

## 1.ACETYL SALICYLIC ACID

**Class:** Antiplatelet Agent

**Indications:**

**Labeled Indications:**

Treatment of mild-to-moderate pain, inflammation, and fever; prevention and treatment of acute coronary syndromes (ST-elevation MI, non-ST-elevation MI, unstable angina), acute ischemic stroke, and transient ischemic episodes; management of rheumatoid arthritis, rheumatic fever, osteoarthritis; adjunctive therapy in revascularization procedures (coronary artery bypass graft [CABG], percutaneous transluminal coronary angioplasty [PTCA], carotid endarterectomy), stent implantation

**Unlabeled:**

Low doses have been used in the prevention of pre-eclampsia, complications associated with autoimmune disorders such as lupus or antiphospholipid syndrome; colorectal cancer; Kawasaki disease; alternative therapy for prevention of thromboembolism associated with atrial fibrillation in patients not candidates for warfarin; pericarditis including pericarditis associated with MI; thromboprophylaxis for aortic valve repair, Blalock-Taussig shunt placement, carotid artery stenosis, coronary artery disease, Fontan surgery, peripheral arterial occlusive disease, peripheral artery percutaneous transluminal angioplasty, peripheral artery bypass graft surgery, prosthetic valves, ventricular assist device (VAD) placement

**Available dosage form in the hospital:** ACETYL SALICYLIC ACID 325MG +ALUMINIUM +MAGNESIUM HYDROXIDE TAB.100MG EC TAB. 500MG TAB.

**Dosage:**

Note: For most cardiovascular uses, typical maintenance dosing of aspirin is 81 mg once daily.

**-Acute coronary syndrome (ST-segment elevation myocardial infarction [STEMI], unstable angina (UA)/non-ST-segment elevation myocardial infarction [NSTEMI]):**

Oral: Initial: 162-325 mg given on presentation (patient should chew nonenteric-coated aspirin especially if not taking before presentation); for patients unable to take oral, may use rectal suppository (300-600 mg [Antman, 2004; Maalouf, 2009]). Maintenance (secondary prevention): 75-162 mg once daily indefinitely (Anderson, 2007) or 81-325 mg once daily; 81 mg once daily preferred (O'Gara, 2013). Note: When aspirin is used with ticagrelor, the recommended maintenance dose of aspirin is 81 mg/day (Jneid, 2012; O'Gara, 2013).

**-UA/NSTEMI: Concomitant antiplatelet therapy (Jneid, 2012):**

-If invasive strategy chosen: Aspirin is recommended in combination with either clopidogrel, ticagrelor, (or prasugrel if at the time of PCI) or an I.V. GP IIb/IIIa inhibitor (if given before PCI, eptifibatid and tirofiban are preferred agents).

-If noninvasive strategy chosen: Aspirin is recommended in combination with clopidogrel or ticagrelor.

**-Analgesic and antipyretic:**

Oral: 325-650 mg every 4-6 hours up to 4 g/day  
Rectal: 300-600 mg every 4-6 hours up to 4 g/day

**-Anti-inflammatory:**

Oral: Initial: 2.4-3.6 g/day in divided doses; usual maintenance: 3.6-5.4 g/day; monitor serum concentrations.

**-Aortic valve repair (unlabeled use):** Oral: 50-100 mg once daily (Guyatt, 2012)

**-Atrial fibrillation (in patients not candidates for oral anticoagulation or at low risk of ischemic stroke) (unlabeled use):** Oral: 75-325 mg once daily (Furie, 2011; Fuster, 2006).

Note: Combination therapy with clopidogrel has been suggested over aspirin alone for those patients who are unsuitable for or choose not to take oral anticoagulant for reasons other than concerns for bleeding (Guyatt, 2012).

As an alternative to adjusted-dose warfarin in patients with atrial fibrillation and mitral stenosis: 75-325 mg once daily with (preferred) or without clopidogrel (Guyatt, 2012)

**-CABG:** Oral: 100-325 mg once daily initiated either preoperatively or within 6 hours postoperatively; continue indefinitely (Hillis, 2011)

**-Carotid artery stenosis (unlabeled use):** Oral: 75-100 mg once daily. Note: When symptomatic (including recent carotid endarterectomy), the use of clopidogrel or aspirin/extended-release dipyridamole has been suggested over aspirin alone (Guyatt, 2012).

**-Coronary artery disease (CAD), established:** Oral: 75-100 mg once daily (Guyatt, 2012)

**-PCI:** Oral:

-Non-emergent PCI: Preprocedure: 81-325 mg (325 mg [nonenteric coated] in aspirin-naive patients) starting at least 2 hours (preferably 24 hours) before procedure.

Postprocedure: 81 mg once daily continued indefinitely (in combination with a P2Y<sub>12</sub> inhibitor [eg, clopidogrel, prasugrel, ticagrelor] up to 12 months) (Levine, 2011)

-Primary PCI: Preprocedure: 162-325 mg as early as possible prior to procedure; 325 mg preferred followed by a maintenance dose of 81 mg once daily even when a stent is deployed (O'Gara, 2013).

Alternatively, in patients who have undergone elective PCI with either bare metal or drug-eluting stent placement: The American College of Chest Physicians recommends the use of 75-325 mg once daily (in combination with clopidogrel) for 1 month (BMS) or 3-6 months (dependent upon DES type) followed by 75-100 mg once daily (in combination with clopidogrel) for up to 12 months. For patients who underwent PCI but did not have stent placement, 75-325 mg once daily (in combination with clopidogrel) for 1 month is recommended. In either case, single antiplatelet therapy (either aspirin or clopidogrel) is recommended indefinitely (Guyatt, 2012).

