**ASPIRIN**
(acetylsalicylic acid)

### Therapeutics

#### Brands
- Bayer Aspirin, Ecotrin, Halfprin, Heartline, Empirin, Alka-Seltzer, Asprimox, Magnaprin, Bufferin, Ascriptin, Aspergum, ZORprin

#### Generic?
Yes

#### Class
- Antiplatelet agent, NSAID, anti-inflammatory

#### Commonly Prescribed For
(FDA approved in bold)
- To reduce risk of myocardial infarction (MI), transient ischemic attack (TIA), or ischemic stroke (IS) due to fibrin platelet emboli
- Angina (unstable or stable)
- Revascularization procedures: coronary artery bypass graft (CABG), angioplasty, and carotid endarterectomy
- Analgesic for mild–moderate pain for relief of headache, muscle aches and pains, toothache, arthritis, menstrual pain
- Fever
- Rheumatic conditions, such as spondyloarthritis, pleurisy associated with systemic lupus erythematosus
- Reducing risk of stroke in high-risk populations, such as nonvalvular atrial fibrillation, when anticoagulants are contraindicated
- Toxemia of pregnancy

#### How the Drug Works
- By acetylatoring cyclo-oxygenase-1 (COX-1), aspirin inhibits synthesis of thromboxane A2, a prostaglandin derivative that is a potent vasoconstrictor and inducer of platelet aggregation
- Irreversibly inhibits platelet aggregation even at low doses
- At larger doses, interferes with COX-1 and COX-2 in arterial walls, interfering with prostaglandin production. Counteracts fever by vasodilation of peripheral vessels, allowing dissipation of excess heat
- Aspirin may also provide analgesia via other (prostaglandin – independent) mechanisms

#### How Long until It Works
- A single dose of aspirin inhibits platelet aggregation for the life of the platelet (7–10 days). In pain, effective within 1–2 hours

### If It Works
- Continue to use for prevention of MI, IS, or TIA and for pain

### If It Doesn’t Work
- Only reduces risk of MI or IS. Warfarin is superior for cardiogenic stroke. Control all IS risk factors such as smoking, hyperlipidemia, and hypertension. For acute events, admit patients for treatment and diagnostic testing. Consider screening for aspirin resistance

#### Best Augmenting Combos for Partial Response or Treatment Resistance
- In stroke prevention, there is no proven benefit to using clopidogrel in combination with aspirin. In clinical trials, there was no significant difference in IS prevention, and AEs (mostly bleeding) were significantly higher
- Consider changing to dipyridamole–aspirin combination for IS prevention
- Pain: In acute migraine, add caffeine and/or acetaminophen, antiemetics, or triptans

#### Tests
- None required

### Adverse Effects (AEs)

#### How Drug Causes AEs
- Antiplatelet effects increase bleeding risk

#### Notable AEs
- Stomach pain, heartburn, nausea, and vomiting

#### Life-Threatening or Dangerous AEs
- GI, intracranial, or intraocular bleeding. Risk increases with higher doses

#### Weight Gain
- Unusual

#### Sedation
- Unusual
**What to Do about AEs**
- For significant GI or intracranial bleeding stop drug

**Best Augmenting Agents for AEs**
- Proton pump inhibitors reduce risk of GI bleeding

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**DOSING AND USE**

**Usual Dose Range**
- MI, TIA, or IS prevention: 50–1300 mg/day
- Pain: 325–1000 mg per dose

**Dosage Forms**
- Chewable tablets: 81 mg
- Tablets: 325 mg, 500 mg
- Gum tablets: 227.5 mg
- Enteric-coated: 81 mg, 165 mg, 325 mg, 500 mg, 650 mg
- Extended- or controlled-release: 650 mg, 800 mg
- Suppositories: 120 mg, 200 mg, 300 mg, 600 mg

**How to Dose**
- Give once daily for prevention of vascular events. For pain, take 325–1000 mg every 4–6 hours as needed up to a maximum of 4000 mg per 24 hours. With extended-release, take 650–1300 mg every 8 hours as needed, maximum 3900 mg/day

**Dosing Tips**
- Taking with food decreases absorption and reduces GI AEs

**Overdose**
- Early: produces respiratory alkalosis, resulting in hyperpnea and tachypnea. Nausea and vomiting, hypokalemia, tinnitus, dehydration, hyperthermia, thrombocytopenia, and easy bruising
- Late: coma, pulmonary edema, respiratory failure, renal failure, hypoglycemia.Mixed respiratory alkalosis and metabolic acidosis may occur. Treat with emesis or gastric lavage and monitor salicylate levels and electrolytes. In severe cases, hemodialysis is effective

