PRODUCT MONOGRAPH

ASPIRIN®
acetylsalicylic acid tablets USP
325mg

ASPIRIN® Extra Strength
acetylsalicylic acid tablets USP
500mg

ASPIRIN® 81mg
acetylsalicylic acid delayed release tablets USP
81mg

ASPIRIN® 81mg Quick Chews
acetylsalicylic acid tablets USP
81mg

Acetylsalicylic acid, USP

Analgesic, anti-inflammatory, antipyretic and

Platelet aggregation inhibitor

BAYER INC.
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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Oral	*ASPIRIN 81mg* acetylsalicylic acid delayed release tablets, USP, 81mg	Lactose
Oral	*ASPIRIN 81 mg Quick Chews* acetylsalicylic acid tablets, USP, 81mg	Not applicable
Oral	*ASPIRIN* acetylsalicylic acid tablets, USP, 325mg	Not applicable
Oral	*ASPIRIN Extra Strength* acetylsalicylic acid tablets, USP, 500mg	Not applicable

For a complete listing see Dosage Forms, Composition and Packaging section.

INDICATIONS AND CLINICAL USE

ASPIRIN® (acetylsalicylic acid, ASA) is indicated for the relief of pain, fever and inflammation of a variety of conditions such as influenza, common cold, low back and neck pain, dysmenorrhea, headache, toothache, sprains and strains, fractures, myositis, neuralgia, synovitis, arthritis, bursitis, burns, injuries, following surgical and dental procedures. ASPIRIN® Extra Strength is also indicated for relief of migraine pain and the associated symptoms of photophobia (sensitivity to light) and phonophobia (sensitivity to sound), and improves overall quality of life.

ASPIRIN® is also indicated for the following uses, based on its platelet aggregation inhibitory properties:

- for reducing the risk of vascular mortality in patients with a suspected acute myocardial infarction;	ASPIRIN® 81mg DIN 02237726 ASPIRIN® 81mg Quick Chews DIN02289970; ASPIRIN® Tablets 325mg DIN02150328
- for reducing the risk of a **first** non-fatal myocardial infarction in individuals deemed to be at sufficient risk of such an event by their physician. - There is no evidence for a reduction in the risk of **first** fatal myocardial infarction. - ASPIRIN® does not reduce the risk of either cardiovascular mortality or **first** strokes, fatal or non-fatal. The decrease in the risk of **first** non-fatal myocardial infarction must be assessed against a much smaller but not insignificant increase in the risk of haemorrhagic stroke as well as gastrointestinal bleeding.	ASPIRIN® 81mg DIN 02237726 ASPIRIN® 81mg Quick Chews DIN 02289970 ASPIRIN® Tablets 325mg DIN02150328;
- for reducing the risk of morbidity and death in patients with unstable angina, with previous myocardial infarction	ASPIRIN® 81mg DIN 02237726 ASPIRIN® 81mg Quick Chews DIN 02289970; ASPIRIN® Tablets 325mg DIN02150328;
- for reducing the risk of transient ischemic attacks (TIA) and for secondary prevention of atherothrombotic cerebral infarction;	ASPIRIN® 81mg DIN 02237726 ASPIRIN® 81mg Quick Chews DIN02289970 ASPIRIN® Tablets 325mg DIN02150328;
- for prophylaxis of venous thromboembolism after total hip replacement;	ASPIRIN® Tablets 325mg DIN02150328;
- for reducing the adhesive properties of platelets in patients following carotid endarterectomy to prevent recurrence of TIA and in hemodialysis	ASPIRIN® Tablets 325mg

patients with a silicone rubber arteriovenous cannula. DIN02150328;

CONTRAINDICATIONS

- Patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container. For a complete listing, see Dosage Forms, Composition and Packaging section of the product monograph.

- Patients with a history of asthma induced by the administration of salicylates or substances with a similar action, notably non-steroidal anti-inflammatory drugs

- Combination with methotrexate at doses of 15mg/week or more

- Last trimester of pregnancy

- Hemorrhagic diathesis
- Active peptic ulcer

WARNINGS AND PRECAUTIONS

General

ASA is one of the most frequent causes of accidental poisonings in toddlers and infants. Tablets should be kept well out of the reach of children.

Salicylates should be administered cautiously to patients with:

- Hypersensitivity to anti-inflammatory or antirheumatic drugs or other allergens
- impaired renal function or hepatic function
- a history of chronic or recurrent gastrointestinal ulcerations and bleeds
- a history of bleeding tendencies, significant anemia and/or hypothrombinemia

Hypersensitivity

ASPIRIN may precipitate bronchospasm and induce asthma attacks or other hypersensitivity reactions. Risk factors are present bronchial asthma, hay fever, nasal polyps, or chronic respiratory disease. This applies also for patients showing allergic reactions (e.g. cutaneous reactions, itching, urticaria) to other substances.

Hematologic

Due to effect on platelet aggregation, ASPIRIN may be associated with an increased risk of bleeding. Caution is necessary when salicylates and anticoagulants are prescribed concurrently, as salicylates can depress the concentration of prothrombin in the plasma.

Peri-Operative Considerations

Due to its inhibitory effect on platelet aggregation ASPIRIN may lead to an increased bleeding tendency during and after surgical operations (including minor surgeries, e.g. dental

extractions).

Special Populations

Pregnant Women:

Use of salicylates in the first 3 months of pregnancy has been associated in several epidemiological studies with an elevated risk of malformations (cleft palate, heart malformations). After normal therapeutic doses this risk seems to be low: a prospective study with exposure of about 32,000 mother-child pairs has not yielded any association with the risk of malformations.

Salicylates should be taken during pregnancy only after strict risk-benefit evaluation.

In the last 3 months of pregnancy administration of salicylates in high doses (>300mg/day) can lead to prolongation of the gestation period, premature closure of the arterial duct and inhibition of uterine contractions. An increased hemorrhagic tendency has been observed in both mother and child.

Administration of ASPIRIN in high doses (> 300 mg/d) shortly before birth can lead to intracranial hemorrhages, particularly in premature babies.

Nursing Women:

ASPIRIN and its metabolites pass into breast milk in small quantities. Since no adverse effects on the infant have been observed after occasional use, interruption of breast-feeding is usually unnecessary. However, on regular use or on intake of high doses, breast feeding should be discontinued early.

Pediatrics

A possible association between Reye's syndrome and the use of salicylates has been suggested but not established. Reye's syndrome has also occurred in many patients not exposed to salicylates. ASPIRIN should not be used in children and teenagers for viral infections with or without fever without consulting a physician. In certain viral illnesses, especially influenza A, influenza B and varicella, there is a risk of Reye’s syndrome, a very rare but possibly life-threatening illness requiring immediate medical action. The risk may be increased when ASPIRIN is given concomitantly; however, no causal relationship has been proven. Should persistent vomiting occur with such diseases; this may be a sign of Reye’s syndrome.

Low Uric Acid Excretion:
At low doses, ASPIRIN reduces excretion of uric acid. This can trigger gout in patients who already tend to have low uric acid excretion.

Monitoring and Laboratory Tests

Salicylates can produce changes in thyroid function tests.

Isolated cases of liver function disturbances (transaminases increase) have been described.

ADVERSE REACTIONS

Many adverse reactions due to ASPIRIN ingestion are dose-related. The following is a list of adverse reactions that have been reported in the literature and from both clinical and post-marketing experience.

Gastrointestinal (the frequency and severity of these adverse effects are dose-related): nausea, vomiting, diarrhea, gastrointestinal bleeding and/or ulceration, dyspepsia, heartburn, hematemesis, melena.

Ear: tinnitus, vertigo, hearing loss.

Hematologic: leukopenia, thrombocytopenia, purpura, anemia.

Dermatologic and hypersensitivity: urticaria, angioedema, pruritus, skin eruptions, asthma, anaphylaxis, Quincke edema.

Miscellaneous: mental confusion, drowsiness, sweating, thirst.

DRUG INTERACTIONS

Overview

ASPIRIN should be used with caution with other products that have anticoagulation or antiplatelet effects, as these effects may be potentiated. Drugs that bind to protein binding sites should also be used cautiously since ASPIRIN may displace drugs from their protein binding site.

Drug-Drug Interactions

Methotrexate, used at 15mg/week or less: Salicylates may retard the elimination of methotrexate by decreasing renal clearance of methotrexate, displacing methotrexate from protein binding sites, and thereby increasing its hematological toxicity.

Anti-coagulants, e.g. warfarin, heparin: Caution is necessary when salicylates and anticoagulants are prescribed concurrently, as salicylates can depress the concentration of prothrombin in the plasma.

Oral hypoglycemics, e.g. insulin, sulfonylureas: Large doses of salicylates have a hypoglycemic action and may enhance the effect of oral hypoglycemic agents. Diabetics receiving concurrent salicylate and hypoglycemic therapy should be monitored closely: reduction of the sulfonylurea hypoglycemic drug dosage may be necessary.

Diuretics: Sodium excretion produced by spironolactone may be decreased by salicylate administration.

Uricosuric Agents: Salicylates in large doses are uricosuric agents; smaller amounts may depress uric acid clearance and thus decrease the uricosuric effects of other drugs.

