1.3 Product Information

1.3.1 Summary of Product Characteristics (SmPC) - Enclosed

SHALSPIRIN CV 75 MG TABLETS

(Aspirin Delayed- Release Tablets USP 75 mg)

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Shalspirin CV 75 mg Tablets (Aspirin Delayed- Release Tablets USP 75 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sr. No.	Name of constituent	Quantity per Tablet
1	Aspirin (Granules) 7017 USP	75.00 mg
2	Microcrystalline Cellulose BP	7.50 mg
3	Colloidal Anhydrous Silica BP	1.00 mg
4	Stearic Acid 1843 Powder USPNF	7.50 mg
5	Wincoat WT-TR-5002 Clear Transparent IH	6.00 mg
6	Isopropyl Alcohol BP#	45.60 mg
7	Methylene Chloride BP #	68.40 mg
8	Wincoat WT-NAQ-1008 White IH	24.00 mg
9	Dummy Granules (White to off white coloured granules) IH (Lactose BP & Maize Starch BP)	158.84 mg

Does not appear in final product

Definitions:

BP: British Pharmacopoeia

USP: United State Pharmacopoeia

IH: In-House Specifications

3. PHARMACEUTICAL FORM

Tablets (Oral)

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the secondary prevention of thrombotic cerebrovascular or cardiovascular disease and following by-pass surgery

4.2 Posology and method of administration

For the management of cardiovascular or cerebrovascular disease: The advice of a doctor should be sought before commencing therapy for the first time. The usual dosage, for long term use, is 75-150mg once daily. In some circumstances a higher dose may be appropriate, especially in the short term, and up to 300mg a day may be used on the advice of a doctor. In general, Aspirin should be used with caution in elderly patients who are more prone to adverse events. The usual adult dose is recommended in the absence of severe renal or hepatic insufficiency.

Treatment should be reviewed at regular intervals.

These tablets should be taken orally with a drink of water.

Children: Shalspirin CV Tablets BP 75mg is not indicated for use in children and young people less than 16 years of age.

Method of administration: Oral

4.3 Contraindications

- Hypersensitivity to salicylic acid compounds or prostaglandin synthetase inhibitors (e.g. certain asthma patients who may suffer an attack or faint and certain patients who may suffer from bronchospasm, rhinitis and urticaria) and to any of the excipients;
- Active, or history of recurrent peptic ulcer and/or gastric/intestinal haemorrhage, or other kinds of bleeding such as cerebrovascular haemorrhages;
- Haemorrhagic diathesis; coagulation disorders such as haemophilia and thrombocytopenia;
- Patients who are suffering from gout;
- Severe hepatic impairment;
- Severe renal impairment;
- Doses >100 mg/day during the third trimester of pregnancy; Methotrexate used at doses >15mg/week

4.4 Special warnings and precautions for use

- Shalspirin CV Tablets 75 mg is not suitable for use as an anti-inflammatory/ analgesic/antipyretic.
- Recommended for use in adults and adolescents from 16 years of age. This medicinal product is not recommended for use in adolescents/children under 16 years unless the expected benefits outweigh the risks. Aspirin may be a contributory factor in the causation of Reye's Syndrome in some children.
- There is an increased risk of haemorrhage particularly during or after operative procedures (even in cases of minor procedures, e.g. tooth extraction). Use with caution before surgery, including tooth extraction. Temporary discontinuation of treatment may be necessary.
- Shalspirin CV Tablets 75mg is not recommended during menorrhagia where it may increase menstrual bleeding.
- Shalspirin CV Tablets 75mg is to be used with caution in cases of hypertension and when patients have a past history of gastric or duodenal ulcer or haemorrhagic episodes or are undergoing therapy with anticoagulants.
- Patients should report any unusual bleeding symptoms to their physician. If gastrointestinal bleeding or ulceration occurs the treatment should be withdrawn.

