SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Lagap Migraine Relief Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

	mg
Aspirin	500.0
Cyclizine Hydrochloride	25.0

3 PHARMACEUTICAL FORM

Tablet

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For relief of migraine pain and alleviation of associated nausea and headache.

4.2 Posology and method of administration

Tablets must be dissolved in water prior to oral administration.

Adults	Two tablets at onset of, or first sign of symptoms. Two further tablets may be taken after four hours if required. Maximum in 24 hours, 8 tablets.
Elderly persons:	As adults.
Children:	Do not give to children under 12 years, and avoid up to and including 15 years of age if feverish.

4.3 Contraindications

As with other aspirin containing products, Femigraine is contraindicated in patients with active peptic ulceration or a history of peptic ulceration, haemophilia, or who are hypersensitive to aspirin.

4.4 Special warnings and precautions for use

If symptoms persist consult your doctor. Keep out of the reach of children. There is a possible association between aspirin and Reye's Syndrome when administered to children with a fever. 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 12 years and should be avoided up to and including 15 years of age if feverish.

4.5 Interaction with other medicinal products and other forms of interaction

Aspirin may enhance the effects of anticoagulants and may inhibit the action of uricosuric agents. Action of cyclizine may be potentiated by alcohol or other centrally acting sedatives.

4.6 Pregnancy and lactation

i) Cyclizine: current knowledge indicates that there are teratogenic problems in animals but not in humans. It is best avoided in pregnancy unless there is medical evidence to the contrary.

ii) There is epidemiological evidence of the safety of aspirin in pregnancy but it may prolong labour and contribute to maternal and neonatal bleeding and so is best avoided during the third trimester.

Aspirin is excreted into breast milk at low concentrations and breast feeding is contraindicated at high doses because of the theoretical risk of affecting clotting mechanisms in the infant.

iii) Femigraine is best avoided during pregnancy except where there is no alternative.

4.7 Effects on ability to drive and use machines

May cause drowsiness and blurred vision in a small number of patients.

4.8 Undesirable effects

Adverse effects of aspirin treatment which have been reported include:

Blood and lymphatic system disorders:

Increased risk of bleeding (due to effect on platelet aggregation): haemorrhagic anaemia, iron deficiency anaemia with the respective laboratory and clinical signs and symptoms. In the case of G6PD deficiency: haemolysis, haemolytic anaemia.

Immune system disorders:
Hypersensitivity, drug hypersensitivity, allergic oedema and angioedema, anaphylactic reaction, anaphylactic shock with respective laboratory and clinical manifestations

Nervous system disorders:

Cerebral and intracranial haemorrhage.

Dizziness

Ear and labyrinth disorders:
Hearing disturbances (such as tinnitus),

Cardiac disorders

In the context of severe allergic reactions: cardio-respiratory distress

Vascular disorders

Haemorrhage, operative haemorrhage, haematoma, muscle haemorrhage

Respiratory, thoracic and mediastinal disorders
Epistaxis, analgesic asthma syndrome, rhinitis, nasal congestion, bronchospasm

Gastrointestinal disorders:
Gastric irritation and inflammation, dyspepsia, gastrointestinal pain, abdominal pain, gingival bleeding, nausea, vomiting, gastrointestinal erosions, ulcerations, gastritis.

In some cases of intensive use may induce gastrointestinal haemorrhage, occasionally major, which may manifest as melaena or haematemesis.

Hepatobiliary disorders:

Liver disorder, transaminases increased

Skin and subcutaneous tissue disorders:
Hypersensitivity reactions including skin rashes, urticarial, pruritus, severe skin reactions.