Valproic Acid: Salicylates may alter valproic acid (VPA) metabolism and may displace VPA from protein binding sites, possibly intensifying the effects of VPA. Caution is recommended when VPA is administered concomitantly with salicylates.

Glucocorticoids (systemic), except hydrocortisone used as replacement therapy in Addison's disease: Decreased blood salicylate levels during corticosteroid treatment and risk of salicylate overdose after this treatment is stopped via increased elimination of salicylates by corticosteroids.

Angiotensin Converting Enzyme (ACE) Inhibitors: The hyponatremic and hypotensive effects of ACE inhibitors *may* be diminished by the concomitant administration of ASPIRIN due to its indirect effect on the renin-angiotensin conversion pathway. The potential interaction may be related to the dose of ASPIRIN (3g/day or more).

Digoxin: Plasma concentrations of digoxin are increased due to a decrease in renal excretion.

ASPIRIN and other NSAIDs:

The use of other non-steroidal anti-inflammatory drugs with salicylates at high doses (≥ 3g/day) may increase the risk of ulcers and gastrointestinal bleeding due to a synergistic effect.

Ibuprofen: Ibuprofen can interfere with the anti-platelet effect of low dose acetylsalicylic acid (81-325 mg per day). Long-term daily use of ibuprofen may render ASA less effective when used for cardioprotection and stroke prevention. To minimize this interaction, regular users of ibuprofen and of low-dose, immediate-release ASA should take the ibuprofen at least one hour after and 11 hours before the daily ASA dose. The use of delayed-release (e.g. enteric-coated) ASA is not recommended when using ibuprofen regularly. Healthcare professionals should advise consumers and patients regarding the appropriate concomitant use of ibuprofen and ASA.

Drug-Food Interactions

Interactions with food have not been established.

Drug-Herb Interactions

Interactions with herb have not been established.

Drug-Laboratory Interactions

Salicylates can produce changes in thyroid function tests.

Drug-Lifestyle Interactions

Patients taking ASPIRIN daily are at an increased risk of developing gastrointestinal bleeding following the ingestion of alcohol.

DOSAGE AND ADMINISTRATION

ASPIRIN tablets should preferably be taken after meals, with plenty of liquid.

Dosing Considerations

Please see below for specific dosing instructions for each indication.

Recommended Dose and Dosage Adjustment

Analgesic and antipyretic:

Adults: 1-2 tablets (325 mg to 650 mg) orally every 4 hours.
Children under 12: 10 to 15 mg/kg every 6 hours, not to exceed a total daily dose of 2.4 g

Migraine pain and associated symptoms:
Adults:1000 mg (2 x 500mg tablets) at onset of pain or symptoms.
Children: Clinical studies to support migraine relief in children have not been conducted with acetylsalicylic acid.

Anti-inflammatory:
Adults:3 tablets (975 mg) 4 to 6 times a day, up to 30 tablets daily, may be required for optimal anti-inflammatory effect. A blood level between 15 and 30 mg per 100 mL is in the desirable therapeutic range.
Children: 60 to 125 mg/kg daily in 4 to 6 divided doses.
Platelet aggregation inhibitor:

Suspected Acute Myocardial Infarction: An initial dose of at least 160 -162.5 mg chewed or crushed to ensure rapid absorption as soon as a myocardial infarction is suspected. The same dose should be given as maintenance over the next 30 days. After 30 days, consider further therapy based on dosage and administration for prevention of recurrent MI (see Prior Myocardial Infarction).

Prevention of a first non-fatal myocardial infarction: 80 - 325 mg once daily, according to the individual needs of the patient, as determined by the physician.

Prior Myocardial Infarction or Unstable Angina Pectoris: 80 - 325 mg daily according to the individual needs of the patient, as determined by the physician.

Transient Ischemic Attack and Secondary Prevention of Atherothrombotic Cerebral Infarction: 80 - 325 mg daily according to the individual needs of the patient, as determined by the physician.

Prophylaxis of Venous Thromboembolism after total hip replacement: 650 mg twice a day (1,300 mg daily), started 1 day before surgery and continued for 14 days.

OVERDOSAGE

Mild Overdose or Early Poisoning - burning in the mouth, lethargy, nausea, vomiting, tinnitus, sweating, thrist, tachycardia or dizziness.

Moderate Overdose - all of the symptoms from mild overdose plus tachypnea, hyperpyrexia, sweating, dehydration, loss of coordination, restlessness, mental confusion.

Severe Overdose - all of the symptoms from moderate overdose plus hypotension, hallucinations, stupor, hypoglycemia, convulsions, cerebral edema, oliguria, renal failure, cardiovascular failure, coma, hemorrhage, metabolic acidosis, respiratory alkalosis and/or failure.

Emergency Management:
1- Immediate transfer to hospital and maintain cardiovascular and respiratory support.

2- Gastric lavage, administration of activated charcoal,
3- Check of acid-base balance and correct if necessary.
4- Alkaline diuresis so as to obtain urine pH between 7.5 and 8 should be considered when plasma salicylate concentration is greater than 500mg/L (3.6 mmol/L) in adults or 300mg/L (2.2 mmol/L) in children
5- Hemodialysis should be considered in severe poisoning 800mg/L (5.8 mmol/L) in adults and 700mg/L (5.0 mmol/L) in children, as renal elimination of salicylates may be slow due to the presence of acidic urine and renal failure. Hemodialysis should also be considered if the patient is experiencing severe systemic metabolic acidosis (arterial pH < 7.2), acute renal failure, pulmonary edema or CNS symptoms such as: drowsiness, agitation, coma or convulsions.
6- Fluid losses should be replaced with hypotonic solution (e.g. half saline) and supplemented with glucose 50 to 100g/L.
7- Symptomatic treatment.

Fatal Dose: varies from 10 to 30g of ASA. However, (in one case) 130g of ASA was ingested without fatal outcome.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

ASPIRIN interferes with the production of prostaglandins in various organs and tissues through acetylation of the enzyme cyclo-oxygenase. Prostaglandins are themselves powerful irritants and produce headaches and pain on injection in man. Prostaglandins also appear to sensitize pain receptors to other noxious substances such as histamine and bradykinin. By preventing the synthesis and release of prostaglandins in inflammation, ASPIRIN may avert the sensitization of pain receptors.

The antipyretic activity of ASPIRIN is due to its ability to interfere with the production of prostaglandin E_1 in the brain. Prostaglandin E_1 is one of the most powerful pyretic agents known.

The inhibition of platelet aggregation by ASPIRIN is due to its ability to interfere with the production of thromboxane A_2 within the platelet. Thromboxane A_2 is, largely, responsible for the aggregating properties of platelets.

In vitro studies have shown that ASPIRIN enhances the activity of the Nitric oxide (NO)-cGMP system and heme oxygenase-1 (HO-1) by acting on endothelial NO synthase site.

Pharmacokinetics

Absorption:
When ASPIRIN is taken orally, it is rapidly absorbed from the stomach and proximal small intestine. The gastric mucosa is permeable to the non-ionized form of acetylsalicylic acid, which passes through the stomach wall by a passive diffusion process.

Optimum absorption of salicylate in the human stomach occurs in the pH range of 2.15 to 4.10. Absorption in the small intestine occurs at a significantly faster rate than in the stomach. After an oral dose of 0.65 g ASPIRIN, the plasma acetylsalicylate concentration in man usually reaches a level between 0.6 and 1.0 mg % in 20 minutes after ingestion and drops to 0.2 mg %

within an hour. Within the same period of time, half or more of the ingested dose is hydrolyzed to salicylic acid by esterases in the gastrointestinal mucosa and the liver, the total plasma salicylate concentration reaching a peak between one or two hours after ingestion, averaging between 3 and 7 mg %. Many factors influence the speed of absorption of ASPIRIN in a particular individual at a given time; tablet disintegration, solubility, particle size, gastric emptying time, psychological state, physical condition, nature and quantity of gastric contents, etc., all affect absorption.

Distribution:
Distribution of salicylate throughout most body fluids and tissues proceeds at a rapid rate after absorption. Aside from the plasma itself, fluids which have been found to contain substantial amounts of salicylate after oral ingestion include spinal, peritoneal and synovial fluids, saliva and milk. Tissues containing high concentrations of the drug are the kidney, liver, heart and lungs. Concentrations in the brain are usually low, and are minimal in feces, bile and sweat.

The drug readily crosses the placental barrier. At clinical concentrations, from 50% to 90% of the salicylate is bound to plasma proteins especially albumin, while acetylsalicylic acid itself is bound to only a very limited extent. However, ASPIRIN has the capacity of acetylating various proteins, hormones, DNA, platelets and hemoglobin, which at least partly explains its wide-ranging pharmacological actions.

