Cardiovascular Health Nova Scotia Guideline Update

Nova Scotia Guidelines for Acute Coronary Syndromes (Updating the 2008 Antiplatelet Section of the Guidelines)

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Non ST Elevation Acute Coronary Syndrome Guidelines: Antiplatelet Update (May 20, 2014)

2008 Recommendation		2014 Update Recommendation		Rationale for change
Immediate Treatment of Suspected Non-ST Elevation Acute Coronary Syndromes (NSTEACS)				
8	**Antiplatelet therapy**			
8a	Acetylsalicylic acid (ASA) (160-325 mg non-enteric coated oral loading dose) should be administered immediately to all patients with suspected ACS who do not have contraindications and who have not been taking ASA previously. [*Class 1, Level B*[1]; *Class 1 Level C*[2]]		Remains the same	
8b	Patients with contraindications to ASA, regardless of age, should be treated immediately with clopidogrel 300 mg oral loading dose. [*Class 1, Level A*[1]; *Class 1 Level B*[2]]		Remains the same	

Additional Immediate and Inpatient Treatment of Definite NSTEACS				
13	**Antiplatelet therapy**	**13**	**Antiplatelet therapy**	
13a	ASA (81–325 mg once daily [OD]) should be continued throughout the hospital stay in all patients with definite NSTEACS and no contraindications. The dose of ASA should be minimized (81 mg daily) in patients also taking clopidogrel or warfarin, to help reduce the risk of bleeding complications. [*Class 1 Level A*[1]]	**13a *(Updated)***	ASA (81 mg once daily [OD]) should be continued throughout the hospital stay in all patients with definite NSTEACS and no contraindications. [*Class 1 Level A*[3][4]]	Modified Recommendations (changed text)
	Clopidogrel	**(*Title updated*)**	***P2Y$_{12}$ Inhibitors***	
13b (moved to 13 c)		**13b *(Updated-formerly 13 d)***	P2Y$_{12}$ inhibitors should be administered acutely to the majority of NSTEACS patients in addition to ASA. Treatment should only be withheld if there are bleeding or other contraindications including a background history suggesting that urgent cardiac surgery is likely to be required e.g. known triple vessel coronary disease with poor left ventricular systolic function. [*AAPI Consensus 2012*[5]]	Modified Recommendation (changed text)

13b	Clopidogrel (300-mg oral loading dose) should be administered In addition to ASA as soon as possible to patients with definite NSTEACS who do not have bleeding or other contraindications. *[Class I, Level A[1]]*	**13c (*Updated-formerly13 b)***	The majority of patients with definite NSTEACS should be treated immediately with clopidogrel (300-mg oral loading dose).[6] *[Strong recommendation, high quality evidence[5]]*	Modified Recommendations (changed text)
13c	At the discretion of the on-call interventional cardiologist a higher loading dose of clopidogrel may be considered in high-risk patients being triaged immediately to the cardiac catheterization laboratory. *[Class II, Level B[2]]*	**13d (*Formerly 13c*)**	At the discretion of the on-call interventional cardiologist a higher loading dose of clopidogrel may be considered in high-risk NSTEACS patients being triaged immediately to the cardiac catheterization laboratory. *[Strong recommendation, moderate quality evidence [4]]*	Recommendation same, new number, updated reference.
13d (moved to 13 b)	Clopidogrel can increase the risk of major bleeding in patients who subsequently go on to have cardiac surgery. However, clopidogrel should not be withheld unless there are clinical features or a background history suggesting that urgent cardiac surgery is very likely to be required, e.g. patients with cardiogenic shock or who are already known to have coronary artery disease (CAD) likely to benefit more from surgical revascularization (e.g. >50% left main stem stenosis or triple vessel coronary disease with poor left		See 13 b	

