 mg
  - Less common: ASA-dipyridamole 20/200 mg BID

DAPT

- Indication:
  - Minor strokes (NIHSS ≤ 3)
  - High-risk TIA (ABCD2 Score ≥ 4)
- Timing: Early (within 12-24 hours)
- Duration: Continued for 21-90 days

ADVOCATE HEALTH

Kleindorfer DO et al. Stroke. 2021;52(7):e364–e467.

Assessment Question #2

A 65-year-old male presents with a non-cardioembolic ischemic stroke. Initial NIHSS is 3. His symptoms began 6 hours ago and have mostly resolved. MRI confirms a small infarct in the right MCA territory. He has no history of atrial fibrillation or bleeding disorders. Following a loading dose, the neurology team asks for a recommendation for dual antiplatelet therapy. **What is an appropriate recommendation for DAPT for this patient?**

A. Ticagrelor 90 mg twice daily + aspirin 325 mg daily for 21 days
B. Clopidogrel 75 mg daily + aspirin 81 mg daily for 21 days
C. Clopidogrel 75 mg + Ticagrelor 90 mg twice daily for 21 days
D. Ticagrelor 90 mg twice daily + aspirin 81 mg daily for 7 days

Neuroendovascular Procedures

ADVOCATE HEALTH

Overview

What are neuroendovascular procedures?

- Minimally invasive techniques performed via blood vessels to treat neurological conditions
- Commonly used for stroke, aneurysms, AVMs, and vascular malformations

Types of procedures

- Mechanical Thrombectomy (for AIS)
- **Intracranial stenting (failed thrombectomy)**
- **Stent-Assisted Coiling (for aneurysms)**
- **Flow Diversion (for complex aneurysms)**
- Embolization (for AVMs, tumors)

Considerations

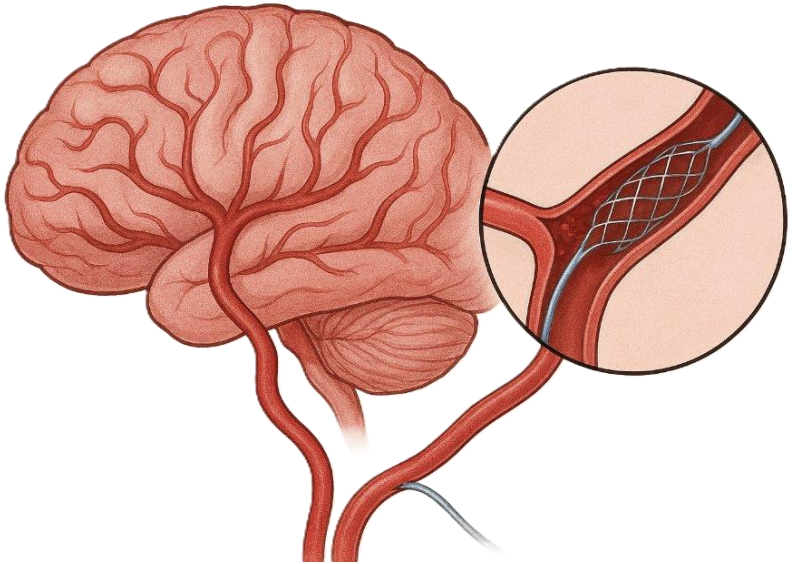
- High risk clot vs bleeding
- IV vs PO therapy

ADVOCATE HEALTH

Riina HA. Neuroendovascular surgery. J Neurosurg. 2019;131(6):1690–1701.