Metabolism:
The liver appears to be the principal site for salicylate metabolism, although other tissues may also be involved. The three chief metabolic products of ASPIRIN or salicylic acid are salicyluric acid, the ether or phenolic glucuronide and the ester or acyl glucuronide. A small fraction is also converted to gentisic acid and other hydroxybenzoic acids. The half-life of ASPIRIN in the circulation is from 13 to 19 minutes so that the blood level drops quickly after absorption is complete. However, the half_life of the salicylate ranges between 3.5 and 4.5 hours, which means that 50% of the ingested dose leaves the circulation within that time.
Excretion:
Excretion of salicylates occurs principally via the kidney, through a combination of glomerular filtration and tubular excretion, in the form of free salicylic acid, salicyluric acid, as well as phenolic and acyl glucuronides. Salicylate can be detected in the urine shortly after its ingestion but the full dose requires up to 48 hours for complete elimination. The rate of excretion of free salicylate is extremely variable, reported recovery rates in human urine ranging from 10% to 85%, depending largely on urinary pH. In general, it can be stated that acid urine facilitates reabsorption of salicylate by renal tubules, while alkaline urine promotes excretion of the drug.

With the administration of 325mg, elimination of ASPIRIN is linear following a first order kinetics. At high concentrations, elimination half life increases.

Special Populations and Conditions:
Absorption and clearance of salicylates are not affected by gender or age.

STORAGE AND STABILITY

ASPIRIN® Tablets: Store between 15-30^{o}C.
ASPIRIN® Caplets: Store between 15-30^{o}C.
ASPIRIN® Extra-Strength Tablets: Store between 15-25^{o}C.
ASPIRIN® 81mg (delayed release tablet): Store between 15-30^{o}C.

ASPIRIN® 81mg Quick Chews: Store between 15-30^{o}C.

DOSAGE FORMS, COMPOSITION AND PACKAGING

ASPIRIN® Tablets: Each round, white tablet with the Bayer Cross* on both sides contains 325 mg acetylsalicylic acid in a formula containing corn starch, hypromellose, powdered cellulose, triacetin. In blister packages of 8 and bottles of 24, 50, 100, 115, 200 and 400.

ASPIRIN® Caplets: Each white capsule-shaped tablet (caplet), with BAYER on one side and score on the other, contains 325 mg acetylsalicylic acid in a formula containing corn starch, hypromellose, powdered cellulose, triacetin. In bottles of 50 and 100.

ASPIRIN® Extra-Strength Tablets: Each round, white tablet, with the Bayer Cross* in red ink on one side, contains 500 mg acetylsalicylic acid in a formula containing carnauba wax, corn starch, D&C Red #7, FD&C Blue #2, FD&C Red #40, hypromellose, powdered cellulose, propylene glycol, shellac, titanium dioxide, triacetin. In bottles of 50 and 100.

ASPIRIN® 81mg (delayed release tablet) Each pale blue coloured enteric coated tablet, with 81 in dark blue ink on one side contains 81 mg acetylsalicylic acid in a formula containing carnauba wax, corn starch, croscarmellose sodium, FD&C Blue #1, FD&C Blue #2, hypromellose, lactose monohydrate, methacrylic acid copolymer, microcrystalline cellulose, polysorbate 80, powdered cellulose, propylene glycol, shellac, sodium laurel sulphate, titanium dioxide, triacetin. In blister packages of 8 and bottles of 30, 120, 180 and 240 tablets.

ASPIRIN® 81mg Quick Chews: Each peach coloured tablet, with pleasant orange taste and the Bayer Cross* on one side contains 81 mg acetylsalicylic acid in a formula containing corn starch, dextrose, FD&C Yellow #6, orange juice flavour, sodium cyclamate. In bottles of 30, and 100 tablets.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

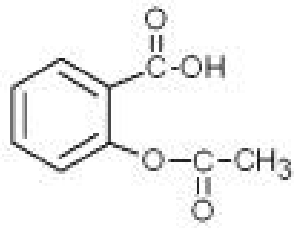
Proper name: acetylsalicylic acid

Chemical name: 2-(Acetyloxy) benzoic acid; salicylic acid acetate

Molecular formula: $C_9H_8O_4$

Molecular mass: 180.16

Structural formula:



Physicochemical properties:

Description: White granules, commonly tabular or needle-like, or white crystalline powder. Odourless or having a faint odour.

Solubility: Slightly soluble in water; freely soluble in alcohol; soluble in chloroform and ether; sparingly soluble in absolute ether.

pK value (25°C): 3.49

Melting Point: 135°C (rapid heating)

CLINICAL TRIALS

Study demographics and trial design

Anti-Platelet Aggregation Studies

Study #/ cross-reference	Trial Design	Dosage, route of administration and duration	Study Subjects (n = number)	Mean age (Range)	Gender
Indication: Reducing the risk of vascular mortality in patients with a suspected acute myocardial infarction.					
ISIS – 2 Ref 102	Multicentre international 2x2 factorial, randomized double blind, placebo controlled study.	160 mg oral for 30 days after suspected acute MI. (Median follow-up to 15 months).	ASA 8587, Streptokinase 8592, ASA + Strep 4292, Placebo 4300	Not available	Not available
Indication: Reducing the risk of a first non-fatal myocardial infarction in individuals deemed to be at sufficient risk of such an event by their physician					
TPT Ref 61	Randomized, factorial, placebo-controlled, parallel-group study	warfarin (mean) 4.1mg, ASA 75mg	warfarin + ASA 1,277 warfarin + ASA placebo 1,268 ASA + warfarin placebo 1,268 ASA placebo + warfarin placebo 1,272	45-69 years	Male
HOT Ref 101	Prospective, randomized, open with blinded endpoint evaluation (PROBE). ASA component was double blinded	ASA 75mg or placebo; felodine 5mg, inhibitors, β-blockers, diuretics mean - 3.8 years	19,567 subjects of which 18,790 were randomized to ASA or Placebo (ASA = 9,399; Placebo = 9,391)	61.5 years - mean (50-80 years)	Male 53% Female 47%
PHS Ref 100	Double blind placebo controlled, 2x2 factorial randomized parallel group	ASA 325mg every other day for 60.2 months	22,071 ASA = 11,037 Placebo = 11,034	40 to 84 years	Male

Platelet Aggregation Studies (continued)

Study #/ cross-reference	Trial Design	Dosage, route of administration and duration	Study Subjects (n = number)	Mean age (Range)	Gender
Indication: Reducing the risk of morbidity and death in patients with unstable angina and in those with previous myocardial infarction					
RISC Ref 76	Prospective randomized, double blind, placebo controlled, multicentre study	ASA 75mg daily for 3 months after initial heparin by IV for 5 days	- Heparin 198 - ASA 189 - Heparin + ASA 210 - Placebo 199	58 years	Male
RISC Trial, 12 month follow-up Ref 89	Prospective randomized, double blind, placebo controlled, multicentre study	ASA 75mg daily for 3 months after initial IV heparin for 5 days	- Heparin 198 - ASA 189 - Heparin + ASA 210 - Placebo 199	58 years	Male
Verheugt et al. Ref 88	Prospective, randomized, placebo-controlled, comparative multicentre study	ASA 100mg for approx. 3 months	ASA 50 Placebo 50	ASA 61 years Placebo 64 years	ASA 72% male Placebo 76% male
SAPAT Ref 54	Prospective, randomized, double blind placebo controlled, multicentred study	ASA 75mg daily for up to 6 years (median 50 months)	ASA 1009 Placebo 1026	52 years	ASA male 51% Placebo males 53%
Indication: Reducing the risk of transient ischemic attacks (TIA) and for secondary prevention of atherothrombotic cerebral infarction					
SALT Ref 81	Prospective, randomized, double blind, placebo controlled, multicentre study	ASA 75mg daily for minimum of 12 months and maximum of 63 months (mean 30.6 months)	ASA 676 Placebo 684	50-79 years ASA mean: 67 years PLA mean: 66.8 years	ASA 65.4% male Placebo 66.2% male
Lindblad et al. Ref 57	Prospective, randomized, double blind placebo controlled study	ASA 75mg daily for 6 months	ASA 117 Placebo 115	66 years (40-81 years)	75% male

Migraine Study

Study #/ cross-reference	Trial Design	Dosage, route of administration and duration	Study Subjects (n = number)	Mean age (Range)	Gender
Lipton et al. Ref 95	Prospective, randomized, double-blind, parallel-group, placebo-controlled	Single dose ASA 1000 mg	ASA = 201 Placebo = 200	ASA = 37.3 PLA = 37.9	ASA = 79 % female PLA = 79 % female

Study results

Platelet Aggregation Studies Results

Study #	**Primary Endpoints**	**Associated value and statistical significance for ASA compared to Placebo**	
Indication: Reducing the risk of vascular mortality in patients with a suspected acute myocardial infarction.			
		Value	ASA vs. Placebo
ISIS – 2 Ref 102	Vascular death after 5 week period	ASA 9.4%, Placebo 11.8% Odds reduction 23%	 2p < 0.00001 ASA was statistically significantly better than placebo
Indication: Reducing the risk of a first non-fatal myocardial infarction in individuals deemed to be at sufficient risk of such an event by their physician			
TPT Ref 61	All ischemic heart disease defined as the sum of fatal and non-fatal events (i.e. coronary death and fatal and non-fatal myocardial infarction).	ASA 10.2%, Placebo 13.3% 20% reduction in IHD	 p = 0.04 ASA was statistically significantly better than placebo
HOT Ref 101	Major cardiovascular events were defined as all (fatal and non-fatal) myocardial infarctions, all (fatal and non-fatal) strokes, and all other cardiovascular deaths.	Reduction in all cardiovascular events by 15 % and all myocardial infarction by 36%	 p=0.03 p = 0.002 ASA was statistically significantly better than placebo
PHS Ref 100	fatal and non-fatal myocardial infarction	325 mg ASA every other day: 44% reduction in risk of MI in ASA vs. Placebo group Relative Risk 0.56, 95% CI 0.45-0.70	p<0.00001 P<0.0001 ASA was statistically significantly better than placebo

