

Summary of Product Characteristics

1. Name of the medicinal product

Sonamoja Tablets

2. Qualitative and quantitative composition

Active Ingredients:

Aspirin BP 600 mg/tablet

Paracetamol Ph Eur 300 mg/tablet

Caffeine anhydrous BP 50 mg/tablet

For excipients see section 6.1

3. Pharmaceutical form

capsule shaped tablet

4. Clinical particulars

4.1 Therapeutic indications

For the treatment of mild to moderate pain including headache, migraine, neuralgia, toothache, sore throat, period pains, symptomatic relief of sprains, strains, rheumatic pain, sciatica, lumbago, fibrositis, muscular aches and pains, joint swelling and stiffness, influenza, feverishness and feverish colds.

4.2 Posology and method of administration

Adults, the elderly and young persons aged 16 and over:

2 tablets every 4 hours to a maximum of 8 tablets in 24 hours.

Do not give to children aged under 16 years, unless specifically indicated (e.g. for Kawasaki's disease).

For migraine indication: use of this medicine is not recommended for children and adolescents (under 18 years of age).

Elderly:

Should be used with caution in elderly patients who are more prone to adverse events (see Warnings and Precautions)

Renal Impairment:

Contraindicated in patients with renal failure (e.g., Glomerular Filtration Rate (GFR) $<15 \text{ mL/min/1.73m}^2$). Aspirin is known to cause sodium and water retention which may exacerbate hypertension, congestive heart failure and renal impairment (see Contraindications, Warnings and Precautions).

Hepatic Impairment:

Contraindicated in patients with hepatic failure (see Contraindications, Warnings and Precautions).

4.3 Contraindications

This combination is contraindicated in the following conditions:

- Hypersensitivity to the active ingredients or to any other excipients.
- Patients in whom asthma, bronchospasm, angioedema, urticaria, or acute rhinitis are precipitated by aspirin or other non-steroidal anti-inflammatory drugs (NSAIDs).
- Peptic ulceration and those with a history of peptic ulceration;
- History of upper gastrointestinal bleeding or perforation, related to previous NSAID therapy.
- History of hemophilia, hypothrombinemia or other clotting disorders
- Renal failure (GFR $< 15 \text{ mL/min/1.73m}^2$).
- Hepatic failure.
- Third trimester of pregnancy
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- children under 16 years and when breast feeding because of possible risk of Reye's Syndrome.

4.4 Special warnings and precautions for use

Serious hypersensitivity reactions or anaphylaxis can occur, bronchospasm may be

precipitated in patients suffering from or with a previous history of asthma, allergic disease or nasal polyps. Aspirin should be used with caution in patients with uncontrolled hypertension (in whom target blood pressure has not been achieved), impaired renal or hepatic function, or in patients who are dehydrated or suffering from diabetes mellitus. The overall benefit-risk should be considered in patients diagnosed with hepatic or renal impairment before use. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.

Contains paracetamol. Do not use with any other paracetamol containing products. The concomitant use with other products containing paracetamol may lead to an overdose.

Do not take if you have a stomach ulcer.

Do not take more medicine than the label tells you to. Paracetamol overdose may cause liver failure which may require liver transplant or lead to death. Talk to your doctor at once if you take too much of this medicine, even if you feel well. This is because too much paracetamol can cause delayed, serious liver damage.

Underlying liver disease increases the risk of paracetamol-related liver damage. The overall benefit-risk should be considered in patients diagnosed with hepatic or renal impairment before use.

If you do not get better, talk to your doctor.

There is a possible association between aspirin and Reye's syndrome when given to children, especially during or immediately after a viral illness. Reye's syndrome is a very rare disease, which affects the brain and liver, and can be fatal. For this reason, aspirin should not be given to children under 16 years, particularly during or immediately after chickenpox, influenza, or other viral infections, unless prescribed by a physician or specifically indicated (e.g.

Kawasaki's disease).

Aspirin decreases platelet adhesiveness and increases bleeding time. Haematological and haemorrhagic effects can occur and may be severe. Patients should report any unusual bleeding symptoms to their physician.

In patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency, aspirin may induce haemolysis or haemolytic anaemia. Factors that may increase the risk of haemolysis are high dosage, fever, or acute infections.