**Long-Term Use**
- Safe for long-term use

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**Habit Forming**
- No

**How to Stop**
- No need to taper

**Pharmacokinetics**
- Aspirin half-life is 20 minutes. Over 99% protein binding. Hepatic metabolism and renal excretion

**Drug Interactions**
- Alcohol increases risk of GI ulceration and may prolong bleeding time
- Urinary acidifiers (ascorbic acid, methionine) decrease secretion and increase drug effect
- Antiacids and urinary alkalinizers may decrease drug effect
- Carbonic anhydrase inhibitors may increase risk of salicylate intoxication, and aspirin may displace acetazolamide from protein binding sites leading to toxicity
- Activated charcoal decreases aspirin absorption and effect
- Corticosteroids may increase clearance and decrease serum levels
- Use with heparin or oral anticoagulants has an additive effect and can increase bleeding risks
- Aspirin may cause unexpected hypotension after treatment with nitroglycerin
- Aspirin use with NSAIDs may decrease NSAID serum levels and increases risk of GI AEs
- May displace valproic acid from binding sites and increase pharmacologic effects
- May blunt effectiveness of beta-blockers and angiotensin-converting enzyme inhibitors
- May decrease effect of loop diuretics and spironolactone
- Increases drug levels of methotrexate
- Reduces the uricosuric effects of probenecid and sulfipyrazone
- Large doses (>2 g/day) may produce hypoglycemia when used with insulin or sulfonylurias in diabetes

**Other Warnings/Precautions**
- The use of aspirin or other salicylates in children or teenagers with influenza or chickenpox may be associated with Reye’s syndrome. Symptoms include vomiting and lethargy that may progress to delirium or coma
- Tinnitus or dizziness are symptoms of aspirin toxicity
Aspirin intolerance is not rare, especially in asthmatics. Symptoms include bronchospasm, angioedema, severe rhinitis, or shock. It is possible to desensitize patients in a hospital setting, but they will need to maintain daily aspirin to avoid recurrence.

### Do Not Use
- Known hypersensitivity to salicylates, acute asthma or hay fever, severe anemia or blood coagulation defects, children or teenagers with chickenpox or influenza symptoms

## Special Populations

### Renal Impairment
- Use with caution in chronic renal insufficiency. May temporarily worsen renal function

### Hepatic Impairment
- Use with caution in patients with significant disease including those with hypoprothrombinemia or vitamin K deficiency. High doses can cause hepatotoxicity

### Cardiac Impairment
- No known effects

### Elderly
- No known effects

### Children and Adolescents
- Not recommended for prevention of IS or TIA in children younger than age 12

### Pregnancy
- Category D: crosses the placenta and is associated with anemia, ante- or postpartum hemorrhage, prolonged gestation and labor, and constriction of ductus arteriosus. Do not use, especially in 3rd trimester

### Breast-Feeding
- Excreted in breast milk in low concentration. Risk to infants and their platelet function is unknown

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**The Art of Pain Pharmacology**

### Potential Advantages
- Effective and inexpensive medication for prevention of both IS and other vascular diseases, such as MI

### Potential Disadvantages
- May be less effective in some patients for IS prevention. Risk of aspirin resistance

### Primary Target Symptoms
- Prevention of the neurological complications that result from IS
- Headache or other pain

### Pearls
- First-line drug for secondary prevention of IS, along with clopidogrel or extended-release dipyridimole plus aspirin
- May be less effective than clopidogrel for patients with peripheral vascular disease
- Aspirin 325 mg in combination with clopidogrel increased bleeding risk in clinical trials and did not prove superior for IS prevention
- Stop aspirin 1 week before any surgical procedure, given its effect on platelet function
- Standard coagulation tests do not accurately reflect the effect of aspirin. Bleeding times are often unreliable. Multiple assays are now available to measure the effect of a given dose of aspirin on platelet function. These include standard platelet aggregometry and tests measuring the effect on COX-1 by measuring thromboxane metabolites
- Increasing aspirin dose may overcome resistance, but patients may develop aspirin resistance over time on a stable dose
- At this point, there are no guidelines to suggest when to screen for aspirin resistance. It is unclear if aspirin failures should simply increase their dose, change to another agent, or take another agent in combination with aspirin
- Antiplatelets may be equally effective compared to anticoagulants for prevention of recurrent arterial dissection
- When compared to warfarin for the prevention of stroke due to symptomatic intracranial disease, aspirin 1300 mg was equal to warfarin and associated with lower rates of MI or major hemorrhage
- In pain/migraine, combination products containing caffeine and/or acetaminophen may be more effective. Adding antiemetics such as metoclopramide is useful in migraine