**-Pericarditis (unlabeled use):** Oral: Initial: 2.4-3.6 g daily in 3-4 divided doses; usual maintenance: 3.6-5.4 g daily in divided doses; gradually taper over 2- to 3-week period as appropriate (Imazio, 2004; Imazio, 2009). In the treatment of postmyocardial infarction pericarditis, an initial dose of 650 mg 4 times daily increased to 975 mg 4 times daily if necessary (after 24 hours) has been used (Berman, 1981; O'Gara, 2013).

**-Peripheral arterial disease (unlabeled use):** Oral: 75-100 mg once daily (Guyatt, 2012) or 75-325 mg once daily; may use in conjunction with clopidogrel in those who are not at an increased risk of bleeding but are of high cardiovascular risk. Note: These recommendations also pertain to those with intermittent claudication or critical limb ischemia, prior lower extremity revascularization, or prior amputation for lower extremity ischemia (Rooke, 2011).

**-Peripheral artery percutaneous transluminal angioplasty (with or without stenting) or peripheral artery bypass graft surgery, postprocedure (unlabeled use):** Oral: 75-100 mg once daily (Guyatt, 2012). Note: For below-knee bypass graft surgery with prosthetic grafts, combine with clopidogrel (Guyatt, 2012).

**-Pre-eclampsia prevention (women at risk) (unlabeled use):** Oral: 75-100 mg once daily starting in the second trimester (Guyatt, 2012)

**-Primary prevention:** Oral:

-American College of Cardiology/American Heart Association: Prevention of myocardial infarction: 75-162 mg once daily. Note: Patients are most likely to benefit if their 10-year coronary heart disease risk is  $\geq 6\%$  (Antman, 2004).

-American College of Chest Physicians: Prevention of myocardial infarction and stroke: Select individuals  $\geq 50$  years of age (without symptomatic cardiovascular disease): 75-100 mg once daily (Guyatt, 2012; Grade 2B, weak recommendation)

**-Prosthetic heart valve: Oral:**

Bioprosthetic aortic valve (patient in normal sinus rhythm) (unlabeled use): 50-100 mg once daily. Note: If mitral bioprosthetic valve, oral anticoagulation with warfarin (instead of aspirin) is recommended for the first 3 months postoperatively, followed by aspirin alone (Guyatt, 2012).

**-Mechanical aortic or mitral valve (unlabeled use):**

-Low risk of bleeding: 50-100 mg once daily (in combination with warfarin) (Guyatt, 2012)

-History of thromboembolism while receiving oral anticoagulants: 75-100 mg once daily (in combination with warfarin) (Furie, 2011)

-Transcatheter aortic bioprosthetic valve (unlabeled use): 50-100 mg once daily (in combination with clopidogrel) (Guyatt, 2012)

**-Stroke/TIA: Oral:**

-Acute ischemic stroke/TIA: Initial: 160-325 mg within 48 hours of stroke/TIA onset, followed by 75-100 mg once daily (Guyatt, 2012). The AHA/ASA recommends an initial dose of 325 mg within 24-48 hours after stroke; do not administer aspirin within 24 hours after administration of alteplase (Jauch, 2013).

-Cardioembolic, secondary prevention (oral anticoagulation unsuitable): 75-100 mg once daily (in combination with clopidogrel) (Guyatt, 2012)

-Cryptogenic with patent foramen ovale (PFO) or atrial septal aneurysm: 50-100 mg once daily (Guyatt, 2012)

-Noncardioembolic, secondary prevention: 75-325 mg once daily (Smith, 2011) or 75-100 mg once daily (Guyatt, 2012). Note: Combination aspirin/extended release dipyridamole or clopidogrel is preferred over aspirin alone (Guyatt, 2012).

-Women at high risk, primary prevention: 81 mg once daily or 100 mg every other day (Goldstein, 2010)

**Renal Impairment:**

-Cl<sub>cr</sub> <10 mL/minute: Avoid use.

-Dialyzable (50% to 100%)

**Hepatic Impairment:**

Avoid use in severe liver disease.

**Common side effect:**

Upper gastrointestinal (UGI) events (eg, symptomatic or complicated ulcers): Low-dose aspirin for cardioprotective effects is associated with a two- to fourfold increase in UGI events. The risks of these events increase with increasing aspirin dose; during the chronic phase of aspirin dosing, doses >81 mg are not recommended unless indicated (Bhatt, 2008).

- Salicylate sensitivity: Patients with sensitivity to tartrazine dyes, nasal polyps, and asthma may have an increased risk of salicylate sensitivity.
- Tinnitus: Discontinue use if tinnitus or impaired hearing occurs.

**Pregnancy Considerations:**

Salicylates have been noted to cross the placenta and enter fetal circulation. Adverse effects reported in the fetus include mortality, intrauterine growth retardation, salicylate intoxication, bleeding abnormalities, and neonatal acidosis. Use of aspirin close to delivery may cause premature closure of the ductus arteriosus. Adverse effects reported in the mother include anemia, hemorrhage, prolonged gestation, and prolonged labor (Østensen, 1998). Aspirin has been used for the prevention of pre-eclampsia; however, the ACOG currently recommends that it not be used in low-risk women (ACOG, 2002). Low-dose aspirin is used to treat complications resulting from antiphospholipid syndrome in pregnancy (either primary or secondary to SLE) (Carp, 2004; Guyatt, 2012; Tincani, 2003). In general, low doses during pregnancy needed for the treatment of certain medical conditions have not been shown to cause fetal harm, however, discontinuing therapy prior to delivery is recommended (Østensen, 2006). Use of safer agents for routine management of pain or headache should be considered.