Gastrointestinal bleeding, ulceration or perforation, which can be fatal, have been reported with all NSAIDs and may occur at any time during treatment, with or without warning symptoms or a previous history of serious GI events. These effects generally have more serious consequences in the elderly (see Interactions)

Cases of hepatic dysfunction/failure have been reported in patients with depleted glutathione levels, such as those who are severely malnourished, anorexic, have a low body mass index or are chronic heavy users of alcohol or have sepsis.

In patients with glutathione depleted states, the use of paracetamol may increase the risk of metabolic acidosis.

Aspirin can reduce uric acid excretions and therefore should be used with care in patients with gout or a history of gout. Keep out of sight and reach of children.

Should be used with caution in elderly patients who are more prone to adverse events. The concomitant use of aspirin with other systemic NSAIDs, including cyclooxygenase-2 selective inhibitors, should be avoided due to the potential for additive undesirable effects (see Interactions).

Excessive intake of caffeine (e.g., coffee, tea and some canned drinks) should be avoided while taking this product.

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment and sepsis, or in patients with malnutrition or other sources of glutathione deficiency (e.g. chronic alcoholism) who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If HAGMA due to pyroglutamic acidosis is suspected, prompt

discontinuation of paracetamol and close monitoring is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.

This medicine contains aspartame (a source of phenylalanine), which may be harmful for people with phenylketonuria (PKU).

Patients with rare hereditary problems of galactose intolerance; the Lapp lactose deficiency or glucose-galactose malabsorption should be advised not to take this medicine.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially "sodium free".

4.5 Interaction with other medicinal products and other forms of interaction

Aspirin, paracetamol and caffeine combination medicines should not be used together with other non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin and cyclo-oxygenase-2 specific inhibitors as these may increase the risk of adverse effects. Aspirin, paracetamol and caffeine combination medicines should be used with caution when taken in combination with the following drugs as interactions have been reported:

Aspirin:

Other NSAIDs and corticosteroids: Do not use in combination with other NSAIDs as these may increase the risk of adverse effects.

Thrombolytics: There is an increased risk of bleeding. Particularly, treatment with aspirin should not be initiated within the first 24 hours after treatment with alteplase in acute stroke patients. Concomitant use is therefore not recommended. (see Warnings and Precautions).

Uricosurics (e.g. probenecid, sulfinpyrazone): Aspirin may reduce the activity of uricosurics (e.g. probenecid, sulfinpyrazone) due to inhibition of tubular resorption, leading to high plasma levels of aspirin.

Loop diuretics (e.g. furosemide), diuretics and antihypertensive agents: Aspirin may reduce the activity of loop diuretics (e.g., furosemide) due to competition and inhibition of urinary prostaglandins. NSAIDs can cause acute kidney failure, especially in dehydrated patients. If a diuretic is administered simultaneously with aspirin, it is necessary to ensure adequate hydration of the patient and to monitor the kidney function and blood pressure, particularly when starting diuretic treatment.

Like other NSAIDs, concomitant use of aspirin with diuretics or antihypertensive agents (e.g., beta-blockers, angiotensin converting enzyme (ACE) inhibitors) may cause a decrease in their antihypertensive effect. Therefore, the combination should be administered with caution and patients, especially the elderly, should have their blood pressure periodically monitored. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy and periodically thereafter, particularly for diuretics and ACE inhibitors, due to the increased risk of nephrotoxicity. Concomitant treatment with potassium-sparing drugs may be associated with increased serum potassium levels, which should therefore be monitored frequently.

Anticoagulants: Aspirin may enhance the effects of oral anticoagulants, such as heparin and coumarins, and of platelet aggregation inhibitors, such as ticlopidine, clopidogrel, and cilostazol, as there is an increased risk of bleeding. Clinical and laboratory monitoring of the bleeding time and prothrombin time should be performed. Metoclopramide: Metoclopramide increases the rate of absorption of aspirin.

However, concurrent use need not be avoided.

Phenytoin: Aspirin increases phenytoin serum levels; serum phenytoin should be well monitored.

