SUMMARY OF PRODUCT CHARACTERISTICS

XALME SPAS

(Mefenamic Acid and Dicyclomine Hydrochloride Tablet)

1. NAME OF THE MEDICINAL PRODUCT

XALME PLUS TABLET

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Mefenamic acid BP 250mg
Dicyclomine hydrochloride 10 mg
For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablets

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Xalme - Spas is indicated in the treatment of pain associated with
Gastro-intestinal biliary colic
Ureteric colic
Primary dysmenorrhea
Menorrhagia

4.2 Posology and method of administration

For oral administration

For relief of colic pain:
One tablet to be taken twice or thrice daily up to a maximum of three days.
For Primary dysmenorrhea and menorrhagia:
On the first day of menstruation, to be taken twice or thrice daily till last day of menstruation.
Xalme-spas tablets should be taken preferably with or after food.

4.3 Contraindications

Xalme-Spas is contraindicated in patients with hypersensitivity to mefenamic acid and dicyclomine or any of the other ingredients of the products, inflammatory bowel disease, gastrointestinal bleeding or perforation, active or history of recurrent peptic ulcer, severe heart failure, hepatic failure, and renal failure and in treatment of pain after coronary artery bypass graft (CABG) surgery.

4.4 Special warnings and precautions for use

Using lowest effective dose for the shortest duration may control symptoms. Patients on prolonged therapy should be kept under regular surveillance.
Appropriate monitoring and caution should be taken while administering to patients suffering from dehydration and renal disease, respiratory disorders, cardiovascular or hepatic impairment, intracranial hemorrhage, bleeding diathesis, gastrointestinal bleeding, ulceration, perforation, SLE, mixed connective tissue disease, skin reactions, epilepsy, elderly patients
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption, known or suspected poor CYP2C9 metabolisers based on previous history/experience with other CYP2C9 substrates, should not take mefenamic acid medicine.
Products containing dicyclomine hydrochloride should be used with caution in any patient with or suspected of having glaucoma or prostatic hypertrophy. Use with care in patients with

hiatus hernia associated with reflux oesophagitis because anticholinergic drugs may aggravate the condition.

4.5 Interaction with other medicinal products and other forms of interaction

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

Mefenamic acid should be cautiously administered with anti-coagulants such as warfarin, lithium, two or more NSAIDs (including aspirin), antidepressents, antihypertensives, diuretics, anti-platelet agents, ciclosporin, corticosteroids, probenecid, quinolone antibiotics, tacrolimus, zidovudine since it may lead to increased side effects or toxicity levels

Administration of mefenamic acid with aminoglycosides, cardiac glycosides, oral hypoglycaemic agents, methotrexate may lead to increased plasma concentrations of the latter. Use of mefenemic acid with mifepristone may lead to decreased effects of the latter drugs.

4.6 Pregnancy and lactation

Pregnancy: Congenital abnormalities have been reported in association with NSAID administration in man; 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 foetal 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. 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 foetus.

Lactation: Trace amounts of mefenamic acid may be present in breast milk and transmitted to the nursing infant. Therefore, mefenamic acid should not be taken by nursing mothers.

Female fertility: The use of mefenamic acid may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of mefenamic acid should be considered.

4.7 Effects on ability to drive and use machines

Undesirable effects such as dizziness, drowsiness, fatigue and visual disturbances are possible after taking NSAIDs. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

The most frequently reported side effects are gastrointestinal disturbances such as diarrhoea, peptic ulcers, perforation or GI bleeding, nausea, vomiting, flatulence, constipation, dyspepsia, abdominal pain, less frequently, gastritis has been observed.

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

Frequencies are not known for the following adverse reactions:

Blood and the lymphatic system disorders such as anemia, thrombocytopenic purpura, leukopenia, agranulocytosis, immune system disorders like asthma, bronchospasm, dyspnoea, skin disorders including rashes of various types, pruritus, urticaria, angioedema, Metabolism and nutritional disorders such as glucose intolerance in diabetic patients, hyponatraemia, pyschiatric disorders inclusive of confusion, depression, hallucinations, nervousness, nervous system disorders including optic neuritis, headaches, paraesthesia, dizziness, drowsiness, reports of aseptic meningitis, blurred vision, convulsions, insomnia, eye disorders, ear and labyrinth disorders, palpitations, hypotension, asthma, dyspnoea, mild hepatotoxicity,

hepatitis, hepatorenal syndrome, oedema, erythema multiforme, perspiration, rash, photosensitivity reaction, dysuria, haematuria, nephrotic syndrome, non-oliguric renal failure, fatigue, malaise, multi-organ failure, pyrexia.
Side-effects seldom occur with dicyclomine tablets. However, in susceptible individuals, dry mouth, thirst and dizziness may occur. On rare occasions, fatigue, sedation, blurred vision, rash, constipation, anorexia, nausea and vomiting, headache and dysuria have also been reported.