Intracranial Stenting

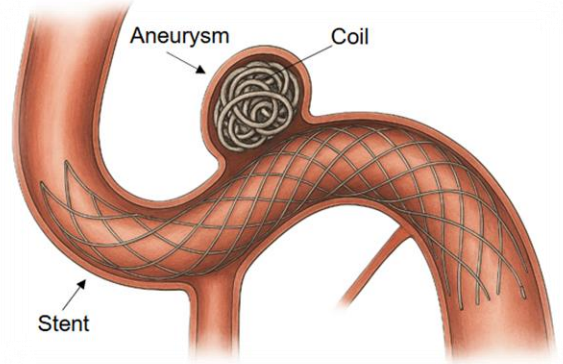
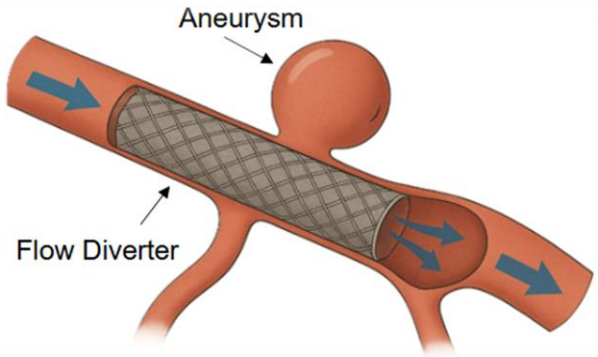
- Rescue treatment to restore blood flow in a severely narrowed or blocked artery
- Commonly used when thrombectomy fails
- Mechanism:
  - Stent placed and permanently positioned to keep vessel open
  - Improves blood flow through blocked artery



Riina HA. Neuroendovascular surgery. J Neurosurg. 2019;131(6):1690–1701.
Image: Intracranial stent [illustration]. Generated by Microsoft Copilot. November 16, 2025.

ADVOCATE HEALTH

Cerebral Aneurysm

Stent-Assisted Coiling	Flow Diversion
	
Used primarily for wide-necked aneurysms	Used primarily for large, complex aneurysms
• Stent placed across neck of aneurysm • Coils inserted into aneurysm to initiate thrombosis • Aneurysm "clots off" and shrinks over time	• Stent placed across neck of aneurysm • Blood flow directed away from aneurysm

Riina HA. Neuroendovascular surgery. J Neurosurg. 2019;131(6):1690–1701.
Image: Copilot AI. Original illustration of Stent-assisted coiling. Created November 17, 2025.
Image: Copilot AI. Original illustration of flow diversion technique. Created November 17, 2025.

ADVOCATE HEALTH

The Role of Antiplatelet Therapy

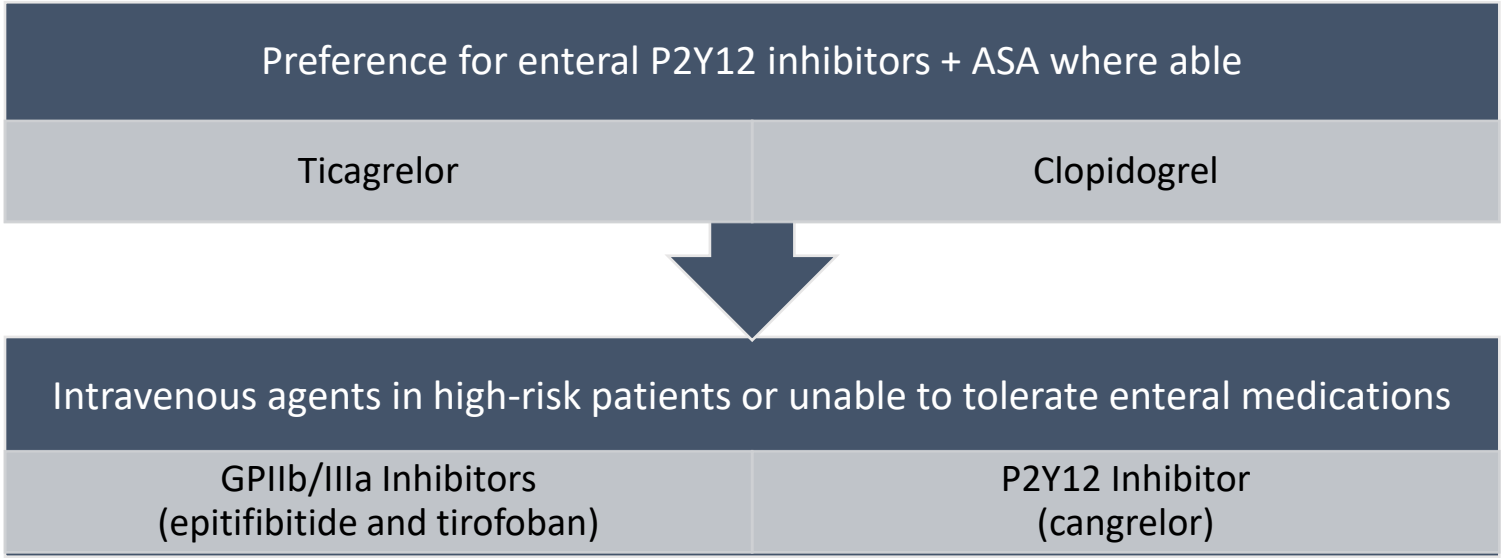
Stents can trigger platelet aggregation and thrombosis