Valproate: Aspirin inhibits valproate metabolism and hence could increase its toxicity; valproate levels should be well monitored

Methotrexate $\leq$ 15 mg/week: The toxicity of methotrexate may be enhanced by

concomitant use of aspirin. In case of concomitant use with aspirin, renal function should be monitored.

Sulphonylureas: Aspirin increases the hypoglycaemic effect of sulphonylureas, thus some downward readjustment of the dosage of the antidiabetic may be appropriate if large doses of salicylates are used. Increased blood glucose controls are recommended.

Alcohol: Co-administration of alcohol and aspirin increases the risk of gastrointestinal haemorrhage. **Antacids:** Antacids may increase the excretion of aspirin by alkalization of the urine.

Selective Serotonin Re-Uptake Inhibitors (SSRIs): Concurrent use of aspirin and SSRIs can increase the risk of gastrointestinal bleeding.

Paracetamol:

Cholestyramine: The speed of absorption of paracetamol is reduced by cholestyramine. Therefore the cholestyramine should not be taken within one hour if maximal analgesia is required.

Metoclopramide and Domperidone: The speed of absorption of paracetamol is increased by metoclopramide and domperidone. However, concurrent use need not be avoided.

Warfarin: The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

Caffeine:

Lithium: Caffeine can increase the elimination of lithium from the body. Concomitant use is therefore not recommended. **Flucloxacillin:**

Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been

associated with high anion gap metabolic acidosis due to pyroglutamic acidosis, especially in patients with risks factors (see section 4.4)

4.6 Fertility, pregnancy and lactation

Fertility

Aspirin

There is some evidence that medicinal products that inhibit cyclo-oxygenase / prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment. However, no accurate data are available on when the reversibility of fertility effects occur after the treatment is suspended. Caution should be exercised when used by women who are planning on becoming pregnant.

Pregnancy

Not recommended for use during pregnancy. This medicine is contraindicated during the third trimester of pregnancy (see Contraindications).

Aspirin

Aspirin should be avoided in the first two trimesters of pregnancy unless the potential benefit to the mother outweighs the risk to the foetus in the view of the treating physician. Aspirin is contraindicated during the third trimester of pregnancy as there is a risk of premature closure of the foetal ductus arteriosus with possible persistent pulmonary hypertension (see Contraindications) and a risk of foetal renal impairment with subsequent oligohydramnios. The onset of labour may be delayed and its duration increased with an increased risk of bleeding tendency in both the mother and child. If the expected benefit to the mother is greater than the possible risk to the foetus, the lowest effective dose and the shortest duration of treatment should be considered.

Paracetamol:

A large amount of data on pregnant women indicate neither malformative, nor fetoneonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed,

paracetamol can be used during pregnancy however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency.

Caffeine:

Caffeine is not recommended for use during pregnancy due to the possible increased risk of spontaneous abortion associated with caffeine consumption.

Lactatio

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Aspirin

Aspirin appears in breast milk, and regular high doses may affect neonatal clotting. Not recommended while breast feeding due to possible risk of Reye's Syndrome as well as neonatal bleeding due to hypoprothrombinaemia.

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Paracetamol

Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding.

Caffeine

Caffeine appears in breast milk. Irritability and poor sleeping pattern in the infant have been reported.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

The following convention has been utilised for the classification of the frequency of adverse reactions: very common ($\geq 1/10$), common ($\geq 1/100$, $< 1/10$), uncommon ($\geq 1/1,000$, $< 1/100$), rare ($\geq 1/10,000$, $< 1/1000$), very rare ($< 1/10,000$), not known (cannot be estimated from available data).

Adverse reactions from historical clinical trial data are both infrequent and from small patient exposure. Accordingly, events reported from extensive post-marketing experience at therapeutic/labeled dose and considered attributable are tabulated below by MedDRA System Organ Class. As these reactions are reported voluntarily from a population of uncertain size, the frequency of these reactions is not known but likely to be rare or very rare ($< 1/1000$).

Adverse events are more likely to occur with increasing dose and duration of use.

