SUMMARY OF PRODUCT CHARACTERISTICS

1.1 Name of the finished pharmaceutical product : MEFTAL – SPAS TABLET

(Invented) name of the medicinal product : Mefenamic Acid and Dicyclomine Hydrochloride Tablets.

1.2 Strength : Mefenamic Acid 250 mg & Dicyclomine Hydrochloride 10mg/ Tablet

1.3 Pharmaceutical form : Oral Solid (Uncoated Tablet)

2. Qualitative and Quantitative composition

Qualitative declaration :

Each Uncoated Tablet Contains :

Mefenamic Acid BP ..... 250 mg

Dicyclomine Hydrochloride BP ..... 10 mg

Excipients ..... q.s.

2.1 Quantitative declaration :

Sr. No	Name of API	Grade	Label claim per Tab in mg	Overages (%)	Input Qty / Tab in mg
1.	Mefenamic Acid	BP	Mefenamic Acid 250 mg	--	250.00
2.	Dicyclomine Hydrochloride	BP	Dicyclomine Hydrochloride 10 mg	--	10.00

3. Pharmaceutical form :

Pale yellow, circular, flat, beveled, uncoated tablets with inscription of a circle and 'MEFTAL – SPAS' embossed on both side.

Packed in printed aluminium / amber coloured PVC blister strip with 'MEFTAL – SPAS ' embossed on PVC side.

4. Clinical particulars :

4.1 Therapeutic indications :

MEFTAL-SPAS Tablets are indicated for symptomatic treatment of:

- Primary spasmodic dysmenorrhea
- IUCD-induced spasm and pain
- Abdominal colic, renal colic, and biliary colic

4.2 Posology and method of administration :

For oral administration: Adults and adolescents: 1 to 2 tablets three times daily or, as prescribed by the physician. Tablets should be taken preferably with or after food.

Therapy should not be given for longer than 7 days at a time.

4.3 Method of administration : By oral route

4.4 Contraindications :

- Known hypersensitivity to mefenamic acid, dicyclomine, or any other ingredients of the formulation
- Pre-existing asthma and aspirin-sensitive asthma
- Active ulceration/bleeding or chronic inflammation of upper or lower GI tract
- Treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery
- Pre-existing renal disease/obstructive uropathy
- Glaucoma
- Myasthenia gravis
- Last trimester of pregnancy
- Lactation

4.5 Special warnings and precautions for use :

MEFENAMIC ACID:

Cardiovascular Effects

I.Cardiovascular Thrombotic Events

Clinical trials of several COX-2 selective and nonselective NSAIDs of up to 3 years duration have shown an increased risk of serious cardiovascular (CV) thrombotic events, myocardial infarction (MI), and stroke, which can be fatal. All NSAIDs, both COX-2 selective and nonselective, may have a similar risk. Patients with known CV disease or risk factors for CV disease may be at greater risk. To minimize the potential risk for an adverse CV event in patients treated with an NSAID, the lowest effective dose should be used for the shortest duration possible. Physicians and patients should remain alert for the development of such events, even in the absence of previous CV symptoms. Patients should be

informed about the signs and/or symptoms of serious CV events and the steps to take if they occur.

II.Hypertension

NSAIDs, including mefenamic acid, can lead to onset of new hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of CV events. Patients taking thiazides or loop diuretics may have impaired response to these therapies when taking NSAIDs. NSAIDS, including mefenamic acid, should be used with caution in patients with hypertension. Blood pressure should be monitored closely during the initiation of NSAID treatment and throughout the course of therapy.

III.Congestive Heart Failure and Edema

Fluid retention and edema have been observed in some patients taking NSAIDs. Mefenamic acid should be used with caution in patients with fluid retention or heart failure.

Gastrointestinal Effects-Risk of Ulceration, Bleeding, and Perforation: NSAIDs, including mefenamic acid, can cause serious GI adverse events including bleeding, ulceration, and perforation of the stomach, small or large intestine, which can be fatal. These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with NSAIDs. Therefore, NSAIDs should be prescribed with extreme caution in those with a prior history of ulcer disease or GI bleeding.

Renal Effects: Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injuries. Those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors, and the elderly are at

greater risk.

Hepatic Effects: Borderline elevations of one or more liver function tests may occur

in some patients receiving mefenamic acid. A patient with symptoms and/or signs suggestive of liver dysfunction, or in whom abnormal liver function tests have occurred, should discontinue the therapy immediately.