Antiplatelet therapy can prevent thrombotic complications during and post-procedure

ADVOCATE HEALTH

Riina HA. Neuroendovascular surgery. J Neurosurg. 2019;131(6):1690–1701.

Antiplatelet Medications



Guideline Recommendations

ADVOCATE HEALTH

Society of Neurointerventional Surgery (2023)

DAPT	
Indication	Duration
Brain aneurysm treatment who have had cardiac stents placed within the last 6–12 months	Recommended during treatment
Following neurointerventional treatment for ICAD	Continued for 3 months
Symptomatic ICAD following secondary stroke treatment	Continued for 3 months
Undergoing coronary artery stenting	Initiate DAPT prior and continue for 3 months

ADVOCATE HEALTH

Schirmer CM et al. J Neurointerv Surg. 2023;15(11):1155–1164.

American Journal of Neuroradiology

2020 Expert Consensus:

- Periprocedural dual IV therapy: ASA + glycoprotein IIb/IIIa inhibitor (PO ASA = alternative where IV is unavailable)
- Transition to oral aspirin + P2Y12 inhibitor within 24 hours post-procedure

ADVOCATE HEALTH

Ospel JM et al. AJNR Am J Neuroradiol. 2020;41(10):1856–1862.

Emerging Therapy: Cangrelor

ADVOCATE HEALTH

Cortez et al. (2020)

Design	Retrospective multicenter study	
Intervention	Ischemic Group (IG)	Aneurysm Group (AG)
	Mechanical thrombectomy, stenting, angioplasty	Flow-diverters, stent-assisted coiling
	Cangrelor Protocol: Loading dose (15–30 µg/kg), maintenance infusion (2–4 µg/kg/min), followed by transition to DAPT	
Outcomes	• Periprocedural symptomatic complications (e.g., hemorrhage, thromboembolic events) • Functional outcomes (mRS 0-2)	
Results	IG: 10% had symptomatic complications; 48% had favorable outcomes at discharge AG: 13% had complications; favorable outcomes at discharge were 56% (ruptured) and 88% (unruptured)	
Conclusion	Cangrelor appears to be a safe and effective alternative for immediate antiplatelet therapy	

ADVOCATE HEALTH

Cortez et al. Neuroradiology. 2021;63(7):925–934.

Cheddad El Aouni et al. (2020)

Design	Single center, retrospective review (n = 112); Patients: 76 (Ticagrelor), 21 (Eptifibatide), 15 (Cangrelor)
Intervention	Ticagrelor (preprocedural) vs. Eptifibatide (during procedure) vs. Cangrelor (during procedure)
Outcomes	• Bleeding • Thromboembolic events, silent infarcts, aneurysm occlusion, functional outcome mRS
Results	• **Symptomatic events (N=8): 4% (Ticagrelor) vs. 14% (Eptifibatide) vs. 13% (Cangrelor) [P=0.106]** • Symptomatic events: AIS, TIA, ICH, Death, and change in mRS at 3-6 months
Conclusion	Cangrelor appears feasible and useful particularly when stenting is unplanned; larger randomized studies are needed

ADVOCATE HEALTH

Cheddad El Aouni M et al. Front Neurol. 2022;13:727026.