Platelet Aggregation Studies Results (continued)

Study #	Primary Endpoints	Associated value and statistical significance for ASA compared to Placebo and Comparator		
Indication: Reducing the risk of morbidity and death in patients with unstable angina and in those with previous myocardial infarction				
		Value	ASA vs. Placebo	ASA vs. Comparator
RISC	Death or non-fatal MI	5 days: Risk Ratio 0.43 (CI 0.21-0.91) 30 days: Risk Ratio 0.31 (CI 0.18-0.53) 90 days: Risk Ratio 0.36 (0.21-0.57)	p=0.03 p<0.0001 p<0.0001 ASA was statistically significantly better than placebo	Heparin was not statistically significantly better than placebo and there was no comparison to ASA
RISC Trial, 12 month follow-up	MI and death	6 months: ASA-35 events, heparin 76 events. Risk Ratio 0.46 (CI 0.31-0.67) 12 months, ASA 44 events, heparin 85 events. Risk Ratio 0.52 (CI 0.37-0.72)	p<0.0001 p=0.0001 ASA was statistically significantly better than placebo	Not Performed
Verheugt et al.	Reinfarction rate	ASA 2 patients (4%), Placebo 9 patients (18%)	p<0.03 ASA was statistically significantly better than placebo	Not Performed
SAPAT	non-fatal or fatal MI or sudden death	ASA 8%, Placebo 12%	p=0.003 ASA was statistically significantly better than placebo	Not Performed

Indication: Reducing the risk of transient ischemic attacks (TIA) and for secondary prevention of atherothrombotic cerebral infarction			
		Value	ASA vs. Placebo
SALT	Risk of stroke or death	18 % reduction in risk: Relative Risk 0.82 (CI 0.67-0.99)	p=0.02 ASA was statistically significantly better than placebo
Lindblad et al.	Stroke (without complete recovery) at 6 months	ASA 2 cases, Placebo 11 cases	p=0.01 ASA was statistically significantly better than placebo

Migraine Study Results

Study #	**Primary Endpoints**	**Associated value and statistical significance for ASA compared to Placebo**	
		Value	ASA vs. Placebo
Lipton et al.	% of subjects experiencing headache response at 2 hr (defined as change in pain intensity from mod. to severe at baseline to mild or none at 2 hr post-medication)	ASA 52 %, Placebo 34%	p<0.001 ASA was statistically significantly better than placebo

DETAILED PHARMACOLOGY

Analgesia:
The analgesic effect of ASPIRIN has been recognized and utilized clinically for more than half a century. The degree of analgesia attained with ASPIRIN is moderate but it has proved highly suitable in the management of pathological pain of mild to moderate severity. As regards site of action, both peripheral and CNS factors appear to contribute significantly to the pain relief afforded by ASPIRIN. As for mechanism of action, the accumulated evidence of recent years indicates that ASPIRIN acts by interfering with the synthesis and release of prostaglandins, thereby averting the sensitization of pain receptors to mechanical stimulation or to other mediators.

Migraine:
Migraines are reoccurring headaches that last 4-72 hours and are characterized by lateralized throbbing, moderate to severe pain intensity and at least one other of the following symptoms: nausea, photophobia, phonophobia. Routine physical activity aggravates the symptoms. Some individuals also experience neurological aura such as blurring of vision before the pain and associated symptoms occur.

Evidence suggests that there are at least three mechanisms involved in the pathophysiology of migraines: extracranial arterial vasodilatation, extracranial neurogenic inflammation and decrease inhibition of central pain transmission. It has been shown that the degree of inflammatory activity is proportional to the intensity of the pain felt and as the blood pulses, the characteristic throbbing emerges.

An estimated two million Canadians have been diagnosed with migraines but many migraineurs never receive a clinical diagnosis; therefore, the actual numbers of Canadians who suffer from migraines could be over 3 million. Over 70% of migraine suffers are women and the majority are aged between 20 and 50 years. This prevalence is based in part due to hormonal fluctuations that women experience related to menstruation, oral contraceptive use, pregnancy, menopause and hormone replacement therapy.

The use of a single dose of ASPIRIN (2 x 500 mg tablets) in patients with a migraine attack was investigated in two placebo-controlled clinical studies conducted by Bayer. Treatment with ASPIRIN resulted in a statistically significant relief of migraine pain and in the associated symptoms of photophobia and phonophobia that continued throughout the 6 hour post-dose observation. The results also showed a significant improvement in overall quality of life for migraine sufferers but there was no difference between ASPIRIN and placebo groups in headache recurrence.

Antipyresis:
Interference with the synthesis and release of prostaglandins is also involved in the antipyretic activity of ASPIRIN. ASPIRIN effects a significant reduction in elevated body temperature, but has little effect on normal body temperature. This latter is maintained by a delicate balance between heat production and heat loss, with the hypothalamus regulating the set point at which body temperature is maintained. Fever is induced by synthesis and release of prostaglandins in this temperature-regulating area and ASPIRIN acts by interfering with this process. Heat production is not inhibited but dissipation of heat is augmented by increased peripheral blood flow and by sweating.

Anti-inflammatory effect:

Components of the anti-inflammatory action of the salicylates are increased capillary resistance, thus reducing capillary leakage in response to local toxins, interference with the production of tissue-destructive lysosomal enzymes and inhibition of the synthesis of prostaglandin E compounds which have been shown to be potent mediators of the inflammatory process. Besides interfering with the synthesis of prostaglandins ASPIRIN also acts by interfering with lymphocyte activation and lymphokine production. Lymphokines are produced by activated thymus lymphocytes which are abundant in the inflammatory tissues of patients suffering from rheumatoid arthritis. They cause increased vascular permeability and white blood cell chemotaxis, activate macrophages and stimulate lymphocyte DNA synthesis. They also induce release of tissue-destructive lysosomal enzymes as well as prostaglandins. The prostaglandins themselves, beside causing many manifestations of inflammation also act as a potent negative feedback mechanism by inhibiting lymphokine production. An indepth review of the effects of ASPIRIN on the lymphocyte-macrophage axis in inflammation has been published.

Effects on platelets: relation to hemostasis and thrombosis.

Platelets play an important role in normal hemostasis and clinical pathologic and experimental evidence indicates that their aggregation may play an equally important role in the evolution of a variety of disease states including cerebrovascular disease, ischemic heart disease and myocardial infarction. ASPIRIN inhibits platelet aggregation by irreversibly acetylating platelet cyclo-oxygenase, thereby blocking the production of prostaglandin endoperoxides PGG_2 and PGH_2 which are precursors of the major platelet-aggregating material, thromboxane A_2, which is also a powerful vasoconstrictor. However, ASPIRIN does not prevent the adherence of platelets to damaged vessel walls or the release of granule contents from these adherent platelets. As the anuclear platelets are unable to synthesize new enzyme molecules to replace those that have been inactivated, inhibition of platelet aggregation by ASPIRIN thus persists for the life of the platelets. Daily administration of 20 to 40 mg of ASPIRIN to healthy volunteers reduced platelet thromboxane production but inhibited platelet aggregation only partially. When administered to patients recovering from myocardial infarction, 50 mg ASPIRIN daily had the same effects on thromboxane production, platelet aggregation and bleeding times as 324 mg daily. Other studies show that ASPIRIN doses of 40 to 325 mg daily suppressed thromboxane production by at least 80%, but 80 mg ASPIRIN daily was the lowest dose required for maximum cumulative thrombocyte function inhibition. The protective effect of ASPIRIN against experimentally induced thrombosis or atherosclerosis has been demonstrated in several animal models.

Besides inhibiting the biosynthesis of thromboxane A_2 by platelets, ASPIRIN also interferes with the production of prostacyclin (PGI_2) by vascular endothelial cells, the above-mentioned prostaglandin endoperoxides being common precursors of both thromboxane A_2 and prostacyclin. This latter compound is one of the most powerfully acting platelet deaggregators and vasodilators and thus it would appear that the interference with the hemostatic processes by ASPIRIN depends on the thromboxane-prostacyclin balance. In fact, it has been suggested that under some conditions, high doses of ASPIRIN may be thrombogenic. However, in contrast to platelets, the vascular endothelial cells are able to regenerate cyclo-oxygenase in a relatively short time and therefore therapeutic doses of ASPIRIN are likely to produce a lesser inhibition of the vascular prostacyclin system than of the platelet thromboxane-forming mechanism. In fact, there is no clinical evidence to indicate that high doses of ASPIRIN would result in an increased risk of thromboembolism. Indeed, quite the contrary was observed and, in a controlled study, paradoxical shortening of the bleeding time was not observed at a daily ASPIRIN dose of 3.6 g. Lower dosages of ASPIRIN make selective blocking of the TxA_2-synthesis without a simultaneous blocking of PGI_2-production possible.