	ventricular systolic function). *[Class I, Level B[1]]*			
		13e *(NEW)*	For NSTEACS patients with high clinical risk (Grace risk score > 140 [See Appendix A] or TIMI risk score 5-7), acute administration of ticagrelor (180 mg oral loading dose) can be considered instead of clopidogrel in the absence of bleeding or other contraindications.[7] [*Conditional recommendation, moderate quality evidence*[5]]	New Recommendation
13e	Clopidogrel (75 mg OD) should be continued throughout the hospital stay in patients with definite NSTEACS who do not have bleeding or other contraindications, and who are not scheduled to undergo early (within 5 days) coronary artery bypass surgery. [Class 1 Level A[1]]	**13f *(Updated)***	$P2Y_{12}$ inhibitor therapy (clopidogrel (75 mg OD)[6] or ticagrelor (90 mg BID)[7] should be continued throughout the hospital stay in the majority of patients with NSTEACS and no contraindications . [*Strong recommendation, high quality evidence*[5]]	Modified Recommendations (changed text)
	Glycoprotein IIb/IIIa receptor inhibitor therapy		***Glycoprotein IIb/IIIa receptor inhibitor therapy***	
13f (updated and changed to 13 g)	For patients with definite NSTEACS and refractory ischemia or other high-risk features, IV infusion of a small molecule platelet glycoprotein IIb/IIIa receptor inhibitor (eptifibatide or tirofiban)	***13g (Updated, formerly 13 f)***	Glycoprotein IIb/IIIa receptor inhibitor therapy is not recommended in the management of acute coronary syndrome patients except in the cardiac catheterization lab.	Modified Recommendation

	should be considered in patients without bleeding or other contraindications. *[Class I, Level B[1]]* Early triage to the cardiac catheterization laboratory should be discussed with the on-call interventional cardiologist. (See *Triage for cardiac catheterization and revascularization*, page 9.)		• For NSTEACS patients with refractory ischemia, the priority should be early triage to the cardiac catheterization laboratory. [*Consensus Nova Scotia 2014*]	
Role of CABG Surgery (antiplatelet recommendations part of this section)				
16	In NSTEACS patients found to have disease that requires coronary artery bypass grafting (CABG), surgery should be prioritized according to the same three risk categories (high, intermediate and low) as for patients undergoing PCI. The timing of CABG should be according to the timelines proposed by the CCS Access to Care Working Group. **-high risk: within 3-5 days** **-intermediate risk: within 2-3 weeks** **-low risk: within 6-8 weeks**	**16a** ***(Updated)***	In NSTEACS patients found to have disease that requires coronary artery bypass grafting (CABG), the timing of CABG should be determined by the patient's coronary anatomy and by their clinical status. [8]	Modified Recommendation (changed text) The CCS access to care working group is no longer in existence. This section has been updated to reflect current practice in Nova Scotia.
17	***Mode of Revascularization*** In general, the factors influencing the most appropriate mode of revascularization (PCI or CABG) in patients with NSTEACS should be the same as for patients with	**16b** **(*Formerly part of 17*)**	Patients with NSTEACS and cardiogenic shock and multi-vessel disease should be considered for emergent CABG and possibly left ventricular assist device implantation .[3] **Notify the**	Modified Recommendation (changed text)

	stable coronary disease. PCI is usually preferred in patients with single-and double-vessel CAD not involving the left main stem. CABG is strongly preferred in patients with left main stem disease and usually preferable in patients with multi-vessel disease, especially when associated with poor left ventricular systolic function and/or diabetes.		**Ventricular Assist Device Team by paging through locating 902-473-2220.**	
		16c (*Updated-formerly 16)*	Patients with NSTEACS and other high-risk angiographic or clinical features should undergo CABG as soon as possible prior to discharge from hospital. The timing of surgery should be determined by weighing the risk of bleeding associated with immediate surgery versus the ischemic risk associated with deferred surgery.[8] [*AAPI Consensus 2012*[5]]	Modified Recommendation (changed text)
		16d (*NEW)*	Patients with NSTEACS and without high-risk features who stabilize with initial medical therapy can potentially be discharged and return for surgery on a semi-urgent basis (within 2-4 weeks). Treadmill testing should be considered prior to discharge	New Recommendation

			to rule out easily inducible ischemia and establish the safety of deferring CABG. [Consensus 2014]	
		16e (*Formerly part of 13e)*	If clinical circumstances permit, clopidogrel or ticagrelor should be discontinued 5 days before CABG.[8] [*Strong recommendation, moderate-quality evidence;*[5]]	Modified Recommendation (changed text)
		16f (*NEW)*	$P2Y_{12}$ inhibitor therapy should be restarted at maintenance dose within 48-72 hours after CABG when deemed safe to do so by the cardiac surgical team.[9] Patients should generally be restarted on the same $P2Y_{12}$ inhibitor that was administered pre-operatively. [*Conditional recommendation, low-quality evidence* [9]]	New Recommendation The importance of restarting $P2Y_{12}$ inhibitors after CABG was not addressed in 2008 guidelines.
Pharmacologic Secondary Preventive Therapy				
19	**Antiplatelet therapy**	**19**	**Antiplatelet therapy**	
19a	ASA (81–325 mg daily) should be continued indefinitely in all NSTEACS patients without contraindications. *[Class I, Level B;*[1] *Class I, Level A*[2]*]* The dose of ASA should be minimized (81 mg daily) in patients also taking clopidogrel or warfarin to help reduce the risk of bleeding	**19a (*Updated*)**	ASA (81 mg OD) should be continued indefinitely in all NSTEACS patients without contraindications.[*Class I, Level A*[3][10]*]*	Modified Recommendation (changed text)