Cangrelor at Advocate

Indications for Use*

- Adult neurointerventional procedures unable to take enteral P2Y12
- Patients with ruptured cerebral aneurysms requiring flow diverting stents not previously on enteral P2Y12
- Patients with acute stroke requiring unplanned stenting
- Patients with planned neurointerventional procedures found to have inadequate response to enteral P2Y12

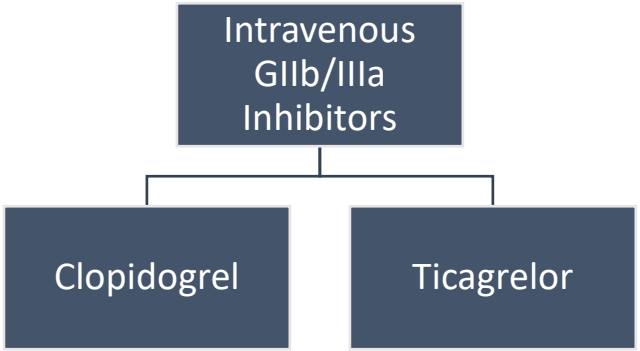
*Not FDA approved (off-label use)

ADVOCATE HEALTH

Transitioning from IV to PO Antiplatelet Therapy

ADVOCATE HEALTH

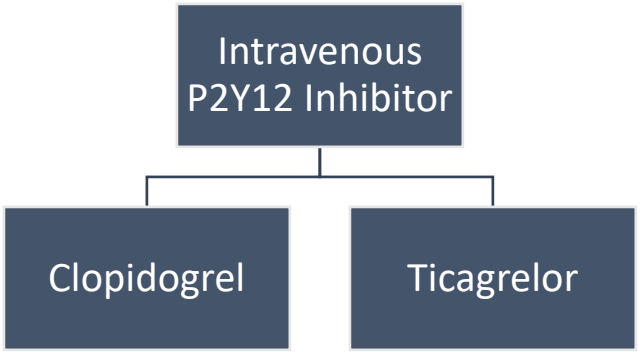
Transition Strategies – GIIb/IIIa Inhibitors



Initiate loading dose after GIIb/IIIa infusion discontinuation:	
Clopidogrel	600 mg
Ticagrelor	180 mg

Brilinta [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2016.
Plavix [package insert]. Bridgewater, NJ: Sanofi-Aventis U.S. LLC; 2019.
Effient [package insert]. Indianapolis, IN: Eli Lilly and Company; 2020.
Integrilin (eptifibatide) injection [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; Revised 2013.
Aggrastat (tirofiban hydrochloride) injection [package insert]. Somerset, NJ: Medicure Pharma, Inc.; Revised 2021.

Transition Strategies – Cangrelor



Oral P2Y12 Inhibitor	When to initiate	Dose
Clopidogrel	After discontinuation of cangrelor infusion	600 mg
Ticagrelor	At the start of cangrelor infusion up to immediately after discontinuation **Note: Infusion overlap of up to 4 hours has been reported**	180 mg

Brilinta [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2016.
Plavix [package insert]. Bridgewater, NJ: Sanofi-Aventis U.S. LLC; 2019.
Effient [package insert]. Indianapolis, IN: Eli Lilly and Company; 2020.
Kengreal [package insert]. Cary, NC: Chiesi USA, Inc.; 2023.

Transition Strategies – Cangrelor

Intravenous P2Y12 Inhibitor

Clinical Pearl: Clopidogrel **should not** be administered during cangrelor infusion because cangrelor competitively inhibits the P2Y12 receptor and prevents clopidogrel from binding and being metabolized into its active form

Oral P2Y12	Dose
Clopid	600 mg
Ticagr	180 mg

Brilinta [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2016.
Plavix [package insert]. Bridgewater, NJ: Sanofi-Aventis U.S. LLC; 2019.
Effient [package insert]. Indianapolis, IN: Eli Lilly and Company; 2020.
Kengreal [package insert]. Cary, NC: Chiesi USA, Inc.; 2023.