Hematological Effects: Anemia is sometimes seen in patients receiving NSAIDs, including mefenamic acid. Patients on long-term treatment with NSAIDs, including mefenamic acid, should have their hemoglobin or hematocrit checked, if they exhibit any signs or symptoms of anemia. NSAIDs inhibit platelet aggregation and have been shown to prolong bleeding time in some patients.

Pre-existing Asthma: Mefenamic acid should be used with caution in patients with pre-existing asthma. It should not be administered to patients with aspirin-sensitive asthma (including bronchospasm), since cross reactivity between aspirin and other NSAIDs has been reported.

DICYCLOMINE:

Cardiovascular Conditions: Dicyclomine hydrochloride needs to be used with caution in conditions characterized by tachyarrhythmia such as thyrotoxicosis, congestive heart failure and in cardiac surgery, where they may further accelerate the heart rate. Investigate any tachycardia before administration of dicyclomine hydrochloride. Care is required in patients with coronary heart disease, as ischemia and infarction may be worsened, and in patients with hypertension.

Peripheral and Central Nervous System: The peripheral effects of dicyclomine hydrochloride are a consequence of their inhibitory effect on muscarinic receptors of the autonomic nervous system. They include dryness of the mouth with difficulty in swallowing and talking, thirst, reduced bronchial secretions, dilatation of the pupils (mydriasis) with loss of accommodation (cycloplegia) and photophobia, flushing and dryness of the skin, transient bradycardia followed by tachycardia, with palpitations and arrhythmias, and difficulty in micturition, as well as reduction in the tone and motility of the gastrointestinal tract leading to constipation.

In the presence of high environmental temperature heat prostration can occur with drug use (fever and heat stroke due to decreased sweating). It should also be used cautiously in patients with fever. If symptoms occur, the drug should be discontinued and supportive measures instituted. Because of the inhibitory effect on muscarinic receptors within the autonomic nervous system, caution should be taken in patients with autonomic neuropathy.

Central nervous system (CNS) signs and symptoms include confusional state, disorientation, amnesia, hallucinations, dysarthria, ataxia, coma, euphoria, fatigue, insomnia, agitation and mannerisms, and inappropriate affect. Psychosis and delirium have been reported in sensitive individuals (such as elderly patients and/or in patients with mental illness) given anticholinergic drugs. These CNS signs and symptoms usually resolve within 12 to 24 hours after discontinuation of the drug.

Myasthenia Gravis: With overdosage, a curare-like action may occur (i.e., neuromuscular blockade leading to muscular weakness and possible paralysis). It should not be given to patients with myasthenia gravis except to reduce adverse muscarinic effects of an anticholinesterase.

Intestinal Obstruction: Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy. In this instance, treatment with this drug would be inappropriate and possibly harmful. Rarely, development of Ogilvie's syndrome (colonic pseudo-obstruction) has been reported. Ogilvie's syndrome is a clinical disorder with signs, symptoms, and radiographic appearance of an acute large bowel obstruction but with no evidence of distal colonic obstruction.

Toxic Dilatation of Intestine (megacolon): Toxic dilatation of intestine and intestinal perforation is possible when anticholinergic agents are administered in patients with Salmonella dysentery.

Ulcerative Colitis: Caution should be taken in patients with ulcerative colitis. Large doses may suppress intestinal motility to the point of producing a paralytic ileus and the use of this drug may precipitate or aggravate the serious complication of toxic megacolon. Dicyclomine is contraindicated in patients with severe ulcerative colitis.

Prostatic Hypertrophy: Dicyclomine should be used with caution in patients with known or suspected prostatic enlargement, in whom prostatic enlargement may lead to urinary retention.

4.6 Paediatric population

Not Applicable

4.7 Interaction with other medicinal products and other forms of interaction :

MEFENAMIC ACID:

Concurrent therapy with other plasma protein binding drugs may necessitate a modification in dosage.

Anti-coagulants: NSAIDs may enhance the effects of anti-coagulants, such as warfarin. Concurrent administration of mefenamic acid with oral anti-coagulant drugs requires careful monitoring of prothrombin time. NSAIDs in combination with warfarin or heparin should be taken under direct medical supervision.

Lithium: A reduction in renal lithium clearance and elevation of plasma lithium levels may occur. Therefore, patients should be observed carefully for signs of lithium toxicity.