4.9 Overdose
It is important that the recommended dose is not exceeded and the regime adhered to since some reports have involved daily dosages exceeding the recommendation.
Possible symptoms include headache, nausea, vomiting epigastric pain, rarely diarrhoea, disorientation, excitation, drowsiness, tinnitus and fainting. Symptoms of dicyclomine overdosage are headache, dizziness, nausea, dry mouth, difficulty in swallowing, dilated pupils and hot dry skin.
Therapeutic measure: Patients should be treated symptomatically within one hour of ingestion of a potentially toxic amount activated charcoal. Alternatively, in adults gastric lavage should be considered within one hour of ingestion of a potentially life-threatening overdose. Good urine output, renal and liver function should be closely monitored. Patients should be observed for at least four hours after ingestion of potentially toxic amounts

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Mefenamic acid is non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory, analgesic and antipyretic properties.
Its anti-inflammatory effect was first established in the UV erythema model of inflammation. Further studies included inhibition of granulation tissue growth into subcutaneous cotton pellets in rats and carrageenin induced rat paw oedema tests. Antipyretic activity was demonstrated in yeast-induced pyresis in rats. In this model its antipyretic activity was roughly equal to that of phenylbutazone and flufenamic acid, but less than that of indomethacin. Analgesic activity was demonstrated in tests involving pain sensitivity of rats paws inflamed by brewers yeast. Mefenamic acid was less potent than flufenamic acid in this model.
Prostaglandins are implicated in a number of disease processes including inflammation, modulation of the pain response, dysmenorrhoea, menorrhagia and pyrexia.
In common with most NSAIDs mefenamic acid inhibits the action of prostaglandin synthetase (cyclo oxygenase). This results in a reduction in the rate of prostaglandin synthesis and reduced prostaglandin levels, which contributes to the pharmacological activity and clinical efficacy of mefenamic acid.
Dicyclomine relieves smooth muscle spasm of the gastrointestinal tract. Animal studies indicate that this action is achieved via a dual mechanism;
(1) a specific anticholinergic effect (antimuscarinic at the ACh-receptor sites) and
(2) a direct effect upon smooth muscle (musculotropic).

5.2 Pharmacokinetic properties
Absorption and Distribution: Mefenamic acid is absorbed from the gastro intestinal tract. Peak levels of 10 mg/l occur two hours after the administration of a 1g oral dose to adults.
Metabolism: Mefenamic acid is predominantly metabolised by cytochrome P450 enzyme CYP2C9 in the liver, first to a 3 hydroxymethyl derivative (metabolite I) and then a 3 carboxyl derivative (metabolite II). Both metabolites undergo secondary conjugation to form glucuronides.

Therefore in patients who are known or suspected to be poor CYP2C9 metabolisers based on previous history/experience with other CYP2C9 substrates, mefenamic acid should be administered with caution as they may have abnormally high plasma levels due to reduced metabolic clearance.
Elimination: Fifty two percent of a dose is recovered from the urine, 6% as mefenamic acid, 25% as metabolite I and 21% as metabolite II. Assay of stools over a 3 day period accounted for 10-20 % of the dose chiefly as unconjugated metabolite II. The plasma levels of unconjugated mefenamic acid decline with a half life of approximately two hours.
After a single oral 20mg dose of dicyclomine in volunteers, peak plasma concentration reached a mean value of 58ng/ml in 1 to 1.5 hours. Studies demonstrated comparable bioavailability from oral and intravenous administration. The principal route of elimination is via the urine.

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, Propylene Glycol, Aerosil, Purified Talc, Sodium Starch Glycollate.

6.2 Incompatibilities
None Known

6.3 Shelf life
36 months

6.4 Special precautions for storage
Store below 30°C.

6.5 Nature and contents of container
Store in dry Place, below 30°C, Protect from light

6.6 Special precautions for disposal and other handling
Not applicable

7. MARKETING AUTHORISATION HOLDER

Bliss GVS Pharma Ltd.

102, Hyde Park, Saki-Vihar Road, Andheri (East), Mumbai – 400072.

APPLICANT: GREENLIFE PHARMACEUTICAL LIMITED, 35A, ASSOCIATION AVENUE, ILUPEJU, LAGOS

8. MARKETING AUTHORISATION NUMBER(S)

NA