Monitoring

Platelet Mapping

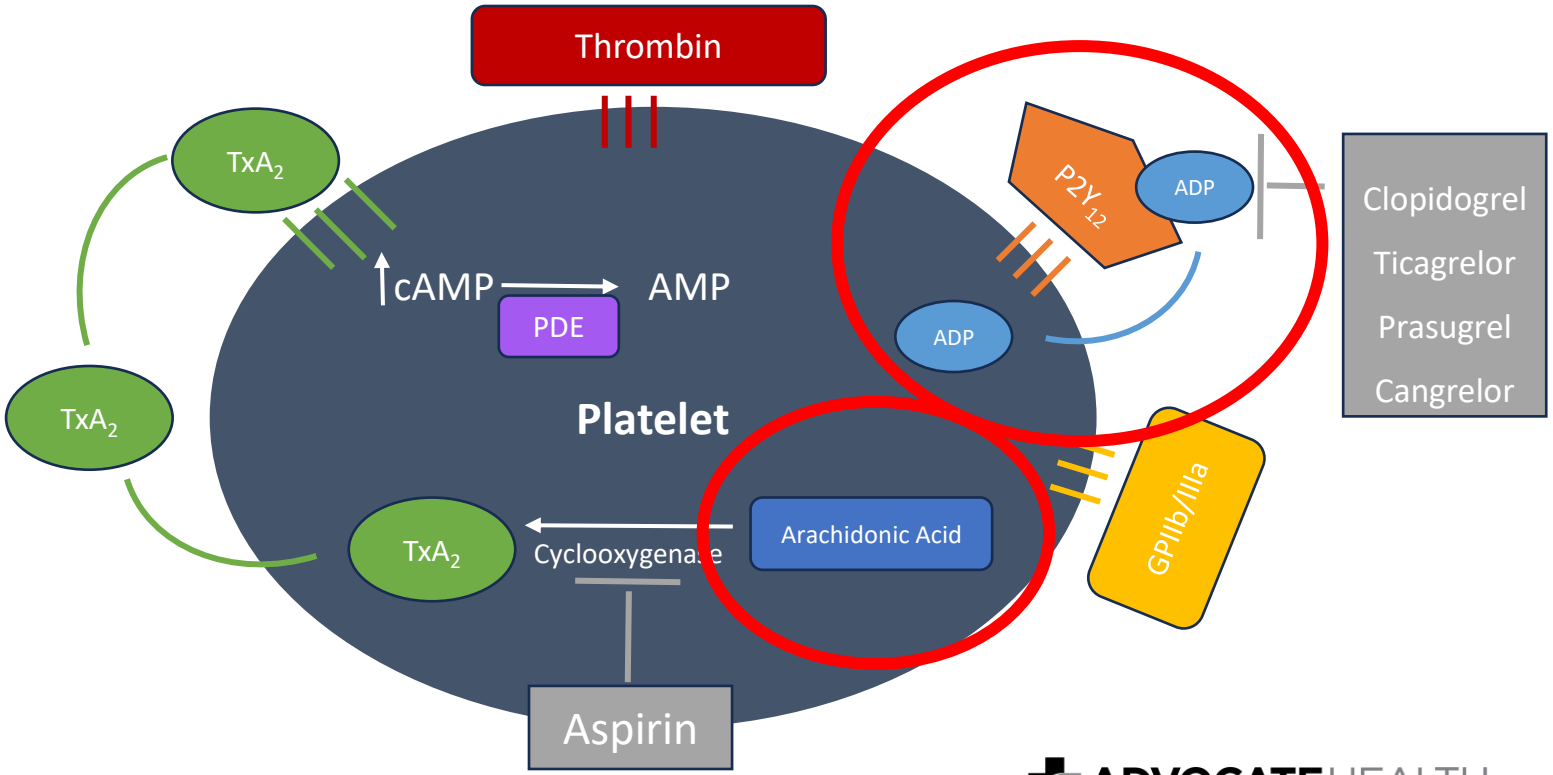
Thromboelastography with Platelet Mapping (TEG/PM)

- Measures the maximum amplitude (MA)
  - Thrombin
  - Fibrin
  - ADP
  - Arachidonic acid
- Percent inhibition calculated

ADVOCATE HEALTH

Smeds et al. J Vasc Surg. 2022;75(5):1687–1694.e4.

TEG-PM



Yun SH et al. *Biomed Res Int.* 2016:9060143.
Kashyap R, Sharma S. StatPearls. StatPearls Publishing; 2023.
Smeds et al. J Vasc Surg. 2022;75(5):1687–1694.e4.