The following interactions have been reported with NSAIDs but have not necessarily been associated with mefenamic acid:

Other analgesics including cyclooxygenase-2 selective inhibitors: Avoid concomitant use of two or more NSAIDs (including aspirin) as this may increase the risk of adverse effects.

Antidepressants: An increase in the risk of gastrointestinal bleeding has been observed with concomitant administration of Selective Serotonin Reuptake Inhibitors (SSRIs).

Antihypertensives and diuretics: A reduction in antihypertensive and diuretic effect has been observed. Diuretics can increase the nephrotoxicity of NSAIDs.

ACE inhibitors and angiotensin-II-receptor antagonists: A reduction in antihypertensive effect and an increased risk of renal impairment especially in elderly patients may be possible. Patients should be adequately hydrated and the renal function assessed in the beginning and during concomitant therapy.

Aminoglycosides: Reduction in renal function (in susceptible individuals); decreased elimination of aminoglycosides.

Anti-platelet agents: Increased risk of gastrointestinal ulceration or bleeding.

Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma cardiac glycoside levels.

Cyclosporine: The risk of nephrotoxicity of cyclosporine may be increased with NSAIDs.

Corticosteroids: Increased risk of gastrointestinal ulceration or bleeding is likely with concomitant use of NSAIDs.

Oral hypoglycaemic agents: Inhibition of metabolism of sulfonylurea drugs, with prolonged half-life and increased risk of hypoglycemia is likely.

Methotrexate: Elimination of the drug can be reduced, resulting in increased plasma levels of methotrexate.

Mifepristone: NSAIDs should not be taken for 8-12 days after mifepristone administration; NSAIDs can reduce the effects of mifepristone.

Probenecid: Reduction in metabolism and elimination of NSAIDs and metabolites may occur.

Quinolone antibiotics: Animal data indicates that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions.

Tacrolimus: Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.

Zidovudine: Increased risk of hematological toxicity when NSAIDs are given with zidovudine.

DICYCLOMINE:

Anti-glaucoma Agents: Anticholinergics antagonize the effects of antiglaucoma agents. Anticholinergic drugs in the presence of increased intraocular pressure may be hazardous when taken concurrently with agents such as corticosteroids. Use of dicyclomine in patients with glaucoma is not recommended.

Other Drugs with Anticholinergic Activity: The following agents may increase certain actions or side effects of anticholinergic drugs including dicyclomine: amantadine, antiarrhythmic agents of Class I (e.g., quinidine), antihistamines, antipsychotic agents (e.g., phenothiazines), benzodiazepines, MAO inhibitors, narcotic analgesics (e.g., meperidine), nitrates and nitrites, sympathomimetic agents, tricyclic antidepressants, and other drugs having anticholinergic activity.

Other Gastrointestinal Motility Drugs: Interaction with other gastrointestinal

motility drugs may antagonize the effects of drugs that alter gastrointestinal motility, such as metoclopramide.

Effect of Antacids: Because antacids may interfere with the absorption of anticholinergic agents including dicyclomine, simultaneous use of these drugs should be avoided.

Effect on Absorption of Other Drugs: Anticholinergic agents may affect gastrointestinal absorption of various drugs by affecting gastrointestinal motility, such as slowly dissolving dosage forms of digoxin; increased serum digoxin concentration may result.

Effect on Gastric Acid Secretion: The inhibitory effects of anticholinergic drugs on gastric acid secretion are antagonized by agents used to treat achlorhydria and those used to test gastric secretion.

4.8 Additional information on special populations :

Not Applicable

4.9 Paediatric population :

Not Applicable

4.10 Fertility, pregnancy and lactation :

MEFENAMIC ACID:

Pregnancy Category C. NSAIDs should not be used during the first two trimesters of pregnancy or labour unless the potential benefit to the patient outweighs the potential risk to the fetus.

Congenital abnormalities have been reported in association with administration of NSAIDs; however, these are low in frequency and do not appear to follow any discernible pattern. In view of the known effects of NSAIDs on the fetal cardiovascular system (risk of closure of the ductus arteriosus), use in the last trimester of pregnancy is contraindicated. The onset of labour may be delayed and the duration increased with an increased bleeding tendency in both mother and child.