The use of ASPIRIN in patients with a suspected acute myocardial infarction was investigated in a

large multi-centre trial involving over 17,000 patients. Treatment with ASPIRIN resulted in a 23% reduction in the risk of vascular mortality versus placebo at 5 weeks. This use translates to a reduction of 24 deaths and 14 non-vascular events per 1000 patients treated.
The effect of time to therapy revealed that patients treated with ASPIRIN "early" (0 to 4 hours) versus "late" (5 to 24 hours) after symptom onset experienced reductions in the odds of vascular death of 25% versus 21%, versus placebo at 5 weeks. 'Early' treatment with ASPIRIN resulted in the saving of 4 additional lives per 1000 patients versus 'late' treatment.

Long term follow-up (up to 10 years) of patients in this study established that the early survival advantage to ASPIRIN persisted long term, and that this prolonged benefit was additive to that of fibrinolytic therapy.

The use of ASPIRIN for secondary prevention of thrombotic events is supported by a comprehensive overview of a number of clinical trials involving patients who already had some type of vascular disease (myocardial infarction, unstable angina, stroke or transient cerebral ischemia). Overall, these studies point to a 26-28 % reduction of the combined endpoints of MI, stroke, or vascular deaths by treatment with ASPIRIN alone at doses of 75 to 325 mg daily. Studies which directly compared low doses with higher doses (30-1200 mg/day), indicated that the incidence of gastrointestinal adverse effects were significantly less common with the lower doses.

In a study in patients undergoing coronary artery bypass surgery (CABG), patients given ASPIRIN at a dosage of 80 mg to 650 mg within 48 hours of revascularization had a risk of dying reduced to 1.3% as compared to 4.0% for those who did not receive treatment ($P<0.001$). There was a reduction in the incidence of myocardial infarction of 2.8% vs. 5.4%, $p < 0.001$. In total, the reduction in fatal and non-fatal outcomes was lower in those who received ASA, 10.6% vs. 18.6% in those who did not ($p<0.001$). The investigators Perioperative Ischemia Research Group (PIRG) concluded that early use of ASPIRIN after coronary by-pass surgery is safe and is associated with a reduce risk of death and ischemic complications involving the heart, brain, kidneys and gastrointestinal tract.
There was no ASPIRIN dose effect observed for either fatal or non-fatal outcomes with total doses lower than 325mg daily.

Recent discussions have focused on the efficacy of ASPIRIN for the primary prevention of myocardial infarction and stroke. Two large scale randomized trials, aimed at evaluating prophylactic use of ASPIRIN, were conducted among apparently healthy male physicians (22,000 in the United States and 5,000 in the United Kingdom) and their results have been published. In the summary overview of the combined results presented by the principal investigators, the authors state that:
"Taken together, these two primary prevention studies demonstrate a significant ($p < 0.0001$) reduction in non-fatal myocardial infarction of about one third."

On the other hand, the same two studies have not indicated any reduction in overall vascular mortality and also suggested a slight increase in the risk of non-fatal disabling stroke. Current controversy exists about the applicability of these findings, obtained in a selected population, to the general public. As well, the optimum dosage regimen still remains an open question in this regard. Thus, the use of ASPIRIN for primary prevention should remain, in the words of the principal investigators:

"a matter of judgment in which the physician considers the cardiovascular risk profile of the patient and balances the known hazards of ASPIRIN...against the clearly established reduction in the incidence of a first myocardial infarction".

Effect of Ibuprofen on Platelet Aggregation, Bleeding and Clotting Times in Normal Volunteers.

Experimental data suggest that ibuprofen may inhibit the effect of low dose ASA (81-325 mg per day) on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg was taken within 8 hours before or within 30 minutes after immediate release ASA dosing (81mg), a decreased effect of acetylsalicylic acid on the formation of thromboxane or platelet aggregation occurred. However, the limitations of these data and the uncertainties regarding extrapolation of *ex vivo* data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use. In a more recent double blind, randomized, placebo-controlled trial with healthy subjects by Cryer et. al, 2005, it has been shown that the drug-drug interaction is absent when immediate release ASA (81 mg) was taken 1 hour before taking ibuprofen (400 mg, TID) and also when ibuprofen was given 11 hours before the intake of low dose ASA. Thus, in order to adequately minimize potential interaction, the recommended dosing schedule for immediate release low dose ASA is to wait at least 11 hours after or 1 hour before taking up to a 400mg dose of ibuprofen.

TOXICOLOGY

The clinical and pathological signs of poisoning from toxic and lethal oral doses of ASA have been extensively described for man, much less extensively for other species.

The acute toxicity of ASA in animals has been studied and reviewed in detail by Boyd. The signs of poisoning in rats from doses in the lethal range are due to varying degrees of gastroenteritis, hepatitis, nephritis, pulmonary edema, encephalopathy, shock and minor toxic effects on other organs and tissues. Death is due to convulsions or cardiovascular shock. The major difference between species appears to be the ability to vomit toxic doses seen in man, cats and dogs, but not in mice, rats and rabbits. Otherwise, the pathological reaction to toxic doses of ASA is similar in all species in which such studies have been reported. The acute oral LD_{50} values have been reported as being over 1.0 g/kg in man, cat and dog, 0.92 g/kg in female and 1.48 g/kg in male albino rats, 1.19 g/kg in guinea pig, 1.1 g/kg in mouse and 1.8 g/kg in rabbit.

Chronic toxicity studies were reported in mice and rats. When ASA was administered at 2 to 20 times the maximum tolerated clinical dose to mice for up to one year, a dose-related deleterious effect was observed on mean survival time, number of young born and number of young raised to weaning age. No evidence of carcinogenic effect was found.

The chronic oral LD_{50} in male albino rats has been reported as 0.24 g/kg/day when given for 100 days. At these daily doses ASA produced no anorexia and no loss of body weight. It did produce polydipsia, aciduria, diuresis, drowsiness, hyperreflexia, piloerection, rapid and deep respiration, tachycardia, and during the second month, soft stools, epistaxis, sialorrhea, dacryorrhea and death in hypothermic coma. Autopsy disclosed the presence of a hypertrophied stomach, renal congestion, mild hepatitis and pneumonitis. While teratogenic effects were noted in animals at near lethal doses, there is no evidence to indicate that ASPIRIN is teratogenic in man.

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PART III: CONSUMER INFORMATION ONLY
PROVIDED BY HEALTH PROFESSIONALS
ASPIRIN® 81mg
acetylsalicylic acid delayed release tablets USP

ASPIRIN® 81mg Quick Chews
acetylsalicylic acid tablets USP

ASPIRIN®
acetylsalicylic acid tablets USP, 325 mg

This leaflet is part III of a three-part "Product Monograph" published when **ASPIRIN® 81mg, ASPIRIN® 81mg Quick Chews and ASPIRIN® 325mg** were approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about **ASPIRIN® 81mg, ASPIRIN® 81mg Quick Chews and ASPIRIN® 325mg**. Contact your doctor or pharmacist if you have any questions about the drug. Also see package insert for additional information.

ABOUT THIS MEDICATION

What the medication is used for:

ASPIRIN 81mg, ASPIRN 81 mg Quick Chews and **ASPIRIN® 325mg** can help save your life in the following situations:

- to help prevent a first heart attack in those who are at increased risk, or
- to help prevent a second heart attack or stroke in those who have already had such an event, or
- when you suspect you are having a heart attack.

FOR PREVENTION OF A FIRST NON-FATAL HEART ATTACK (DAILY THERAPY):

Your doctor may recommend you take ASPIRIN 81mg, ASPIRIN 81mg Quick Chews or ASPIRIN 325mg to help reduce the risk of a first non-fatal heart attack because you are at risk of having a heart attack. There is no evidence that this product reduces the risk of a first fatal heart attack, nor first strokes (fatal and non-fatal), nor death due to any cardiovascular problems. Your doctor will assess the appropriate balance of possible benefit of this product against the potential risk of stomach bleeding and stroke. Factors that increase your risk include high blood pressure, high cholesterol, diabetes, family history of heart disease, increased age, overweight and smoking. You should follow your doctor's instructions carefully. Please notify your doctor if you intend to stop taking this medication.

USE DURING A HEART ATTACK

If you think you are having a heart attack, *call an ambulance* and immediately chew or crush two ASPIRIN 81mg or ASPIRIN 81mg Quick Chews tablets or one ASPIRIN 325mg tablet. It is important to chew or crush the product, to ensure this medicine quickly works. Then get to a hospital immediately for medical attention. Taking ASPIRIN 81mg, ASPIRIN 81mg Quick Chews or ASPIRIN 325mg at the first signs and symptoms can reduce your risk of dying from the heart attack.

The signs and symptoms of a heart attack include:

- uncomfortable pressure, fullness, squeezing or pain in the centre of the chest that lasts more than a few minutes, or goes away quickly and comes back,
- pain that spreads to the shoulders, neck or arms,
- chest discomfort with lightheadedness, fainting, sweating, nausea or shortness of breath.

At the hospital, the doctor will then recommend appropriate therapy.