	complications.			
19b	Clopidogrel (75 mg OD), in addition to ASA, is recommended on discharge for all definite NSTEACS patients in the absence of contraindications. The duration of clopidogrel therapy should be tailored according to patient risk and the type of stent inserted in those who undergo PCI.[11]	**19b (*Updated*)**	Clopidogrel (75 mg OD)[6], or ticagrelor (90 mg BID)[7] in addition to ASA, is recommended on discharge for all definite NSTEACS patients in the absence of contraindications. [*Strong recommendation, moderate-quality evidence*[5]]	Modified Recommendation (changed text)
		19c (*NEW)*	Ticagrelor should generally only be administered to patients at higher risk [7] [See Appendix A] of recurrent events [*Strong recommendation, moderate-quality evidence* [5]] and continued for 12 months. [7][12]	New Recommendation
		19d (*Formerly part of 19 b*)	The duration of clopidogrel therapy should be tailored according to patient risk and to the type of stent inserted in those who undergo PCI. (See Table 1) [13] [14]	Modified Recommendation (changed text)

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2. Bassand JP, Hamm CN, Ardissino D, et al; for the Task Force for Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndromes of European Society of Cardiology. Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes. *Eur Heart J*. 2007; 28(13):1598-1600.

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10. Jneid H, Anderson JL, Wright RS, et al. 2012 ACCF/AHA focused update of the guideline for the management of patients with unstable angina/non–ST-elevation myocardial infarction (updating the 2007 guideline and replacing the 2011 focused update): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2012; 126: 875-910.

11. Love MP, Schampaert E, Cohen EA: et al; for the Canadian Association of Interventional Cardiology and the Canadian Cardiovascular society. The Canadian Association of Interventional Cardiology and the Canadian Cardiovascular Society Joint Statement on Drug-eluting Stents. *Can J Cardiol.* 2007; 23(2):121-123.

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13. *Nova Scotia Guidelines for Acute Coronary Syndromes.* Halifax, NS: Cardiovascular Health Nova Scotia; 2008.

14. Nova Scotia Department of Health and Wellness. Nova Scotia Provincial Pharmacare Programs. Request for coverage of clopidogrel. Retrieved from: http://novascotia.ca/dhw/pharmacare/documents/forms/Clopidogrel-Plavix-Form.pdf January 24, 2014.

Table 1. Recommended duration of clopidogrel therapy

Recommended clopidogrel duration	Patients not undergoing PCI	Patients undergoing PCI
3 months	Patients at low risk of recurrent events	Patients at low risk of recurrent events treated only with bare metal stents (BMS)
12 months	Patients at increased risk of recurrent events[a]	Patients receiving ≥1 drug eluting stent (DES) or who are at increased risk of recurrent events[a] regardless of stent type
>12 months	Patients at very high risk of recurrent events[b]	Some patients receiving multiple (≥3) DES or undergoing complex PCI[c] or patients at very high risk of recurrent events[b] regardless of stent type

[a] *e.g. second ACS within 12 months, complex or extensive CAD (especially if not amenable to revascularization), associated peripheral arterial or cerebrovascular disease*

[b] *e.g. patients with degenerate saphenous vein bypass grafts or who also have peripheral vascular and cerebrovascular disease*

[c] *DES implanted in left main stem or bifurcation configuration*

From: *Nova Scotia Guidelines for Acute Coronary Syndro*mes, 2008.

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Appendix A GRACE risk score

Risk Calculator for 6-Month Postdischarge Mortality After Hospitalization for Acute Coronary Syndrome

Record the points for each variable at the bottom left and sum the points to calculate the total risk score. Find the total score on the x-axis of the nomogram plot. The corresponding probability on the y-axis is the estimated probability of all-cause mortality from hospital discharge to 6 months.