DICYCLOMINE:

Pregnancy Category B. Epidemiological studies in pregnant women with products containing dicyclomine hydrochloride (at doses up to 40 mg/day) have not shown

that dicyclomine hydrochloride increases the risk of fetal abnormalities if administered during the first trimester of pregnancy. Reproduction studies have been performed in rats and rabbits at doses of up to 100 times the maximum recommended dose (based on 60 mg/day for an adult person) and have revealed no evidence of impaired fertility or harm to the fetus due to dicyclomine. Since the risk of teratogenicity cannot be excluded with absolute certainty for any product, the drug should be used during pregnancy only if clearly needed.

MEFTAL-SPAS Tablets should not be used during the first two trimesters of pregnancy or during labour unless the potential benefit to the patient outweighs the possible risk to the fetus. MEFTAL-SPAS Tablets are contraindicated for use in the third trimester of pregnancy.

Nursing Mothers

Trace amounts of mefenamic acid may be present in breast milk and transmitted to the nursing infant. But, the risk to the infant seems to be limited.

Dicyclomine has been reported to be excreted in human milk. Use of dicyclomine is contraindicated in nursing mothers.

Because of the potential for serious adverse reactions in nursing infants, MEFTAL-SPAS Tablets are contraindicated for use in lactation.

Pediatric Use

This formulation is not intended for use in children. Both, mefenamic acid and dicyclomine are not recommended in infants less than 6 months of age.

Use in Elderly

As with any NSAID, caution should be exercised regarding use of mefenamic acid in the elderly (65 years and older). This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to

monitor renal function.

Dicyclomine hydrochloride should be used with caution in elderly who may be more susceptible to its adverse effects.

Thus, MEFTAL-SPAS Tablets should be used with caution in geriatric patients.

Hepatic and Renal Impairment

MEFTAL-SPAS Tablets should be used with caution in patients with known hepatic and renal impairment.

4.11 Effects on ability to drive and use machines :

Undesirable effects such as dizziness, drowsiness, fatigue and visual disturbances are possible after taking NSAIDs including mefenamic acid. Dicyclomine may produce drowsiness, dizziness or blurred vision. Thus, patients should be warned not to engage in activities requiring mental alertness, such as operating a motor vehicle or other machinery or performing hazardous work while taking MEFTAL-SPAS Tablets.

4.12 Undesirable effects :

MEFENAMIC ACID:

The most frequently reported side effects associated with mefenamic acid involve the gastrointestinal tract. Diarrhea occasionally occurs following the use of mefenamic acid.

Frequencies are not known for the following adverse reactions:

Gastrointestinal disorders: The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur. Nausea, vomiting, diarrhea, flatulence, constipation, dyspepsia, abdominal pain, malaena, hematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease have been reported following administration. Less frequently, gastritis has been observed.

Elderly or debilitated patients seem to tolerate gastrointestinal ulceration or bleeding less well than other individuals; indeed, most spontaneous reports of fatal GI events are in this population.

Anorexia, colitis, enterocolitis, gastric ulceration with or without hemorrhage, pancreatitis, steatorrhea may occur.

Blood and the lymphatic system disorders: Hemolytic anemia (reversible), decrease in hematocrit, hypoplastic bone marrow, aplastic anemia, pancytopenia, thrombocytopenia, neutropenia, agranulocytosis; temporary lowering of white

blood cell count (leukopenia) with a risk of infection, sepsis, and disseminated intravascular coagulation.

Immune system disorders: Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of non-specific allergic reactions and anaphylaxis; respiratory tract reactivity comprising asthma, bronchospasm, or dyspnea; or, assorted skin disorders including rashes of various types, pruritus, urticaria, purpura, angioedema, and more rarely exfoliative or bullous dermatoses (including epidermal necrolysis and erythema multiforme).

Metabolism and nutritional disorders: Glucose intolerance in diabetic patients, hyponatraemia

Psychiatric disorders: Confusion, depression, hallucinations, nervousness can develop albeit rarely.

Nervous system disorders: Optic neuritis, blurred vision, headaches, paresthesia, dizziness, drowsiness, insomnia, convulsions, reports of aseptic meningitis (especially in patients with existing auto-immune disorders, such as systemic lupus erythematosus, mixed connective tissue disease), with symptoms such as stiff neck, headache, nausea, vomiting, fever or disorientation have been reported.

Eye disorders: Eye irritation, reversible loss of color vision, visual disturbances may occur.