MedDRA SOC	Adverse Reaction	Frequency
Aspirin		
Blood and lymphatic system disorders	Prolonged bleeding time, thrombocytopenia, ecchymosis.	Not known
Immune system disorders	Hypersensitivity reactions (e.g. anaphylaxis, angioedema, bronchospasm, urticaria, skin reactions and rhinitis).	Not known
Respiratory, thoracic and mediastinal disorders	Aspirin-exacerbated respiratory disease	Very rare
Metabolism and Nutrition disorders	Sodium and fluid retention.	Not known
Ear and labyrinth disorders	Temporary hearing loss, tinnitus.	Not known
Gastrointestinal disorders	Gastrointestinal haemorrhage, gastrointestinal ulceration, vomiting, gastritis, nausea, and dyspepsia.	Not known
Hepatobiliary disorders	Reye's syndrome (see Warnings and Precautions). Elevation in aminotransferase levels.	Not known
Renal and urinary disorders	Renal dysfunction, increased blood uric acid levels.	Not known

Paracetamol		
Blood and lymphatic system disorders	Thrombocytopenia.	Very rare
Immune system disorders	Anaphylaxis Cutaneous hypersensitivity reactions including, among others, skin rashes, angioedema, Stevens-Johnson syndrome and Toxic Epidermal Necrolysis.	Very rare
Respiratory, thoracic and mediastinal disorders	Bronchospasm in patients sensitive to aspirin and other NSAIDs.	Very rare
Hepatobiliary disorders	Hepatic dysfunction.	Very rare
Metabolism and Nutrition Disorders	High anion gap metabolic acidosis Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.	Not known
Caffeine		
Central Nervous System	Dizziness, headache.	Not known
Cardiac disorders	Palpitation.	Not known
Psychiatric disorders	Insomnia, restlessness, anxiety and irritability, nervousness.	Not known
Gastrointestinal disorders	Gastrointestinal disturbances.	Not known
<i>When the recommended aspirin-paracetamol-caffeine dosing regimen is combined with dietary caffeine intake, the resulting higher dose of caffeine may increase the potential for caffeine-related adverse effects.</i>		

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to the marketing authorisation holder, or, if available, via the national reporting system.

4.9 Overdose

This product contains both paracetamol and aspirin, and as such, any overdose events should be assessed using information available on both active substances. Liver damage is possible in adults who have taken 10g or more of paracetamol. Adults who have consumed more than 5g of paracetamol, may experience liver damage if they have one of the following risk factors:

- long term treatment with either anti-infectives, anti-epileptics or St John's Wort, or any other drugs that induce liver enzymes
- regular consumption of ethanol in excess of recommended amounts
- likely to be glutathione deplete e.g. eating disorder, cystic fibrosis, HIV infection, starvation, cachexia.

Salicylate poisoning is usually associated with plasma concentrations >350mg/L (2.5mmol/L). Most adult deaths occur in patients whose concentrations exceed 700mg/L (5.1mmol/L).

Single doses less than 100mg/kg are unlikely to cause serious poisoning.

Symptoms: Common features exist for both active substances when taken in overdose, but these can be tabulated as follows:

Paracetamol	Aspirin	Caffeine
Symptoms of paracetamol overdose in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage is possible in adults who have taken 10g or more of paracetamol. Adults who have consumed more than 5g of paracetamol, may experience liver damage if they have one of the following risk factors: •long term treatment with either anti-infectives, anti-epileptics or St John's Wort, or any other drugs that induce liver enzymes •regular consumption of ethanol in excess of recommended amounts •likely to be glutathione deplete e.g. eating disorder, cystic fibrosis, HIV infection, starvation, cachexia Symptoms of paracetamol overdose after 12-48 hours are: •Liver damage •Abnormalities of glucose metabolism and metabolic acidosis •Severe poisoning: Hepatic failure may progress to Encephalopathy, Haemorrhage, Hypoglycaemia, cerebral oedema, and death. •With or without severe liver damage: Acute renal failure with acute tubular necrosis strongly suggested by loin pain, haematuria and proteinuria.	Common: Vomiting, Dehydration, Tinnitus, Vertigo, Deafness Sweating Warm extremities with bounding pulses Increased respiratory rate Hyperventilation Acid base disturbance Mixed respiratory alkalosis and metabolic acidosis with normal or high arterial pH (normal or reduced hydrogen ion concentration) in adults and children aged over 4 years. In children aged 4 years or less, a dominant metabolic acidosis with low arterial pH (raised hydrogen ion concentration) is common. Acidosis can increase salicylate transfer across the blood brain barrier. Uncommon: Haematemesis, Hyperpyrexia Hypoglycaemia, Hypokalaemia Thrombocytopenia, Increased INR/PTR Intravascular coagulation, Renal failure Non-cardiac pulmonary oedema Confusion, disorientation, coma and convulsions are more common in children than adults.	Other symptoms of overdosage, associated with the caffeine component, include: CNS stimulation; agitation, anxiety, nervousness, restlessness, insomnia, excitement, muscle twitching, confusion, convulsions Cardiac: tachycardia, cardiac arrhythmia Gastric: Abdominal or stomach pains, vomiting Other: diuresis, facial flushing For clinically significant symptoms of caffeine overdose to occur with this product, the amount ingested would be associated with serious paracetamol-related liver toxicity.

