TARGET AUDIENCE: All Canadian health care professionals.

OBJECTIVE:
To review the use of antiplatelet agents and oral anticoagulants for the secondary prevention of ischemic cardiac disease in patients presenting with non-ST elevation acute coronary syndrome.

ABBREVIATIONS:

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACS</td>
<td>acute coronary syndrome</td>
</tr>
<tr>
<td>ADP</td>
<td>adenosine diphosphate</td>
</tr>
<tr>
<td>ASA</td>
<td>acetyl salicylic acid</td>
</tr>
<tr>
<td>CABG</td>
<td>coronary artery bypass graft</td>
</tr>
<tr>
<td>DAPT</td>
<td>dual antiplatelet therapy</td>
</tr>
<tr>
<td>NSTEACS</td>
<td>non ST-elevation acute coronary syndrome</td>
</tr>
<tr>
<td>MI</td>
<td>myocardial infarction</td>
</tr>
<tr>
<td>PCI</td>
<td>percutaneous coronary intervention</td>
</tr>
<tr>
<td>TIA</td>
<td>transient ischemic attack</td>
</tr>
</tbody>
</table>

BACKGROUND:
New approaches to antithrombotic therapies have become available to treat patients with non-ST elevation acute coronary syndrome (NSTEACS). This document summarizes to possible treatment combinations according to the method of revascularization (percutaneous coronary intervention [PCI] versus coronary artery bypass graft [CABG] versus medical therapy).

MECHANISM OF ACTION:
Acetyl salicylic acid (ASA) is an antiplatelet agent acting via the inhibition of thromboxane production. Clopidogrel (Plavix™), ticagrelor (Brilinta™) and prasugrel (Effient™) act by blocking platelet adenosine diphosphate (ADP) receptors of subtype P2Y12. Ticagrelor is a reversible blocker whereas prasugrel and clopidogrel are irreversible. Rivaroxaban is an anticoagulant acting via direct inhibition of the coagulation factor Xa.
**INDICATION:**
See treatment algorithm below for details. The initial decisions should be based on whether the patient was treated with PCI, CABG or with medical therapy only.

**NSTE-ACS**

- **PCI**
  - ASA 81mg indefinitely (or clopidogrel 75mg if intolerant to ASA)
  - Ticagrelor 90mg twice daily for 12 months
  - Prasugrel 10mg daily for 12 months
  - **Or**
  - Clopidogrel 75mg daily for 12 months if not eligible to ticagrelor or prasugrel

- **CABG**
- **Medical**

**Anti-platelet therapy**

- Note 1: Prasugrel should be avoided if prior stroke or TIA.
- Note 2: In patients older than 75 years of age or with a body weight < 60 Kg, a dose of 5mg daily can be considered

**Continuation of ticagrelor, prasugrel or clopidogrel for more than 12 months can be considered in patients with high thrombosis risk and low bleeding risk**

**The triple association of rivaroxaban, clopidogrel and ASA should not be considered over the use of dual antiplatelet therapy for the secondary prevention of acute coronary syndrome**

**The association of an oral anticoagulation (including vitamin K antagonist) with a dual antiplatelet therapy can be appropriate in selected patients, such as those with atrial fibrillation and mechanical heart valve**

**Dabigatran and apixaban should not be used in combination with antiplatelet therapy for the secondary prevention of ACS**

© 2013 Thrombosis Canada.
**AGENTS AND DOSING:**

a) **ASA**: 81 mg daily indefinitely in all patients unless allergic or intolerant, in which case it should be replaced by clopidogrel.

b) **Clopidogrel**: 75 mg daily. A maintenance dose of 150 mg daily can be considered for the first 6 days in patients treated with PCI.

c) **Ticagrelor**: 90 mg twice daily.

d) **Prasugrel**: 10 mg daily. A dose of 5 mg daily can be considered in patients ≥75 years of age or with a body weight < 60 kg. Prasugrel is currently not recommended for patients with prior stroke or transient ischemic attack (TIA).

e) **Rivaroxaban** is not approved by Health Canada for the secondary prevention of ischemic cardiac disease post-acute coronary syndrome (ACS).

**MONITORING:**

No laboratory monitoring is required for patients taking aspirin, clopidogrel, ticagrelor or prasugrel.

**ADVERSE EFFECTS:**

Ticagrelor has been associated with ventricular pauses, bradycardia and short-term mild to moderate dyspnea at the start of treatment. Dyspnea has not been associated with adverse outcomes.

**PERI-PROCEDURAL MANAGEMENT:**

**Non-CABG**

The use of antiplatelet agents is known to increase the risk of bleeding and transfusion requirements associated with surgery and other invasive procedures. However, discontinuation of dual antiplatelet therapy (DAPT) within 12 months of drug-eluting stent implantation or within 6 weeks of bare-metal stent implantation is associated with a large increased risk of major adverse cardiovascular events and stent thrombosis. For this reason, procedures associated with significant bleeding risk should be delayed beyond these time frames if possible, and, if not possible, done with the patient remaining on therapy. If prasugrel can be stopped safely, it should be discontinued at least 7 days prior to surgery. For ticagrelor and clopidogrel, stopping 5 days prior to a procedure is sufficient.

**CABG**

In stable patients with ACS without critical coronary anatomy who are clinically stabilized, clopidogrel and ticagrelor should be withheld for 5 days and prasugrel for 7 days before CABG. In
patients with ACS, dual antiplatelet therapy should be restarted at maintenance dose within 48-72 hours post-operatively when deemed safe by the cardiac surgical team.

**SPECIAL CONSIDERATIONS:**

The P2Y12 receptor inhibitors (clopidogrel, ticagrelor or prasugrel) initially selected at hospital discharge should not be switched to another P2Y12 inhibitor unless there is a compelling clinical reason to do so. Such reasons may include but are not limited to stent thrombosis, allergy intolerance and bleeding.

The P2Y12 receptor inhibitors (clopidogrel, ticagrelor or prasugrel) can be continued for more than 12 months in patients with a high thrombosis risk and a low bleeding risk. In such patients, consultation with a specialist is always preferable before discontinuing the medication.

In P2Y12 inhibitor-naive patients, it is recommended that the coronary anatomy has been defined and the PCI planned before prasugrel is administered over clopidogrel or ticagrelor.

Triple therapy with rivaroxaban, clopidogrel and ASA is more effective than the dual combination of clopidogrel and ASA on the composite outcome of cardiovascular death, myocardial infarction and stroke. However, this triple therapy has been associated with a 4-fold increase in the risk of major bleeding and with a 3-fold increase in the risk of intracranial hemorrhage. For this reason, the combination is not recommended over DAPT with ticagrelor or prasugrel plus ASA.

**PEDIATRICS**

In general, the etiology of myocardial infarction (MI) in children is different from that of adults. There are no studies confirming safety and efficacy of antithrombotic therapy in children. However, there are case reports using different therapies (anticoagulant, antiplatelet and thrombolytic) in acute MI in children. Consultation with a pediatric hematologist is recommended.

**REFERENCES**


Please note that the information contained herein is not to be interpreted as an alternative to medical advice from your doctor or other professional healthcare provider. If you have any specific questions about any medical matter, you should consult your doctor or other professional healthcare providers, and as such you should never delay seeking medical advice, disregard medical advice or discontinue medical treatment because of the information contained herein.