- Aspirin should be used with caution in patients with moderately impaired renal or hepatic function (contraindicated if severe), or in patients who are dehydrated since the use of NSAIDs may result in deterioration of renal function. Liver function tests should be performed regularly in patients presenting slight or moderate hepatic insufficiency.
- Aspirin may promote bronchospasm and asthma attacks or other hypersensitivity reactions. Risk factors are existing asthma, hay fever, nasal polyps or chronic respiratory diseases. The same applies for patients who also show allergic reaction to other substances (e.g. with skin reactions, itching or urticaria).
- Serious skin reactions, including Steven-Johnsons syndrome, have rarely been reported in association with the use of acetylsalicylic acid. Shalspirin CV Tablets 75mg should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.
- Elderly patients are particularly susceptible to the adverse effects of NSAIDs, including Aspirin especially gastrointestinal bleeding and perforation which may be fatal. Where prolonged therapy is required, patients should be reviewed regularly.
- Concomitant treatment with Shalspirin CV Tablets 75mg and other drugs that alter haemostasis (i.e. anticoagulants such as warfarin, thrombolytic and antiplatelet agents, anti-inflammatory drugs and selective serotonin reuptake inhibitors) is not recommended, unless strictly indicated, because they may enhance the risk of haemorrhage. If the combination cannot be avoided, close observation for signs of bleeding is recommended.
- Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration, such as oral corticosteroids, selective serotonin-reuptake inhibitors and deferasirox. Aspirin in low doses reduces uric acid excretion. Due to this fact, patients who tend to have reduced uric acid excretion may experience gout attacks.
- The risk of hypoglycaemic effect with sulfonylureas and insulins may be potentiated with Shalspirin CV Tablets 75mg taken at over dosage.
- Shalspirin CV should be avoided in late pregnancy and generally during breast feeding.
- Shalspirin CV Tablets 75mg contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Pregnancy:

During the first and second trimester of pregnancy, Aspirin should not be given unless clearly necessary. If Aspirin is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:

- Cardiopulmonary toxicity (with premature closure of the ductusarteriosus and pulmonary hypertension);
- Renal dysfunction, which may progress to renal failure with oligo-hydroamniosis; the mother and the neonate, at the end of pregnancy, to:
- Possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses.
- Inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently, Aspirin at doses of 100 mg/day and higher is contraindicated during the third trimester of pregnancy.

Lactation:

Low quantities of salicylates and of their metabolites are excreted into the breast milk. Since adverse effects for the infant have not been reported up to now, short-term use of the recommended dose does not require suspending breastfeeding. In cases of long-term use and/or administration of higher doses, breastfeeding should be discontinued.

4.5 Interaction with other medicinal products and other forms of interaction

Contraindicated combinations:

Methotrexate (used at doses >15mg/week): The concomitant use of methotrexate (at doses >15mg/week) with Shalspirin CV Tablets BP 75mg is contraindicated.

Not recommended combinations:

Uricosuric agents, e.g. probenecid: Salicylates reverse the effect of probenecid. The combination should be avoided.

Combinations requiring precautions for use or to be taken into account

Anticoagulants e.g. coumarin, heparin, warfarin and phenindione: Increased risk of bleeding due to inhibited thrombocyte function, injury of the duodenal mucosa and displacement of oral anticoagulants from their plasma protein binding sites. The bleeding time should be monitored.

Anti-platelet agents (e.g clopidogrel and dipyridamole) and selective serotonin re-uptake inhibitors (SSRIs; such as sertraline or paroxetine): Increased risk of gastrointestinal bleeding.

Antidiabetics, e.g. sulphonylureas: Salicylics may increase the hypoglycaemic effect of sulphonylureas.

Digoxin and lithium: Aspirin impairs the renal excretion of digoxin and lithium, resulting in increased plasma concentrations. Monitoring of plasma concentrations of digoxin and lithium is recommended when initiating and terminating treatment with acetylsalicylic acid. Dose adjustment may be necessary.

Diuretics and antihypertensives: NSAIDs may decrease the antihypertensive effects of diuretics and other antihypertensive agents. As for other NSAIDs concomitant administration with ACE-inhibitors increases the risk of acute renal insufficiency.

