Cardiovascular Health Nova Scotia Update to Antiplatelet Sections of *Nova Scotia Guidelines for Acute Coronary Syndromes*, 2008

Non ST Elevation Acute Coronary Syndrome Guidelines: Antiplatelet Update (May 20, 2014)	
Immediate Treatment of Suspected Non-ST Elevation Acute Coronary Syndromes (NSTEACS)	
8 Antiplatelet therapy-ASA	
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]]
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]]
Additional Immediate and Subsequent Inpatient Treatment of Definite NSTEACS	
13 Antiplatelet therapy-ASA, $P2Y_{12}$ Inhibitors and Glycoprotein IIb/IIIa receptor inhibitor therapy	
13a	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]]
13b	$P2Y_{12}$ 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]]
13c	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]*]*
13d	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]*]*
13e	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]]
13f	$P2Y_{12}$ 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]]
13g	Glycoprotein IIb/IIIa receptor inhibitor therapy is not recommended in the management of acute coronary syndrome patients except in the cardiac catheterization lab.

Non ST Elevation Acute Coronary Syndrome Guidelines: Antiplatelet Update (May 20, 2014)	
	• For NSTEACS patients with refractory ischemia, the priority should be early triage to the cardiac catheterization laboratory. [*Consensus Nova Scotia 2014*]
16 Role of CABG Surgery (and antiplatelet recommendations part of this section)	
16a	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]
16b	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 Ventricular Assist Device Team by paging through locating 902-473-2220.**
16c	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]]
16d	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 to rule out easily inducible ischemia and establish the safety of deferring CABG. [Consensus 2014]
16e	If clinical circumstances permit, clopidogrel or ticagrelor should be discontinued 5 days before CABG.[8] [*Strong recommendation, moderate-quality evidence;*[5]]
16f	$P2Y_{12}$ 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]]
Pharmacologic Secondary Preventive Therapy	
19 Antiplatelet therapy-ASA, $P2Y_{12}$ Inhibitors	
19a	ASA (81 mg OD) should be continued indefinitely in all NSTEACS patients without contraindications.[*Class I, Level A*[3][10]]
19b	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]]
19c	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][11]
19d	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) [12] [13]

References:

1. Anderson JL, Adams CD, Antman EM, et al. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction) developed in collaboration with the American College of Emergency Physicians, the Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation and the Society for Academic Emergency Medicine. *J Am Coll Cardiol*. 2007; 50(7):e1-e57.

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.

3. Hamm CW, Bassand JP, Agewall S, et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J.* 2011; 32: 2999-3054.

4. Mehta SR, Tanguay JF, Eikelboom JW, et al. Double-dose versus standard-dose clopidogrel and high-dose versus low-dose aspirin in individuals undergoing percutaneous coronary intervention for acute coronary syndromes (CURRENT-OASIS 7): a randomised factorial trial. *Lancet*. 2010; 376: 1233–1243.

5. Love MP, Bergin P, Paddock v, et al. Atlantic Canadian Guidelines for the acute use of oral antiplatelet therapy in patients with acute coronary syndromes: Atlantic Cardiovascular Society. April 18, 2012. Available at http://ac-society.org/cms/node/45. Accessed July 23, 2013.

6. Yusuf S, Zhao F, Mehta SR, et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med.* 2001; 345: 494-502.

7. Wallentin L, Becker RC, Budaj A, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med.* 2009; 361: 1045-57.

8. Fitchett D, Eikelboom, J, Fremes, et al. Dual antiplatelet therapy in patients requiring urgent coronary artery bypass grafting surgery: A position of the Canadian Cardiovascular society. *Can J Cardiol.* 2009; 25(12): 683-689.

9. Tanguay JF, Bell AD, Ackman ML, et al. Focused 2012 Update of the Canadian Cardiovascular Society Guidelines for the use of antiplatelet therapy. *Can J Cardiol*. 2013; 29: 1334-1345.

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. Nova Scotia Department of Health and Wellness. Pharmacare news (physician's edition). December 2012; vol 12-11. Retrieved from : http://novascotia.ca/dhw/pharmacare/pharmacare-news-bulletins.asp, January 6, 2014.

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

13. 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.

CardioVascular HEALTH NOVA SCOTIA

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

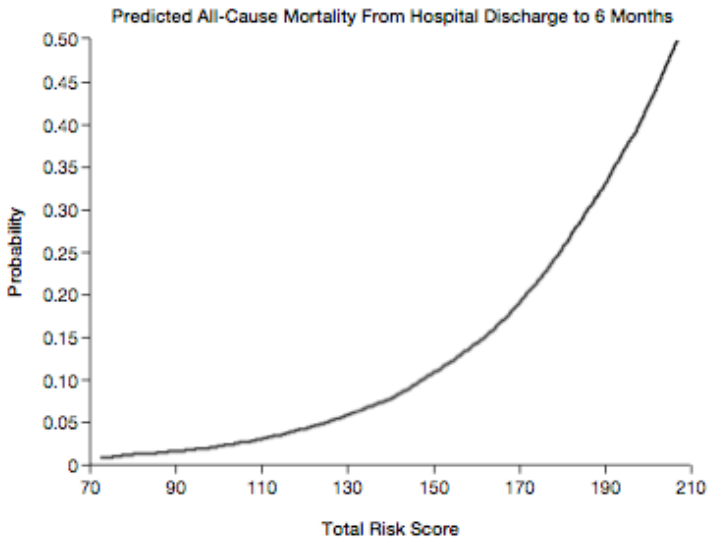
⑨ No In-Hospital Percutaneous Coronary Invervention — 14

Points

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

Total Risk Score _____ (Sum of Points)

Mortality Risk _____ (From Plot)



Eagle KA, Lim MJ, Dabbous OH, et al. A validated prediction model for all forms of acute coronary syndrome: estimating the risk of 6 month post discharge death in an international registry. *JAMA* 2004; 291: 2727-2733.

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.

Excerpt from Nova Scotia Department of Health and Wellness. Pharmacare news (physician's edition). December 2012; vol 12-11. Retrieved from : http://novascotia.ca/dhw/pharmacare/pharmacare-news-bulletins.asp, January 6, 2014.