Ear and labyrinth disorders: Ear pain, tinnitus, vertigo may occur.

Cardiac/Vascular disorders: Edema, hypertension and cardiac failure have been reported in association with NSAID treatment. Clinical trial and epidemiological data suggest that use of some NSAIDs (particularly at high doses and in long term treatment) may be associated with an increased risk of arterial thrombotic events (e.g. myocardial infarction or stroke).

Palpitations and Hypotension may occur.

Respiratory, thoracic and mediastinal disorders: Asthma, dyspnea have been reported.

Hepato-biliary disorders: Borderline elevations of one or more liver function tests, hepatitis, cholestatic jaundice, hepato-renal syndrome have been reported.

Skin and subcutaneous tissue disorders: Angioedema, laryngeal edema,

erythema multiforme, face edema, bullous reactions including Lyell's syndrome (toxic epidermal necrolysis) and Stevens-Johnson syndrome, perspiration, rash, photosensitivity reaction, pruritus and urticaria.

Renal and urinary disorders: Allergic glomerulonephritis, acute interstitial nephritis, dysuria, hematuria, nephrotic syndrome, non-oliguric renal failure (particularly in dehydration), proteinuria, renal failure including renal papillary necrosis.

General disorders: Fatigue, malaise, multi-organ failure, pyrexia may occur.

Investigations: A positive reaction in certain tests for bile in the urine of patients receiving mefenamic acid has been demonstrated to be due to the presence of the drug and its metabolites and not to the presence of bile.

DICYCLOMINE:

Most adverse reactions reported in clinical trials conducted with dicyclomine were typically anti-cholinergic in nature such as dry mouth, dizziness, blurred vision, nausea, light-headedness, drowsiness, weakness and nervousness.

Other adverse reactions reported with dicyclomine and pharmacologically similar drugs, e.g. other anti-cholinergics and antispasmodics were:

Gastrointestinal: Vomiting, constipation, bloated feeling, abdominal pain, taste loss, anorexia may occur.

Central Nervous System: Tingling, headache, numbness, mental confusion and/or excitement (especially in elderly persons), dyskinesia, lethargy, syncope, speech disturbance, insomnia have been reported.

Ophthalmologic: Diplopia, mydriasis, cycloplegia, increased ocular tension.

Dermatologic/Allergic: Rash, urticaria, itching, and other dermal manifestations; severe allergic reaction or drug idiosyncrasies including anaphylaxis.

Genitourinary: urinary hesitancy, urinary retention.

Cardiovascular: tachycardia, palpitations.

Respiratory: dyspnea, apnea, asphyxia.

Other: decreased sweating, nasal stuffiness or congestion, sneezing, throat congestion, impotence, suppression of lactation.

4.13 Overdose :

MEFENAMIC ACID:

Symptoms: Symptoms following acute NSAID overdose are usually limited to lethargy, drowsiness, nausea, vomiting, and epigastric pain, which are generally reversible with supportive care. Mefenamic acid overdose has been associated with CNS toxicity, especially with convulsions. Occurrence of coma has been reported rarely.

Management: Patients should be managed by symptomatic and supportive care following an NSAID overdose. There are no specific antidotes. Emesis and/or activated charcoal and/or osmotic cathartic may be indicated.

DICYCLOMINE:

Symptoms : Symptoms of dicyclomine overdosage are headache, nausea, vomiting, blurred vision, dilated pupils, hot dry skin, dizziness, dryness of the mouth, difficulty in swallowing, and CNS stimulation. A curare-like action may occur (i.e., neuromuscular blockade leading to muscular weakness and possible paralysis).

Management : Treatment should consist of gastric lavage, emetics, and activated charcoal. It is not known whether dicyclomine is dialyzable. Sedatives (barbiturates/ benzodiazepines) may be used for management of overt signs of excitement. If indicated, an appropriate parenteral cholinergic agent may be used as an antidote.

5. Pharmacological properties

Mefenamic acid belongs to a class of non-steroidal anti-inflammatory drugs (NSAIDs) which exhibit anti-inflammatory, analgesic, and antipyretic properties. Like NSAIDs in general, mefenamic acid acts by inhibiting the enzyme cyclooxygenase (COX) that is responsible for formation of prostaglandins.

Dicyclomine is an antispasmodic and anticholinergic agent. Its action is achieved via a dual mechanism: a specific anticholinergic effect at the acetylcholine-receptor sites, and a direct effect upon smooth muscle.