Management

Paracetamol:

Immediate treatment is essential in the management of overdose due to the paracetamol content of the product.

If overdose is confirmed or suspected, seek immediate advice from your Poison Centre and refer patient to nearest Emergency Medical Centre for management and expert treatment. This should happen even in patients without symptoms or signs of overdose due to the risk of delayed liver damage. Where a Poison Information Centre is not available, refer patient to the nearest Emergency Medical Centre for management and expert treatment.

There may be few or no initial symptoms, and these can be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines, see BNF overdose section.

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour.

Plasma paracetamol concentrations should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable).

Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol; however, the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after this time. If required the patient should be given intravenous N-acetylcysteine, in line with the

established dosage schedule. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital.

Management of patients who present with serious hepatic dysfunction, or are under 10 years or over 70, beyond 24h from ingestion should be discussed with the National Poisons Information Service (NPIS) or a liver unit.

Salicylates:

Give activated charcoal if an adult presents within one hour of ingestion of more than 120 mg/kg. Plasma salicylate concentrations should be measured although the severity of poisoning cannot be determined from this alone and the clinical and biochemical features must be taken into account.

Elimination of aspirin is increased by urinary alkalisation, which is achieved by the administration of 1.26% sodium bicarbonate. The urine pH should be monitored.

Metabolic acidosis should be corrected with intravenous 8.4% sodium bicarbonate (first check serum potassium). Forced diuresis should not be used since it does not enhance salicylate excretion and may cause pulmonary oedema.

Haemodialysis is the treatment of choice for severe poisoning and should be considered in patients with plasma salicylate concentrations >700mg/L (5.1mmol/L), or lower concentrations associated with severe clinical or metabolic features.

Patients under 10 years or over 70 years of age may be at an increased risk of salicylate toxicity and may require dialysis at an earlier stage.

Caffeine:

Treatment of caffeine overdose is primarily symptomatic and supportive. Diuresis should be treated by maintaining fluid and electrolyte balance and CNS symptoms can be controlled by intravenous administration of diazepam.

5. Pharmacological properties

5.1 Pharmacodynamic

properties ASPIRIN

Mechanisms of action/effect

Salicylates inhibit the activity of the enzyme cyclo-oxygenase to decrease the formation of precursors of prostaglandins and thromboxanes from arachidonic acid. Although many of the therapeutic effects may result from inhibition of prostaglandin synthesis (and consequent reduction of prostaglandin activity) in various tissues, other actions may also contribute significantly to the therapeutic effects.

Analgesic

Produces analgesia through a peripheral action by blocking pain impulse generation and via a central action, possibly in the hypothalamus.

Anti-inflammatory (Non-steroidal)

Exact mechanisms have not been determined. Salicylates may act peripherally in inflamed tissue probably by inhibiting the synthesis of prostaglandins and possibly by inhibiting the synthesis and/or actions of other mediators of the inflammatory response.

Antipyretic

May produce antipyresis by acting centrally on the hypothalamic heat regulating centre to produce peripheral vasodilation resulting in increased cutaneous blood flow, sweating and heat loss.

PARACETAMOL

Mechanism of action/effect

Analgesic - the mechanism of analgesic action has not been fully determined.

Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the central nervous system (CNS) and, to a lesser extent, through a peripheral action by blocking pain-impulse generation.

The peripheral action may also be due to inhibition of prostaglandin synthesis or to inhibition of the synthesis or actions of other substances that sensitize pain receptors to mechanical or chemical stimulation.

Antipyretic - paracetamol probably produces antipyresis by acting centrally on the hypothalamic heat-regulation centre to produce peripheral vasodilation resulting in

increased blood flow through the skin, sweating, and heat loss. The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus.

CAFFEINE

Mechanisms of action/effect

Central nervous system stimulant - caffeine stimulates all levels of the CNS, although its cortical effects are milder and of shorter duration than those of amphetamines.

Analgesia adjunct

Caffeine constricts cerebral vasculature with an accompanying decrease in the cerebral blood flow and in the oxygen tension of the brain. It is believed that caffeine helps to relieve headache by providing more rapid onset of action and/or enhanced pain relief with lower doses of analgesic. Recent studies with ergotamine indicate that the enhancement of effect by the addition of caffeine may also be due to improved gastrointestinal absorption of ergotamine when administered with caffeine.

5.2 Pharmacokinetic

properties ASPIRIN

Absorption and fate

Absorption is generally rapid and complete following oral administration. It is largely hydrolysed in the gastrointestinal tract, liver and blood to salicylate which is further metabolised primarily in the liver.

PARACETAMOL

Absorption and Fate

Paracetamol is readily absorbed from the gastro-intestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion. It is metabolised in the liver and excreted in the urine mainly as the glucuronide and sulfate conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half-life varies from about 1 to 4 hours. Plasma-protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.

A minor hydroxylated metabolite which is usually produced in very small amounts by mixed-function oxidases in the liver and which is usually detoxified by conjugation with liver glutathione may accumulate following paracetamol overdosage and cause liver damage.

CAFFEINE

Absorption and fate

Caffeine is completely and rapidly absorbed after oral administration with peak concentrations occurring between 5 and 90 minutes after dose in fasted subjects. There is no evidence of pre-systemic metabolism. Elimination is almost entirely by hepatic metabolism in adults.

In adults, marked individual variability in the rate of elimination occurs. The mean plasma elimination half life is 4.9 hours with a range of 1.9 - 12.2 hours. Caffeine distributes into all body fluids. The mean plasma protein binding of caffeine is 35%. Caffeine is metabolised almost completely via oxidation, demethylation and acetylation and is excreted in the urine. The major metabolites are 1-methylxanthine, 7-methylxanthine, 1,7-dimethylxanthine (paraxanthine). Minor metabolites include 1-methyluric acid and 5-acetylamino-6-formylamino-3-methyluracil (AFMU).

5.3 Preclinical safety data

Non-clinical safety data on aspirin, paracetamol and caffeine have not revealed findings which are of relevance to the recommended dosage and use of the product and which are not already addressed in the clinical data section. (See Fertility, Pregnancy and Lactation)

6. Pharmaceutical particulars

6.1 List of excipients

- Maize Starch BP
- Gelatin BP
- Propyl Hydroxy Benzoate BP

- Purified Water BP
- Colloidal Silicon Dioxide USP/NF
- Maize Starch BP
- Microcrystalline Cellulose BP
- Croscarmellose Sodium USP/NF
- Purified Talc BP
- Stearic Acid BP

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in a cool and dry place below 30°C. Protect from direct sunlight. Keep medicine out of reach of children.

6.5 Nature and contents of container

50 strips containing 2 tablets in a carton and 10 strips containing 2 tablets in a carton.

6.6 Special precautions for disposal and other handling

No special requirement

7. Marketing authorisation holder

SHALINA

HEALTHCARE

DMCC, 30th Floor,

Almas Towers,

Jumeirah Lakes

Towers Dubai-UAE.

Manufacturing Site

Address:

Bal Pharma Limited,

21 & 22,

Bommasandra

Industrial Area,

Bangalore-560 099,

India

8. Marketing authorisation number(s)

H2008/18960/173/R1

9. Date of first authorisation/renewal of the authorisation

22/06/2026

10. Date of revision of the text

22/06/2026