



### OBJECTIVE:

To provide information on the use of acetylsalicylic acid in the prevention of vascular thromboembolic events.

### BACKGROUND:

Acetylsalicylic acid (ASA) is well-established in the management of acute myocardial infarction and in the secondary prevention of cardiovascular disease among both men and women, based on large randomized trials. ASA may also be considered in selected patients for prevention of recurrent venous thromboembolism (VTE) and for prevention of VTE following joint arthroplasty. In addition, in select patients, ASA may be considered for primary prevention of cardiovascular events. The net benefit of ASA use depends on weighing the anticipated reduction in cardiovascular events against the increased risk of gastrointestinal and intracranial bleeding.

### MECHANISM OF ACTION OF ASA:

ASA irreversibly inhibits platelet aggregation by inhibiting thromboxane A<sub>2</sub> (TxA<sub>2</sub>) synthesis.

### INDICATIONS FOR ASA<sup>1</sup>:

Antiplatelet therapy with ASA is recommended for all patients with the following, unless contraindicated:

- 1) **Cardiac:** For all patients with symptomatic coronary artery disease (CAD), including:
  - i. History of acute coronary syndrome (ACS) with and without ST segment elevation
  - ii. Chronic stable angina
  - iii. Following percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG)
    - a. In combination with clopidogrel (elective PCI), prasugrel, or ticagrelor (PCI for ACS) while the patient remains at very high risk for subsequent coronary events (usually one year) [see **Clinical Guide: Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease**]
    - b. In combination with clopidogrel and oral anticoagulation in patients with an indication for anticoagulation, for the shortest possible duration, while the patient is at extremely high risk for subsequent coronary events [see **Clinical Guide: Anticoagulation in Patients Requiring Antiplatelet Therapy**].
    - c. May be considered in combination with rivaroxaban 2.5 mg twice daily for patients with coronary artery disease or peripheral artery disease for prevention of stroke,

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<sup>1</sup>Unless otherwise indicated, ASA refers to enteric-coated ASA

myocardial infarction and cardiovascular death, and for the prevention of acute limb ischemia and mortality [see **Clinical Guide: Rivaroxaban (Xarelto®)**]

iv. Prosthetic heart valves:

- a. ASA 81 mg daily is recommended in addition to vitamin K antagonist (VKA) in selected high-risk patients with a mechanical valve prosthesis [see **Clinical Guide: Mechanical and Bioprosthetic Heart Valves: Anticoagulant Therapy**]
- b. ASA 81 mg daily is reasonable in all patients with a bioprosthetic aortic or mitral valve who are not taking an oral anticoagulant [see **Clinical Guide: Mechanical and Bioprosthetic Heart Valves: Anticoagulant Therapy**]

**2) Cerebrovascular:**

- i. For patients with history of non-cardioembolic ischemic stroke or transient ischemic attack (TIA) [see **Clinical Guide: Stroke: Secondary Prevention**]
- ii. Following carotid endarterectomy

**3) Peripheral arterial disease (PAD):**

- i. Symptomatic patients with or without a history of vascular intervention [see **Clinical Guide: Peripheral Arterial Disease**]

**4) Primary prevention of cardiovascular morbidity and mortality:** The use of ASA is not recommended for **primary prevention** of a first vascular event.

- i. This recommendation pertains to individuals with or without vascular risk factors who have **not** had a vascular event.
- ii. The net benefit of ASA in individuals with diabetes or with asymptomatic atherosclerosis (i.e. asymptomatic coronary or carotid atherosclerosis) is uncertain.

**5) Secondary prevention of recurrent VTE:**

- i. In patients at high risk of VTE recurrence following completion of initial anticoagulant therapy for a minimum of 3-6 months, ASA may be considered as an option to decrease recurrent VTE only if extended anticoagulant therapy is not acceptable to the patient. [see **Clinical Guide: Venous Thromboembolism: Duration of Treatment**]

**6) Thromboprophylaxis following joint arthroplasty:**

- i. For patients not at high risk of VTE, consideration can be given to rivaroxaban 10 mg orally per day until post-operative day 5, followed by ASA 81 mg daily for an additional 9 days following total knee arthroplasty or for 30 days after total hip arthroplasty. [see **Clinical Guide: Thromboprophylaxis: Orthopedic Surgery**]

**7) Prevention of Preeclampsia in Pregnancy**

- i. For patients at moderate to high risk of preeclampsia

**DOSING OF ASA:**

- The usual antiplatelet dose of ASA is 81 mg daily. Higher doses are not associated with any evidence of increased efficacy or bleeding risk, but with lower treatment adherence.
- A single initial dose of 162 mg chewed or crushed is recommended in patients suffering an ACS event, and then indefinite therapy with 81 mg daily.