Diuretics: Risk of acute renal failure due to the decreased glomerular filtration via decreased renal prostaglandin synthesis. Hydrating the patient and monitoring renal function at the start of the treatment is recommended.

Carbonic anhydrase inhibitors (acetazolamide): May result in severe acidosis and increased central nervous system toxicity.

Systemic corticosteroids: The risk of gastrointestinal ulceration and bleeding may be increased when Aspirin and corticosteroids are co-administered.

Methotrexate (used at doses <15mg/week): The combined drugs, methotrexate and acetylsalicylic acid, may increase haematological toxicity of methotrexate due to decreased renal clearance of methotrexate by acetylsalicylic acid.

Increased risk of ulcerations and gastrointestinal bleeding due to synergistic effects.

Ibuprofen: Experimental data suggest that ibuprofen may inhibit the effect of low dose Aspirin on platelet aggregation when they are dosed concomitantly. 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.

Ciclosporin, tacrolimus: Concomitant use of NSAIDs and ciclosporin or tacrolimus may increase the nephrotoxic effect of ciclosporin and tacrolimus. The renal function should be monitored in case of concomitant use of these agents and acetylsalicylic acid.

Valproate: Aspirin has been reported to decrease the binding of valproate to serum albumin, thereby increasing its free plasma concentrations at steady state.

Phenytoin (an antiepileptic): Salicylate diminishes the binding of phenytoin to plasma albumin. This may lead to decreased total phenytoin levels in plasma, but increased free phenytoin fraction. The unbound concentration, and thereby the therapeutic effect, does not appear to be significantly altered.

Alcohol: Concomitant administration of alcohol and Aspirin increases the risk of gastrointestinal bleeding. Antacids will reduce the effect of Shalspirin CV. Principle incompatibilities are iron salts, carbonates and alkali hydroxides.

4.6 Pregnancy and lactation

Pregnancy:

During the first and second trimester of pregnancy, Aspirin should not be given unless clearly necessary. If Aspirin is used by a woman attempting to conceive, or during the first and second

trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

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Lactation:

Low quantities of salicylates and of their metabolites are excreted into the breast milk. Since adverse effects for the infant have not been reported up to now, short-term use of the recommended dose does not require suspending breastfeeding. In cases of long-term use and/or administration of higher doses, breastfeeding should be discontinued.

4.7 Adverse Reactions

Side effects are grouped on the basis of System Organ Class. Within each system organ class the frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000) and not known (cannot be estimated from the available data)

Blood and lymphatic system disorders	Common	Increased bleeding tendencies
	Rare	Thrombocytopenia, Granulocytosis, aplastic anaemia.
	Not Known	Cases of bleeding with prolonged bleeding time such as epistaxis, gingival bleeding. Symptoms may persist for a period of 4–8 days after Aspirin discontinuation. As a result there may be an increased risk of bleeding during surgical procedures. Existing (haematemesis, melaena) or occult gastrointestinal bleeding, which may lead to iron deficiency anaemia (more common at higher doses).
Immune system disorders	Rare	Hypersensitivity reactions angio-oedema, allergic oedema, anaphylactic reactions including shock.
Metabolism and digestive system disorders	Not known	Hyperuricemia
Nervous system disorders	Rare	Intracranial haemorrhage
	Not known	Headache, vertigo
Ear and labyrinth disorders	Not known	Reduced hearing ability; tinnitus
Vascular disorders	Rare	Hemorrhagic vasculitis
Respiratory, thoracic and mediastinal disorders	Uncommon	Rhinitis, dyspnoea
	Rare	Bronchospasm, asthma attacks
Reproductive system and mammary disorders	Rare	Menorrhagia
	Not known	Stevens-Johnson syndrome
Gastrointestinal disorders	Common	Dyspepsia
	Rare	Severe gastrointestinal haemorrhage, nausea, vomiting
	Not known	Gastric or duodenal ulcers and perforation, diarrhoea
Hepatobiliary disorders	Not known	Hepatic insufficiency
Skin and subcutaneous tissue disorders	Uncommon	Urticaria
	Rare	Steven-Johnsons syndrome, Lyells syndrome, purpura, erythema nodosum, erythemamultiforme
Renal and urinary tract disorders	Not known	Impaired renal function, salt and water retention