5.1 Pharmacodynamic properties :

Pharmacotherapeutic group : Analgesic/Antispasmodic

ATC Code : Mefenamic Acid M01AG01

Dicyclomine Hydrochloride A03AA07

MEFENAMIC ACID:

Mefenamic acid belongs to a class of non-steroidal anti-inflammatory drugs (NSAIDs) that exhibit anti-inflammatory, analgesic, and antipyretic activities. Like all other NSAIDs, the mechanism of action of mefenamic acid is related to prostaglandin inhibition. This results in a reduction in the rate of prostaglandin synthesis and reduced prostaglandin levels. Cyclooxygenase (COX) is an enzyme that is responsible for formation of prostaglandins (inflammatory mediators). Mefenamic acid is a potent inhibitor of COX with both central and peripheral action. Additionally, mefenamic acid also binds to prostaglandin receptors to prevent the effects of preformed prostaglandins. Mefenamic acid therefore both inhibits the synthesis and response to prostaglandins. This double blockade may well be important in their mode of action.

DICYCLOMINE:

Dicyclomine is an anti-spasmodic and anti-muscarinic agent. Dicyclomine has a dual effect on visceral smooth muscles. It relaxes the smooth muscle by:

1. A specific anti-cholinergic effect (anti-muscarinic) at the acetylcholine-receptor sites.
2. Direct effect upon smooth muscle (musculotropic).

5.2 Pharmacokinetic properties :

MEFENAMIC ACID:

Mefenamic acid is rapidly absorbed after oral administration. Peak plasma levels are attained in 2 to 4 hours. More than 90% of mefenamic acid is bound to plasma proteins, mainly albumin. Mefenamic acid is metabolized by cytochrome P450 enzyme [CYP2C9] to 3-hydroxymethyl mefenamic acid. Approximately 52% of a mefenamic acid dose is excreted into the urine and up to 20% of the dose is excreted by fecal route. The elimination half-life of mefenamic acid is approximately 2 hours. Because both renal and hepatic routes are significant pathways of elimination, dosage adjustments in patients with renal or hepatic dysfunction may be necessary.

DICYCLOMINE:

In man, dicyclomine is rapidly absorbed after oral administration, reaching peak values within 60-90 minutes. Mean volume of distribution following a 20 mg oral dose is approximately 3.65 l/kg, suggesting extensive distribution in tissues. The metabolism of dicyclomine was not studied. The principal route of excretion is via the urine (79.5% of the dose). Excretion also occurs in the feces, but to a lesser extent (8.4%). Mean half-life of plasma elimination in one study was determined to be approximately 1.8 hours when plasma concentrations were measured for 9 hours after a single dose. In subsequent studies, plasma concentrations were followed for up to 24 hours after a single dose, showing a secondary phase of elimination with a somewhat longer half-life.

5.3 Preclinical safety data :

Preclinical safety data does not add anything of further significance to the prescriber.

6. Pharmaceutical particulars

6.1 List of excipients :

Microcrystalline Cellulose
Maize Starch
Povidone K-30
Propylene Glycol
Colour Tartrazine
Purified Water
Sodium Starch Glycolate
Purified Talc
Colloidal Silicon Dioxide
Magnesium Stearate

6.2 Incompatibilities :

None Known

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store below 30^0C in a dry place.

Protect from light.

6.5 Nature and contents of container :

Blister Strip : 30 Tablets (1 Combi - Strip of 3 x 10 Tablets)

Carton : 2 Combi strip alongwith one package leaflet

Shipper : 96 cartons arranged in two layers in 3 x 16 Style . Packed the shipper and seal with BOPP tape in 'H' type packing on bottom and top side.

6.6 Special precautions for disposal and other handling

No special requirements

7. Marketing Authorisation Holder and Manufacturing Site Addresses

Blue Cross Laboratories Pvt Ltd.

L – 17, Verna Industrial Estate, Verna, GOA – 403 722.

8 Marketing Authorisation Number

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9. Date of First Registration/Renewal of the Registration

Renewal of the Registration

10. DATE OF REVISION OF THE TEXT

Not Applicable

11. DOSIMETRY (IF APPLICABLE)

Not Applicable

12. 1NSTRUCTIONS FOR PREPARATION OFRADIOPHARMACEUTICALS (IF APPLICABLE)

Not Applicable