FOR PREVENTION OF A SECOND HEART ATTACK OR STROKE (DAILY THERAPY)

Your doctor may recommend you take ASPIRIN 81mg, ASPIRIN 81mg Quick Chews or ASPIRIN 325mg daily to help prevent a second heart attack or stroke. After having experienced a first heart attack or stroke, you can be at increased risk of experiencing a second one. You may also be at risk for heart disease and stroke because you may be overweight, a smoker, have an inactive lifestyle, high blood pressure, are under stress or have high blood cholesterol.

Following your doctor's instructions concerning the use of ASPIRIN 81mg, ASPIRIN 81mg Quick Chews or ASPIRIN 325mg and the changes in diet, exercise and lifestyle he/she may have prescribed, will provide you with your best opportunity to avoid experiencing a second heart attack or stroke. Always contact your doctor if you experience any difficulties.

What it does:

ASPIRIN 81mg, ASPIRIN 81mg Quick Chews or ASPIRIN 325mg belongs to a group of medicines called antiplatelet drugs. Platelets are very small structures in blood, smaller than red or white blood cells, which clump together during blood clotting. By preventing this clumping, antiplatelet drugs reduce the chances of blood clots forming (a process called thrombosis).

When it should not be used:

ASPIRIN should not be used if you:

- are allergic to ASA or any ingredient within the formulation
- have active stomach ulcer
- have a history of asthma induced by salicylates or other anti-inflammatory drugs. Talk to your doctor.
- are using methotrexate at doses of 15 mg/week or more
- are in the last trimester of pregnancy
- are prone to bleeding

What the medicinal ingredient is:

acetylsalicylic acid (ASA)

What the important nonmedicinal ingredients are:

ASPIRIN® 81mg – carnauba wax, corn starch, croscarmellose sodium, FD&C Blue #1, FD&C Blue #2, hypromellose, lactose monohydrate, methacrylic acid copolymer, microcrystalline cellulose, polysorbate 80, powdered cellulose, propylene glycol, shellac, sodium laurel sulphate, titanium dioxide, triacetin.
ASPIRIN® 81mg Quick Chews – corn starch, dextrose, FD&C Yellow #6, orange juice flavour, sodium cyclamate.
ASPIRIN® 325mg – corn starch, hypromellose, powdered cellulose, triacetin.

What dosage forms it comes in:

ASPIRIN® 81mg, ASPIRIN® 81mg Quick Chews and ASPIRIN® 325mg comes as enteric coated (delayed release), chewable tablets and tablets.

WARNINGS AND PRECAUTIONS

Your doctor will have asked you many questions about your health, lifestyle, and medications before recommending ASPIRIN 81mg, ASPIRIN 81mg Quick Chews and ASPIRIN 325mg. That is why it is very important that you tell your doctor all such information. If you have forgotten to tell your doctor about any of the following, call your doctor or pharmacist before you take this medicine (or any medicine):

- allergy to salicylates;
- asthma;
- stomach problems;
- peptic ulcer;
- severe liver/kidney disease;

- history of blood clotting defects;
- have severe anemia;
- are pregnant or breast-feeding or
- will be having surgery in five to seven days

REMEMBER: This product is not recommended for children or teenagers. This package contains enough drug to seriously harm a child. Keep out of children's reach. Do not administer to children and teenagers for chicken pox or flu symptoms before a doctor is consulted. Reye's Syndrome which can occur in children or teenagers is a rare but serious illness reported to be associated with ASA.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor if you are taking any prescription or non-prescription drugs including blood thinners, anti-inflammatory drugs, anticonvulsants, anti-diabetic medicine, gout medicine, other medications containing salicylates and acetaminophen, or are taking simultaneously with alcohol. Ibuprofen may interfere with the heart protective benefits of ASPIRIN. Patients should talk to their doctor if they are on an ASPIRIN regimen and take ibuprofen for pain.

PROPER USE OF THIS MEDICATION

Usual dose:

During a heart attack: Immediately chew or crush 2 – ASPIRIN 81mg or ASPIRIN 81mg Quick Chews tablets or 1 – ASPIRIN 325mg tablet and call an ambulance.

For prevention of a first heart attack or for the prevention of a second heart attack or stroke: ASPIRIN 81mg or ASPIRIN 81mg Quick Chews: Take 1 to 4 tablets daily, depending on your doctor's instructions. ASPIRIN 325mg: Take 1 tablet daily, depending on your doctor's instructions. You should take this medicine at the same time every day. This will help you to remember to take your medication. For maximum effectiveness, it is very important to take ASPIRIN 81mg, ASPIRIN 81mg Quick Chews or ASPIRIN 325mg *every day* as directed by your doctor. Do not take more tablets than your doctor recommends. Your doctor may tell you to take ASPIRIN 81mg, ASPIRIN 81mg Quick Chews or ASPIRIN 325mg with other medications; he or she may also tell you to eat special foods, exercise or take other steps to safeguard your health.

For daily therapy ASPIRIN 81mg**,** tablets should be swallowed whole for the medicine to work properly. ASPIRIN 81mg tablets have a special coating, *enteric coating*, which allows the tablets to pass undissolved through the stomach and on into the intestine. By dissolving in the intestine rather than the stomach, the risk of stomach upset is reduced in those with a sensitive stomach. Therefore, to maintain this protection, the tablets should not be crushed or broken.

For daily therapy with **ASPIRIN 81mg Quick Chews,** tablets could be chewed or swallowed whole.

For daily therapy with ASPIRIN® 325mg, tablets could be swallowed whole.

Can I Continue to Take ASPIRIN for Relief of Headache, Fever or Arthritis Pain?

ASPIRIN 81mg or ASPIRIN 81mg Quick Chews is specially designed to reduce your risk of dying during a heart attack, to help prevent a first heart attack in those who are at increased risk and to help prevent a second heart attack or stroke. It is a smaller dose than you would need to take for a headache or other types of pain and is unlike other pain reliever products such as acetaminophen (Tylenol®) and ibuprofen (Advil®). Ask your doctor or pharmacist about other ASPIRIN products available (or other pain relievers such as acetaminophen or ibuprofen) and the correct dosage for the relief of your headache, fever or arthritic pain.

Always consult with your doctor or pharmacist before taking other medications.

Overdose:

In case of accidental overdose call a doctor or poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you forget to take your medication, take it when you remember. But do not take *extra* medication to compensate for a missed dosage unless instructed by your doctor.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, ASPIRIN may occasionally produce unwanted side effects. You should call your doctor if you experience any of the following: nausea, vomiting; stomach irritation, ringing or buzzing in the ears or pain; if you notice that you are 'bruising' more easily than you were before starting a daily dose of ASPIRIN.

Regular daily use of alcohol while on ASPIRIN daily therapy may increase your risk of developing gastrointestinal bleeding.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Stop use and call your doctor if you experience an allergic reaction (skin rash, hives, itching, swelling of eyes, face, lips, tongue, or throat, wheezing or breathing difficulties); stomach bleeding (bloody vomit, vomit that looks like coffee grounds, bright red blood in stools, black or tarry stools); loss of hearing or bleeding.

HOW TO STORE IT

Keep out of reach of children.

Store at room temperature, 15-30°C.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- **Report online at www.healthcanada.gc.ca/medeffect**
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting form and:**
  - **Fax toll-free to 1-866-678-6789**
  - **Mail to:**
    Canada Vigilance Program
    Health Canada
    Postal Locator 0701D
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web Site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:www.Bayer.ca
This leaflet was prepared by Bayer Inc. , Toronto, ON M9W 1G6
Last revised: March 21, 2012

PART III: CONSUMER INFORMATION
ASPIRIN® 81mg
acetylsalicylic acid (ASA) delayed-release tablets, USP

This leaflet is part III of a three-part "Product Monograph" published when **ASPIRIN® 81 mg** was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about **ASPIRIN® 81 mg**. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

- ASPIRIN 81mg is for doctor supervised long-term preventative therapy.

What it does:

ASPIRIN 81mg is for doctor supervised long-term preventative therapy.

When it should not be used:

ASPIRIN should not be used if you:

- are allergic to ASA or any ingredient within the formulation
- have active stomach ulcer
- have a history of asthma induced by salicylates or other anti-inflammatory drugs. Talk to your doctor.
- are using methotrexate at doses of 15 mg/week or more
- are in the last trimester of pregnancy because it may cause problems in the unborn child or complications during delivery
- are prone to bleeding

What the medicinal ingredient is:

acetylsalicylic acid (ASA)

What the important nonmedicinal ingredients are:

carnauba wax, corn starch, croscarmellose sodium, dextrose, FD&C Blue #1, FD&C Blue #2, hypromellose, lactose monohydrate, methacrylic acid copolymer, microcrystalline cellulose, polysorbate 80, powdered cellulose, propylene glycol, shellac, sodium lauryl sulphate, titanium dioxide, triacetin.