- A single initial dose of 325 mg chewed or crushed is recommended in patients prior to angioplasty (if not already receiving chronic daily ASA).
- An initial dose of 81 mg once daily should be utilized in patients suffering a TIA or ischemic stroke of noncardiac origin.

**Note:** For patients with a history of, or at high risk of, gastrointestinal bleeding, consider co-administration of a gastroprotective agent (i.e. proton pump inhibitor [PPI], H<sub>2</sub> antagonist) or using an alternate antiplatelet agent such as clopidogrel.

### **ADVERSE EFFECTS OF ASA:**

- Bruising and other minor bleeding is very common with use of ASA
- Dyspepsia
- The most common serious adverse effect of ASA is bleeding into the gastrointestinal tract (which is dose-related)
- Allergic reactions, aspirin-induced asthma (may be severe)

### **PERI-PROCEDURAL MANAGEMENT FOR PATIENTS TAKING ASA:**

Patients receiving ASA and:

- 1) Undergoing an invasive diagnostic test,
  - i. associated with a low risk of bleeding, should continue ASA without interruption.
  - ii. associated with a high risk of bleeding, should discontinue ASA 7 to 10 days prior to the procedure.
  - iii. Patients with coronary stents deserve special consideration, and consultation with a specialist is advised.
- 2) Undergoing arthrocentesis, continue ASA through the time of the procedure.
- 3) Undergoing a minor surgery, dental, eye, or skin procedure, generally continue ASA around the time of the procedure.
- 4) Undergoing elective major non-cardiac surgery, should discontinue ASA 7 to 10 days prior to the procedure except in those undergoing carotid endarterectomy, or with recent coronary artery stenting (consultation with a specialist is advised). When ASA is interrupted, it should be resumed when the risk of bleeding related to surgery has passed, between 8 to 10 days after major noncardiac surgery (See Clinical Guide: Perioperative Management of Antiplatelet Therapy).
- 5) Undergoing coronary artery bypass grafting (CABG), should continue ASA (See **Clinical Guide: Perioperative Management of Antiplatelet Therapy**).

### **SPECIAL CONSIDERATIONS:**

- 1) **Concomitant use of therapeutic doses of anticoagulants and ASA** is discouraged and should only be considered in patients with an indication for anticoagulation who are at relatively low bleeding risk AND have one of the following indications:

- i. Very recent ACS and/or PCI +/- coronary artery stent (short duration of ASA in combination with clopidogrel and an anticoagulant, after which dual pathway with clopidogrel and an anticoagulant alone is preferred)
- ii. High risk prosthetic heart valve (e.g. older generation valve or mitral valve replacement with atrial fibrillation, left ventricle (LV) dysfunction or previous systemic embolus on therapeutic anticoagulation)
- iii. Proven TIA/ischemic stroke while on therapeutic doses of anticoagulation alone

In **most** other patients taking ASA, if anticoagulation is started, the ASA should be stopped.

- 2) Patients taking ASA for vascular protection should avoid the concomitant use of **NSAIDs**. If a patient taking low-dose ASA for vascular protection requires an anti-inflammatory agent, specific cyclooxygenase-2 inhibitors should be chosen over traditional NSAIDs.
- 3) ASA should be avoided or used with caution in patients with **asthma or nasal polyps**, in those at **high risk of bleeding** or with recent major bleeding, and in patients with **severe thrombocytopenia** or with familial or **acquired bleeding disorders**.

#### **PEDIATRICS:**

When possible, pediatricians with expertise in thromboembolism should be involved when ASA is being considered for antiplatelet therapy. When this is not possible, a combination of a neonatologist/pediatrician and an adult hematologist, supported by consultation with an experienced pediatric hematologist, is recommended.

#### **OTHER RELEVANT THROMBOSIS CANADA CLINICAL GUIDES:**

- Mechanical and Bioprosthetic Heart Valves: Anticoagulant Therapy
- Perioperative Management of Antiplatelet Therapy
- Peripheral Arterial Disease
- Stroke: Secondary Prevention
- Thromboprophylaxis: Orthopedic Surgery
- Venous Thromboembolism: Duration of Treatment

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