ADVOCATE HEALTH

Verify Now

Point-of-care test

- Results within minutes

Evaluates platelet reactivity to antiplatelet drugs

Aspirin

- Aspirin reaction units (ARU) > 550 = poor response

P2Y12i

- P2Y12 reaction units (PRU) > 208 = poor response

Can use results to assess percent inhibition

ADVOCATE HEALTH

Smeds et al. J Vasc Surg. 2022;75(5):1687–1694.e4.

Clopidogrel Considerations

- Clopidogrel is a prodrug requiring activation by the CYP2C19 enzyme
- Genetic polymorphisms in CYP2C19 significantly affect clopidogrel's efficacy
- FDA Boxed Warning: Reduced effectiveness in poor metabolizers
- Historically, highest prevalence in eastern asian populations

ADVOCATE HEALTH

Plavix [package insert]. Bridgewater, NJ: Sanofi-Aventis U.S. LLC; 2019.

Genetic Polymorphisms

Metabolizer Phenotype	Genotype	US Population	Response to clopidogrel
Ultrarapid	2 increased function alleles (*17/*17)	1–5%	Normal or increased antiplatelet response
Rapid	1 increased function and 1 normal function allele (*1/*17)	20-30%	Normal or increased antiplatelet response
Normal	Absence of any tested increased function or LOF alleles (*1/*1)	35-50%	Normal antiplatelet response
Intermediate	1 LOF allele (*1/*2, *1/3, *2/17, and *3/*17)	20-30%	Reduced antiplatelet response
Poor	2 LOF alleles (*2/*2, *2/3, *3/*3)	1-5%	Significantly reduced antiplatelet response

ADVOCATE HEALTH

Klein et al. Arterioscler Thromb Vasc Biol. 2019;39(4):647–652.

CHANCE-2 (2021)

Population *N=6,412*	• Adults ≥ 40 with NIHSS ≤ 3 or ABCD2 ≥ 4 and symptom onset within 24 hours • **CYP2C19 LOF alleles** (identified via point-of-care testing)		
Intervention	**Ticagrelor + ASA**	vs	**Clopidogrel + ASA**
	Ticagrelor: 180 mg x1, followed by 90 mg BID x 90 days ASA: 75–300 mg x1, followed by 75 mg daily x 21 days		Clopidogrel group: 300 mg x1, followed by 75 mg daily x 90 days ASA: 75–300 mg x1, followed by 75 mg daily x 21 days
Outcomes	• Efficacy: Stroke (ischemic or hemorrhagic) within 90 days • Safety: moderate-to-severe bleeding event		
Results	• **Lower rate of stroke** with ticagrelor: 6.0% (ticagrelor) vs 7.6% (clopidogrel) → p = 0.008 • No significant difference in **major bleeding** events		
Conclusion	Ticagrelor + ASA is **more effective** than clopidogrel + ASA in reducing stroke risk in patients with CYP2C19 LOF alleles		

ADVOCATE HEALTH

Wang Y et al. JAMA. 2021;326(3):231–239.

Assessment Question #3

A 58-year-old male presents with AIS and undergoes stent-assisted coiling for an intracranial aneurysm. Post-procedure, DAPT (clopidogrel + ASA) is initiated. The patient's CYP2C19 genotype shows he is a poor metabolizer (CYP2C19 *2/*2). **What is the most appropriate pharmacologic intervention for optimizing this patient's antiplatelet therapy?**

A. Add cilostazol to increase platelet inhibition

B. Increase the dose of clopidogrel to 150 mg daily

C. Discontinue antiplatelet therapy and start anticoagulation instead

D. Discontinue clopidogrel and start ticagrelor

Summary

- There are many mechanisms by which medications can inhibit platelet activity
- Antiplatelet therapy is recommended for non-cardioembolic CVA or TIA for reduction of recurrence
- New evidence supports the use of antiplatelet medications for high-risk neurovascular procedures
- Genetic testing and platelet mapping help individualize antiplatelet therapy

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ADVOCATE HEALTH

Questions?

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