What dosage forms it comes in:

ASPIRIN® 81mg comes as enteric-coated tablets

WARNINGS AND PRECAUTIONS

Your doctor will have asked you many questions about your health, lifestyle, and medications before recommending ASPIRIN 81mg. That is why it is very important that you tell your doctor all such information. If you have forgotten to tell your doctor about any of the following, call your doctor or pharmacist before you take this medicine (or any medicine):

- allergy to salicylates;
- asthma;
- stomach problems;
- peptic ulcer;
- severe liver/kidney disease;
- history of blood clotting defects;
- have severe anemia;
- are pregnant or breast-feeding or
- will be having surgery in five to seven days

REMEMBER: This product is not recommended for children or teenagers. This package contains enough drug to seriously harm a child. Keep out of children's reach. Do not administer to children and teenagers for chicken pox or flu symptoms before a doctor is consulted. Reye's Syndrome which can occur in children or teenagers is a rare but serious illness reported to be associated with ASA.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor if you are taking any prescription or nonprescription drugs including blood thinners, anti-inflammatory drugs, anticonvulsants, anti-diabetic medicine, gout medicine, other medications containing salicylates and acetaminophen, or if you are taking simultaneously with alcohol. Do not use ibuprofen if you are taking **ASPIRIN® 81 m**g for preventative therapy without talking to a doctor or pharmacist. Ibuprofen may interfere with the preventive benefits of **ASPIRIN® 81 m**g.

PROPER USE OF THIS MEDICATION

Usual dose: **For doctor supervised long-term preventative therapy**: Take 1 to 4 tablets daily, depending on your doctor's instructions. You should take this medicine at the same time every day. This will help you to remember to take your medication. For maximum effectiveness, it is very important to take ASPIRIN 81mg *every day* as directed by your doctor. Do not take more tablets than your doctor recommends. Your doctor may tell you to take ASPIRIN 81mg with other medications; he or she may also tell you to eat special foods, exercise or take other steps to safeguard your health. ASPIRIN 81 mg tablets have a special coating, *enteric coating*, which allows them to pass undissolved through the stomach and into the intestine. By dissolving in the intestine rather than the stomach, the risk of stomach upset is reduced. Therefore, to maintain this protection, the tablets should not be crushed or broken.

Can I Continue to Take ASPIRIN for Relief of Headache, Fever or Arthritis Pain?

ASPIRIN 81mg is specially designed for doctor supervised long-term preventative therapy. It is a smaller dose than you would need to take for a headache or other types of pain and is unlike other pain reliever products such as acetaminophen and ibuprofen. Ask your doctor or pharmacist about other ASPIRIN products available (or other pain relievers such as acetaminophen or ibuprofen) and the correct dosage for the relief of your headache, fever or arthritic pain. Always consult with your doctor or pharmacist before taking other medications.

Overdose:

In case of accidental overdose call a doctor or poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you forget to take your medication, take it when you remember. But do not take *extra* medication to compensate for a missed dosage unless instructed by your doctor.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, ASPIRIN may occasionally produce unwanted side effects. You should call your doctor if you experience: nausea, vomiting; stomach irritation, ringing or buzzing in the ears or pain; if you notice that you are 'bruising' more easily than you were before starting a daily dose of ASPIRIN. Regular daily use of alcohol while on ASPIRIN daily therapy may increase your risk of developing gastrointestinal bleeding.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Stop use and call your doctor if you experience an allergic reaction (skin rash, hives, itching, swelling of eyes, face, lips, tongue, or throat, wheezing or breathing difficulties); stomach bleeding (bloody vomit, vomit that looks like coffee grounds, bright red blood in stools, black or tarry stools); loss of hearing or bleeding.

HOW TO STORE IT

Keep out of reach of children.
Store at room temperature, 15-30°C.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- **Report online at www.healthcanada.gc.ca/medeffect**
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting form and:**
  - **Fax toll-free to 1-866-678-6789**
  - **Mail to:**
    Canada Vigilance Program
    Health Canada
    Postal Locator 0701D
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web Site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:. This leaflet was prepared by Bayer Inc., Toronto, ON M9W 1G6. Last revised: March 21, 2012

PART III: CONSUMER INFORMATION

ASPIRIN® 81mg Quick Chews
acetylsalicylic acid (ASA) tablets USP

This leaflet is part III of a three-part "Product Monograph" published when **ASPIRIN® 81mg Quick Chews** were approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about **ASPIRIN® 81mg Quick Chews**. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
- ASPIRIN 81mg Quick Chews is for doctor supervised long-term preventative therapy.

What it does:
ASPIRIN 81mg Quick Chews is for doctor supervised long-term preventative therapy.

When it should not be used:
ASPIRIN should not be used if you:
- are allergic to ASA or any ingredient within the formulation
- have active stomach ulcer
- have a history of asthma induced by salicylates or other anti-inflammatory drugs. Talk to your doctor.
- are using methotrexate at doses of 15 mg/week or more
- are in the last trimester of pregnancy because it may cause problems in the unborn child or complications during delivery
- are prone to bleeding

What the medicinal ingredient is:
acetylsalicylic acid (ASA)

What the important nonmedicinal ingredients are:
corn starch, dextrose, FD&C Yellow #6, orange juice flavour, sodium cyclamate.

What dosage forms it comes in:
ASPIRIN® 81mg Quick Chews comes as chewable tablets

WARNINGS AND PRECAUTIONS

Your doctor will have asked you many questions about your health, lifestyle, and medications before recommending ASPIRIN 81mg Quick Chews. That is why it is very important that you tell your doctor all such information. If you have forgotten to tell your doctor about any of the following, call your doctor or pharmacist before you take this medicine (or any medicine):

- allergy to salicylates;
- asthma;
- stomach problems;
- peptic ulcer;
- severe liver/kidney disease;
- history of blood clotting defects;
- have severe anemia;
- are pregnant or breast-feeding or
- will be having surgery in five to seven days

REMEMBER: This product is not recommended for children or teenagers. This package contains enough drug to seriously harm a child. Keep out of children's reach. Do not administer to children and teenagers for chicken pox or flu symptoms before a doctor is consulted. Reye's Syndrome which can occur in children or teenagers is a rare but serious illness reported to be associated with ASA.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor if you are taking any prescription or nonprescription drugs including blood thinners, anti-inflammatory drugs, anticonvulsants, anti-diabetic medicine, gout medicine, other medications containing salicylates and acetaminophen, or if you are taking simultaneously with alcohol.

Do not use ibuprofen if you are taking **ASPIRIN® 81mg Quick Chews** for preventative therapy without talking to a doctor or pharmacist. Ibuprofen may interfere with the preventive benefits of **ASPIRIN® 81mg Quick Chews**.

PROPER USE OF THIS MEDICATION

Usual dose: For doctor supervised long-term preventative therapy: Take 1 to 4 tablets daily, depending on your doctor's instructions. You should take this medicine at the same time every day. This will help you to remember to take your medication. For maximum effectiveness, it is very important to take ASPIRIN 81mg Quick Chews *every day* as directed by your doctor. Do not take more tablets than your doctor recommends. Your doctor may tell you to take ASPIRIN 81mg Quick Chews with other medications; he or she may also tell you to eat special foods, exercise or take other steps to safeguard your health. For daily therapy with ASPIRIN 81mg Quick Chews, tablets could be chewed or swallowed whole.

Can I Continue to Take ASPIRIN for Relief of Headache, Fever or Arthritis Pain?
ASPIRIN 81mg Quick Chews is specially designed for doctor supervised long-term preventative therapy. It is a smaller dose than you would need to take for a headache or other types of pain and is unlike other pain reliever products such as acetaminophen and ibuprofen. Ask your doctor or pharmacist about other ASPIRIN products available (or other pain relievers such as acetaminophen or ibuprofen) and the correct dosage for the relief of your headache, fever or arthritic pain.
Always consult with your doctor or pharmacist before taking other medications.

Overdose:
In case of accidental overdose call a doctor or poison control centre immediately, even if there are no symptoms.
Missed Dose:
If you forget to take your medication, take it when you remember. But do not take *extra* medication to compensate for a missed dosage unless instructed by your doctor.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, ASPIRIN may occasionally produce unwanted side effects.

You should call your doctor if you experience: nausea, vomiting; stomach irritation, ringing or buzzing in the ears or pain; if you notice that you are 'bruising' more easily than you were before starting a daily dose of ASPIRIN.

Regular daily use of alcohol while on ASPIRIN daily therapy may increase your risk of developing gastrointestinal bleeding.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Stop use and call your doctor if you experience an allergic reaction (skin rash, hives, itching, swelling of eyes, face, lips, tongue, or throat, wheezing or breathing difficulties); stomach bleeding (bloody vomit, vomit that looks like coffee grounds, bright red blood in stools, black or tarry stools); loss of hearing or bleeding.

HOW TO STORE IT

Keep out of reach of children.
Store at room temperature, 15-30°C.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- **Report online at www.healthcanada.gc.ca/medeffect**
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting form and:**
  - **Fax toll-free to 1-866-678-6789**
  - **Mail to:**
    Canada Vigilance Program
    Health Canada
    Postal Locator 0701D
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web Site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice..

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:. This leaflet was prepared by Bayer Inc. Last revised: March 21, 2012

PART III: CONSUMER INFORMATION
ASPIRIN®

acetylsalicylic acid (ASA) tablets, USP, 325 mg

This leaflet is part III of a three-part "Product Monograph" published when **ASPIRIN®** was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about **ASPIRIN®**. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
- ASPIRIN is for fast and effective relief of headaches, fever, the pain and discomfort of colds and flu, pain of inflammation, arthritic or rheumatic pain, minor aches and pain, pain due to muscle sprains and strains, joint and body pain, pain of menstrual cramps, toothache and pain of dental work or intervention.
ASPIRIN is also for doctor supervised long-term preventative therapy.