4.8 Symptoms of Overdosage & Treatment

- Salicylate poisoning is usually associated with plasma concentrations >350mg/L (2.5 mmol/L). Most adult deaths occur in patients whose concentrations exceed 700mg/L (5.1 mmol/L). Single doses less than 100mg/kg are unlikely to cause serious poisoning.
- Common features of salicylate poisoning include vomiting, dehydration, tinnitus, vertigo, deafness, sweating, warm extremities with bounding pulses, increased respiratory rate and hyperventilation. Some degree of acid-base disturbance is present in most cases.
- A mixed respiratory alkalosis and metabolic acidosis with normal or high arterial pH (normal or reduced hydrogen ion concentration) is usual in adults and children over the age of 4 years. In children aged 4 years or less, a dominant metabolic acidosis with low arterial pH (raised hydrogen ion concentration) is common. Acidosis may increase salicylate transfer across the blood brain barrier.
- Uncommon features of salicylate poisoning include haematemesis, hyperpyrexia, hypoglycaemia, hypokalaemia, thrombocytopaenia, increased INR/PTR, intravascular coagulation, renal failure and non-cardiac pulmonary oedema.
- Central nervous system features including confusion, disorientation, coma and convulsions, are less common in adults than in children.
- Give activated charcoal if an adult presents within one hour of ingestion of more than 250mg/kg. The plasma salicylate concentration 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 is increased by urinary alkalinisation, which is achieved by the administration of 1.26% sodium bicarbonate.
- The urine pH should be monitored. Correct metabolic acidosis 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.

5. PHARMACOLOGICAL PROPERTIES

Pharmacological action:

Aspirin has an antithrombotic action which is mediated through inhibition of platelet activation.

Pharmacotherapeutic Group: Antithrombotic agents, platelet aggregation inhibitors.

ATC Code: B01AC06

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: ATC Code: B01AC06 Antithrombotic agents, platelet aggregation inhibitors.

Mechanism of action: Aspirin inhibits platelet aggregation by inactivation of platelet cyclo-oxygenase, the enzyme that produces the cyclic endoperoxide precursor of Thromboxane A2. Thromboxane A2 is a powerful inducer of platelet aggregation and vasoconstriction.

5.2 Pharmacokinetic properties

Non ionised Aspirin is absorbed from the stomach. There is also absorption of acetylsalicylates from the intestines. Aspirin appears rapidly in all body tissues. It does cross the placenta and appears in breast milk and it is moderately bound to plasma proteins. Excretion is a salicylic acid and as compounds in the urine and increases as the pH rises.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline Cellulose BP, Colloidal Anhydrous Silica BP, Stearic Acid 1843 Powder USPNF, Wincoat WT-TR-5002 Clear Transparent IH, Isopropyl Alcohol BP, Methylene Chloride BP, Wincoat WT-NAQ-1008 White IH, Dummy Granules (White to off white coloured granules) IH (Lactose BP & Maize Starch BP)

6.2 Incompatibilities

None

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 30°C. Keep out of reach of children. Store in the original package in order to protect from sunlight and moisture

6.5 Nature and contents of container

Blister Pack of 10 Tablets and such 03 blisters are packed in inner carton along with pack insert.

7. MARKETING AUTHORISATION HOLDER

M/s SHALINA HEALTHCARE DMCC

Physical and Postal Address:

30th Floor, Almas Towers,

Jumeirah Lakes Towers Dubai-UAE.

Country: Dubai

8. MARKETING AUTHORISATION IN OTHER COUNTRIES

Product is registered in Democratic Republic of Congo.