

Cardiovascular Drugs and Therapies

ANTIPLATELET AGENTS (Oral)

Generic Name	ASA, Acetylsalicylic Acid	Clopidogrel	Prasugrel	Ticagrelor
Trade Name	ASPIRIN, generics	PLAVIX	EFFIENT	BRILINTA
Dosage Forms	81 mg, 325 mg enteric coated and non-enteric coated tablets 80 mg chewable tablet.	75 mg tablet	10 mg tablet	90 mg tablet
Indication	ACS treatment. Secondary prevention of cardiovascular events in coronary artery disease. Secondary stroke prevention. Adjunctive therapy in revascularization procedures (CABG, PCI, carotid endarterectomy). Alternative for prevention of thromboembolic events, including stroke, in patients with atrial fibrillation who are not candidates for anticoagulants.	UA/NSTEMI managed medically or with PCI (with or without stent) or CABG. STEMI (with or without reperfusion therapy with PCI or CABG). Secondary stroke prevention. Secondary prevention of cardiovascular events in patients with ASA allergy. In lieu of ASA, as an alternative for prevention of thromboembolic events, in patients with atrial fibrillation with ≥ 1 risk factor for vascular events, unsuitable for treatment with an anticoagulant and at a low risk for bleeding.	ACS treatment in patients who are undergoing PCI.	ACS treatment in patients who are managed medically or with PCI or CABG.
Dosing	Acute MI (initial): 162-325 mg 81-325 mg once daily	300-600 mg load, followed by 75 mg daily	60 mg load, followed by 10 mg daily	180 mg load, followed by 90 mg BID (in combination with 81 mg ASA)

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<p>ACS = Acute Coronary Syndromes CABG = Coronary Artery Bypass Graft PCI = Percutaneous Coronary Intervention UA/STEMI - Unstable Angina/Non-ST Segment Elevation Myocardial Infarction</p>				
Contraindications/ Precautions	Active bleed	Active bleed, severe hepatic impairment	Active bleed, severe hepatic impairment, history of intracranial hemorrhage, stroke/TIA (CI), ≥75 years old, under 60 kg, or at high risk of bleeding, patients on oral anticoagulants	Active bleed, moderate to severe hepatic impairment, history of intracranial hemorrhage, stroke, or high risk of bleeding, co-administration with oral anticoagulants or strong CYP3A4 inhibitors Caution in patients with bradycardia, hyperuricemia and in patients likely to have dyspnea
Mechanism of Action	Inhibits COX-1 and COX-2, blocking synthesis of TXA2 and PGI2	Thienopyridine PRODRUG irreversibly binds to P2Y12 receptor on platelets	Thienopyridine PRODRUG irreversibly binds to P2Y12 receptor on platelets	Cyclopentyltriazolopyrimidine reversibly binds to P2Y12 receptor on platelets
Onset	1 hour 3-4 hours (enteric coated)	2 hours	30 minutes	30 minutes
Metabolism	Hepatic: hydrolyzed to salicylate (active metabolite)	Hepatic: hydrolysis to an inactive metabolite; also 2 CYP-dependent steps (primarily involving CYP2C19) to active metabolite	Hepatic: rapid intestinal and serum metabolism via esterase-mediated hydrolysis to a thiolactone (inactive), which is then converted, via CYP3A4 and CYP2B6 oxidation, to an active metabolite	Hepatic: via CYP3A4 to an active metabolite
Elimination	Renal	Renal/fecal	Renal/fecal	Renal/fecal
CYP Interaction	No	Yes (CYP2C19) *potential for inter-patient variability	No	Yes (moderate CYP3A4 inhibitor)

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PGP Interaction	No	No	No	Yes (weak PGP inhibitor)
Safety	GI toxicity (dose dependent), Bleeding	Bleeding (GI hemorrhage, hematoma, epistaxis), bruising, rash, pruritus	Bleeding (more major and life-threatening bleeding in TRITON-TIMI38 compared to clopidogrel)	Bleeding, dyspnea (mild, short lived), asymptomatic ventricular pauses >3s (resolving in 30 days), increase in SCr and uric acid during treatment
Clearance Considerations	Renal: Avoid if CrCl<10 mL/min Hepatic: Avoid with severe liver disease	Hepatic: caution in hepatic impairment	None	None
Unit Cost*	\$0.03/ 325 mg \$0.05/ 650 mg	\$0.66/ 75 mg	\$2.70/ 10 mg	\$1.50/ 90 mg
30 Day # Patient cost	\$0.97 (325 mg daily) \$1.60 (650 mg daily)	\$21.40 (75 mg daily)	\$88 (10 mg daily)	\$96 (90 mg bid)
ODB^a	No (81 mg) Yes (325 mg)	Yes	Limited Use Code (In combo with ASA for pts with: 1. STEMI undergoing primary PCI who have not received antiplatelet therapy prior to the catheterization 2. ACS who failed clopidogrel and ASA as defined by definite stent thrombosis or recurrent STEMI/ NSTEMI/ UA after prior revascularization via PCI	Limited Use Code (For pts with STEMI/NSTEMI/UA and ONE of the following: 1. Failure on optimal clopidogrel and ASA as defined by definite stent thrombosis or recurrent STEMI/ NSTEMI/ UA after prior revascularization via PCI 2. STEMI and undergoing revascularization via PCI 3. NSTEMI or UA with high risk angiographic features and undergoing revascularization via PCI)
MSH^b	Yes	Yes	No	No

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<i>UHN</i>^b	Yes	Yes	Yes	Yes

* List prices from the Ontario Drug Benefit (ODB) Formulary, Ontario Ministry of Health. Last Updated: 01/04/2011 Version 2.2. All prices represent the generic medication option.

30 day patient costs represented by ODB generic price + 8% markup. These prices do not include a dispensing fee, which can range from 4.99 – 11.99. Pricing is based on a typical dosing regimen.

a - ODB - indicates an item on the Ontario Drug Benefit (ODB) Formulary

b - MSH - indicates an item on the Mount Sinai Hospital Formulary; UHN - indicates an item on the University Health Network Formulary

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References

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3. Eikelboom JW, Hirsh J, Spencer FA, et al. Antiplatelet drugs: Antithrombotic therapy and prevention of thrombosis, 9th ed. American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141(2 Suppl):e89S-119S.
4. Wiviott SD, Braunwald E, McCabe CH, Montalescot G, et al. Prasugrel versus clopidogrel in patients with acute coronary syndromes (TRITON-TIMI38). N Engl J Med. 2007;357:2001-15.
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The contents of this Handbook are approved and endorsed by the UHN Cardiovascular Subcommittee of the Pharmacy and Therapeutics Committee.

1. Purpose of the Pharmacotherapy Handbook.

Notice to Healthcare Providers:

The Pharmacotherapy Handbook is intended to be used as a tool to aid in the appropriate prescribing and administration of cardiovascular formulary agents.

This information in this Handbook is intended for use by and with experienced physicians and pharmacists. The information is not intended to replace sound professional judgment in individual situations, and should be used in conjunction with other reliable sources of information. Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about Cardiovascular illness and the treatments in question.

Due to the rapidly changing nature of cardiovascular treatments and therapies, users are advised to recheck the information contained herein with the original source before applying it to patient care.

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