Medical History

① Age in Years	Points
≤29	0
30–39	0
40–49	18
50–59	36
60–69	55
70–79	73
80–89	91
≥90	100

② History of Congestive Heart Failure	24
③ History of Myocardial Infarction	12

Findings at Initial Hospital Presentation

④ Resting Heart Rate, beats/min	Points
≤49.9	0
50–69.9	3
70–89.9	9
90–109.9	14
110–149.9	23
150–199.9	35
≥200	43

⑤ Systolic Blood Pressure, mm Hg	
≤79.9	24
80–99.9	22
100–119.9	18
120–139.9	14
140–159.9	10
160–199.9	4
≥200	0

	1
⑥ ST-Segment Depression	11

Findings During Hospitalization

⑦ Initial Serum Creatinine, mg/dL	Points
0–0.39	1
0.4–0.79	3
0.8–1.19	5
1.2–1.59	7
1.6–1.99	9
2–3.99	15
≥4	20

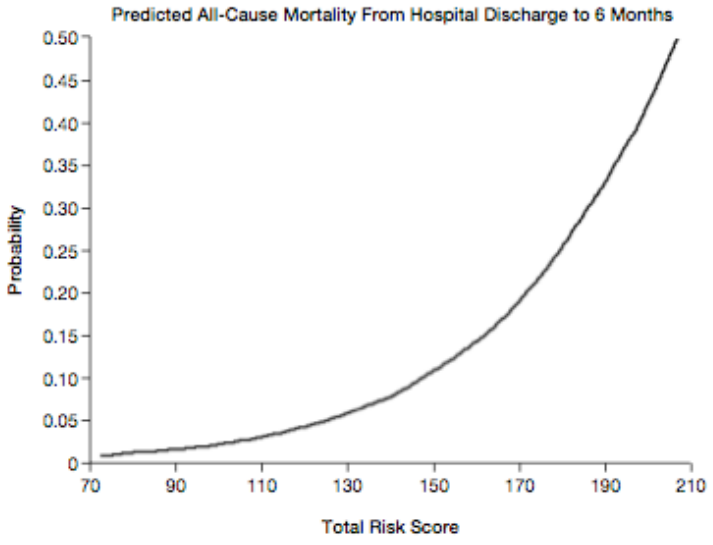
⑧ Elevated Cardiac Enzymes	15
⑨ No In-Hospital Percutaneous Coronary Invervention	14

Points

① _____
② _____
③ _____
④ _____
⑤ _____
⑥ _____
⑦ _____
⑧ _____
⑨ _____

Total Risk Score _____ (Sum of Points)

Mortality Risk _____ (From Plot)



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Appendix B: Department of Health and Wellness Pharmacare Criteria for Ticagrelor

New Exception Status Benefits

The following product was reviewed by the Canadian Drug Expert Committee (CDEC) and will be listed as exception status benefits, with the following criteria, effective **December 1, 2012.**

PRODUCT	STRENGTH	DIN	PRESCRIBER	BENEFIT STATUS	MFR
Brilinta®(ticagrelor)	90mg Tab	02368544	DNP	E (SF)	AZE
Criteria	To be taken in combination with ASA 75 mg -150mg daily[1] for patients with acute coronary syndrome (i.e. ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), or unstable angina (UA), as follows: - **STEMI** [2][3] • STEMI patients undergoing primary percutaneous coronary intervention (PCI) -**NSTEMI or UA**[2][3] • Presence of high risk features irrespective of intent to perform revascularization: -High GRACE risk score (>140) -TIMI risk score (5-7) - Second ACS within 12 months - Complex or extensive coronary artery disease e.g. diffuse three vessel disease -Definite documented cerebrovascular or peripheral vascular disease - Previous CABG **OR** -Undergoing PCI + highrisk angiographic anatomy[4] - Coverage duration 12 months				

	NOTE: **Criteria Code 30** (written on the prescription) may be used for the initial 30 day coverage period, however a written request submitted to the Pharmacare office is required to allow coverage for the remaining duration of treatment. [1] Co-administration of ticagrelor with high maintenance dose ASA (>150 mg daily) is not recommended. [2] In the PLATO study more patients on ticagrelor experienced non CABG related major bleeding than patients on clopidogrel, however, there was no difference between the rate of overall major bleeding, between patients treated with ticagrelor and those treated with clopidogrel. As with all other antiplatelet treatments the benefit/risk ratio of antithrombotic effect vs. bleeding complications should be evaluated. [3] Ticagrelor is contraindicated in patients with active pathological bleeding, in those with a history of intracranial hemorrhage and moderate to severe hepatic impairment. [4] High risk angiographic anatomy is defined as any of the following: left main stenting, high risk bifurcation stenting (i.e., two-stent techniques), long stents ≥38 mm or overlapping stents, small stents ≤2.5 mm in patients with diabetes.

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