What it does:
ASPIRIN quickly and effectively relieves pain. ASPIRIN is an effective pain reliever which is easy-to-swallow and dissolves quickly because of its micro-thin coating. It doesn't dissolve in the mouth, so there's no bitter taste. ASPIRIN contains the same trusted ingredient as Extra Strength ASPIRIN and is recommended for doctor supervised adult long-term preventative therapy. Speak to your doctor to determine if ASPIRIN for long-term preventative therapy is right for you.

When it should not be used:
ASPIRIN should not be used if you:
- are allergic to ASA or any ingredient within the formulation
- have active stomach ulcer
- have a history of asthma induced by salicylates or other anti-inflammatory drugs. Talk to your doctor.
- are using methotrexate at doses of 15 mg/week or more
- are in the last trimester of pregnancy because it may cause problems in the unborn child or complications during delivery
- are prone to bleeding

What the medicinal ingredient is:
acetylsalicylic acid (ASA)
What the important nonmedicinal ingredients are:
corn starch, hypromellose, powdered cellulose, triacetin.
What dosage forms it comes in:
ASPIRIN® comes in tablets and caplets

WARNINGS AND PRECAUTIONS

Your doctor will have asked you many questions about your health, lifestyle, and medications before recommending ASPIRIN. That is why it is very important that you tell your doctor all such information. If you have forgotten to tell your doctor about any of the following, call your doctor or pharmacist before you take this medicine (or any medicine):

- allergy to salicylates;
- asthma;
- stomach problems;
- peptic ulcer;
- severe liver/kidney disease;
- history of blood clotting defects;
- have severe anemia;
- are pregnant or breast-feeding or
- will be having surgery in five to seven days

REMEMBER: This product is not recommended for children or teenagers. This package contains enough drug to seriously harm a child. Keep out of children's reach. Do not administer to children and teenagers for chicken pox or flu symptoms before a doctor is consulted. Reye's Syndrome which can occur in children or teenagers is a rare but serious illness reported to be associated with ASA.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor if you are taking any prescription or nonprescription drugs including blood thinners, anti-inflammatory drugs, anticonvulsants, anti-diabetic medicine, gout medicine, other medications containing salicylates and acetaminophen, or if you are taking simultaneously with alcohol. Do not use ibuprofen if you are taking **ASPIRIN®** for preventative therapy without talking to a doctor or pharmacist. Ibuprofen may interfere with the preventive benefits of **ASPIRIN®**.

PROPER USE OF THIS MEDICATION

Usual dose:
Adult Dose For Pain And Fever: 1-2 ASPIRIN tablets/caplets with milk or water; may be repeated every 4 hours as necessary, up to a maximum of 12 tablets/caplets daily.
If these doses do not bring relief of pain or fever, or fever lasts beyond 3 days or pain lasts beyond 5 days, consult doctor. It is hazardous to exceed the maximum recommended dose unless advised by a doctor.
In conditions affecting children under 12 years, consult your doctor.

For doctor supervised long-term preventative therapy: Take 1 tablet/caplet daily as directed by your doctor.
Overdose:
In case of accidental overdose call a doctor or poison control centre immediately, even if there are no symptoms.
Missed Dose:
If you forget to take your medication, take it when you remember. But do not take *extra* medication to compensate for a missed dosage unless instructed by your doctor.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, ASPIRIN may occasionally produce unwanted side effects.

You should call your doctor if you experience: nausea, vomiting; stomach irritation, ringing or buzzing in the ears or pain; if you notice that you are 'bruising' more easily than you were before starting a daily dose of ASPIRIN.

Regular daily use of alcohol while on ASPIRIN daily therapy may increase your risk of developing gastrointestinal bleeding.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Stop use and call your doctor if you experience an allergic reaction (skin rash, hives, itching, swelling of eyes, face, lips, tongue, or throat, wheezing or breathing difficulties); stomach bleeding (bloody vomit, vomit that looks like coffee grounds, bright red blood in stools, black or tarry stools); loss of hearing or bleeding.

HOW TO STORE IT

Keep out of reach of children.
Store at room temperature, 15-30°C.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- **Report online at www.healthcanada.gc.ca/medeffect**
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting form and:**
  - **Fax toll-free to 1-866-678-6789**
  - **Mail to:**
    Canada Vigilance Program
    Health Canada
    Postal Locator 0701D
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web Site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice..

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at: www.Bayer.ca
This leaflet was prepared by Bayer Inc.
Last revised: March 21, 2012
Bayer Inc., Toronto, ON M9W 1G6

PART III: CONSUMER INFORMATION
ASPIRIN® Extra Strength
acetylsalicylic acid (ASA) tablets, USP, 500 mg

This leaflet is part III of a three-part "Product Monograph" published when **ASPIRIN® Extra Strength** was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about **ASPIRIN® Extra Strength**. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
- ASPIRIN is for fast and effective relief of headaches, fever, the pain and discomfort of colds and flu, pain of inflammation, arthritic or rheumatic pain, minor aches and pain, pain due to muscle sprains and strains, joint and body pain, pain of menstrual cramps, toothache and pain of dental work or intervention. ASPIRIN Extra Strength is also clinically proven to relieve migraine pain and associated symptoms (sensitivity to light and sound) to improve the overall quality of life and let you get on with your day.

What it does:
ASPIRIN quickly and effectively relieves pain. ASPIRIN is an effective pain reliever which is easy-to-swallow and dissolves quickly because of its micro-thin coating. It doesn't dissolve in the mouth, so there's no bitter taste. For your tough pain, try Extra Strength ASPIRIN (500 mg).

When it should not be used:
ASPIRIN should not be used if you:
- are allergic to ASA or any ingredient within the formulation
- have active stomach ulcer
- have a history of asthma induced by salicylates or other anti-inflammatory drugs. Talk to your doctor.
- are using methotrexate at doses of 15 mg/week or more
- are in the last trimester of pregnancy because it may cause problems in the unborn child or complications during delivery
- are prone to bleeding

What the medicinal ingredient is:
acetylsalicylic acid (ASA)
What the important nonmedicinal ingredients are:
carnauba wax, corn starch, D&C Red # 7, FD&C Blue #2, FD&C Red #40, hypromellose, powdered cellulose, propylene glycol, shellac, titanium dioxide, triacetin
What dosage forms it comes in:
ASPIRIN® Extra Strength comes in tablets

WARNINGS AND PRECAUTIONS

Call your doctor or pharmacist before you take this medicine (or any medicine) if you have any of the following:

- allergy to salicylates;
- asthma;
- stomach problems;
- peptic ulcer;
- severe liver/kidney disease;
- history of blood clotting defects;
- have severe anemia;
- are pregnant or breast-feeding or
- will be having surgery in five to seven days

REMEMBER: This package contains enough drug to seriously harm a child. Keep out of children's reach. Do not administer to children and teenagers for chicken pox or flu symptoms before a doctor is consulted. Reye's Syndrome which can occur in children or teenagers is a rare but serious illness reported to be associated with ASA.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor if you are taking any prescription or nonprescription drugs including blood thinners, anti-inflammatory drugs, anticonvulsants, anti-diabetic medicine, gout medicine, other medications containing salicylates and acetaminophen, or if you are taking simultaneously with alcohol.

PROPER USE OF THIS MEDICATION

Usual dose:
Adult Dose For Pain And Fever: 1-2 ASPIRIN tablets/caplets with milk or water; may be repeated every 4 hours as necessary, up to a maximum of 8 tablets/caplets daily.
If fever lasts beyond 3 days or non-migraine pain lasts beyond 5 days, consult doctor. ASPIRIN Extra Strength is not a standard dosage unit; use only on advice of a doctor. It is hazardous to exceed the maximum recommended dose unless advised by a doctor.
In conditions affecting children under 12 years, consult your doctor.
Adult Dose For Migraine and Associated Symptoms (light and sound sensitivity): At onset of pain or symptoms, take 2 tablets with water. Repeat every 4 hours as needed, not to exceed the maximum of 8 tablets/day.
Overdose:
In case of accidental overdose call a doctor or poison control centre immediately, even if there are no symptoms.
Missed Dose:
If you forget to take your medication, take it when you remember. But do not take *extra* medication to compensate for a missed dosage unless instructed by your doctor.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, ASPIRIN may occasionally produce unwanted side effects.

You should call your doctor if you experience: nausea, vomiting; stomach irritation, ringing or buzzing in the ears or pain; bruising.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Stop use and call your doctor if you experience an allergic reaction (skin rash, hives, itching, swelling of eyes, face, lips, tongue, or throat, wheezing or breathing difficulties); stomach bleeding (bloody vomit, vomit that looks like coffee grounds, bright red blood in stools, black or tarry stools); loss of hearing or bleeding.

HOW TO STORE IT

Keep out of reach of children.
Store at room temperature, 15-25°C.

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- **Report online at www.healthcanada.gc.ca/medeffect**
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting form and:**
  - **Fax toll-free to 1-866-678-6789**
  - **Mail to:**
    Canada Vigilance Program
    Health Canada
    Postal Locator 0701D
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web Site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice..

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at: This leaflet was prepared by Bayer Inc. Last revised: March 21, 2012