Renal and urinary disorders:

Impaired renal function

Adverse effects of *cyclizine* treatment which have been reported include:

Blood and lymphatic system disorders: Agranulocytosis

Cardiac disorders: Tachycardia

Eye disorders: Blurred vision, oculogyric crisis

Gastrointestinal disorders: Dry mouth, dry nose, dry throat, constipation

General disorders and administration site conditions: Asthenia

Hepatobiliary disorders: Hepatic dysfunction, hypersensitivity hepatitis, cholestatic jaundice, cholestatic hepatitis

Immune system disorders: Hypersensitivity reactions including anaphylaxis

Musculoskeletal and connectivbe tissue disorders: Twitching, muscle spasms

Nervous system disorders: Somnolence, headache, dystonia, dyskinesia, extrapyramidal motor disturbances, tremor, convulsions, dizziness, decreased consciousness, transient speech disorders, paraesthesia, generalised chorea

Psychiatric disorders: Disorientation, restlessness, nervousness, insomnia, auditory and visual hallucinations

Renal and urinary disorders: Urinary retention

Respiratory, thoracis and mediastinal disorders: Bronchospasm, apnoea

Skin and subcutaneous tissue disorders: Urticaria, drug rash, angioedema, allergic skin reactions, fixed drug eruption

Vascular disorders: Hypertension

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 via the Yellow Card Sceme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Symptoms of overdose include drowsiness, dizziness, convulsions, respiratory depression and tinnitus. Rarely, agitation, ataxia and hallucinations may occur. Treatment comprises gastric lavage, forced alkaline diuresis and supportive measures. Restoration of acid-base balance may be necessary. Convulsions can be controlled with diazepam injections.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Aspirin is an antipyretic, anti-inflammatory analgesic agent. For relief of mild to moderate pain and reduction of fever in upper respiratory tract infections, and painful or febrile disorders such as influenza, neuralgia, rheumatic pain, dysmenorrhoea and migraine.

Aspirin inhibits prostaglandin synthesis, so that the prostaglandin induced sensitivity of peripheral nerve endings to kinins and other inflammation and pain mediators is eliminated. It inhibits platelet aggregation by blocking thromboxane A2 synthesis in the platelets.

Cyclizine is an anti-emetic/anti-nauseant used widely for prevention or treatment of sickness.

5.2 Pharmacokinetic properties

Aspirin is rapidly absorbed from the gastro-intestinal tract after oral administration and is rapidly distributed throughout the whole body. It is hydrolysed to its active primary metabolite salicylic acid and completely excreted in the urine, principally as glucuronic acid and glycine conjugates of salicylic acid, but also as salicylic acid itself. Salicylates are extensively bound to plasma proteins. Maximum plasma concentrations are reached after 10-40 minutes (acetyl salicylic acid) and 0.3-2 hours (total salicylate). The elimination half-life of acetyl salicylic acid is dose dependant typically 4 hours after a 1g dose.

Cyclizine is extensively metabolised to form norcyclizine 1-1.8mg of which is excreted in the urine in four days after a 50mg dose. Peak blood concentrations following a single oral dose of 50mg has been reported to be 0.069 µg/ml in 2 hours. Plasma concentrations (of norcyclizine) were in the range 0.004-0.022 µg/ml following oral doses of 50mg thrice daily to four subjects.

5.3 Preclinical safety data

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol

Polyvinylpyrrolidone

Malic Acid

Sodium Dioctyl Sulphosuccinate

Sodium Bicarbonate

Citric Acid (Anhydrous)

Dextrates (Anhydrous)

Sodium Carbonate (Anhydrous)
Saccharin Sodium

Lemon Permaseal

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original container.

6.5 Nature and contents of container

Polythene coated foil 'Strip Packs'.

Foil strips of 4 or 6 tablets in a cardboard carton.

Pack sizes: 4, 12, 16, 18, 24.

6.6 Special precautions for disposal

No special precautions necessary.

7 MARKETING AUTHORISATION HOLDER

Cullen & Davison Ltd.
Killenaule Road
Fethard

Co. Tipperary
Ireland

8 MARKETING AUTHORISATION NUMBER(S)

PL 08977/0036

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

05/11/2000

10 DATE OF REVISION OF THE TEXT

20/09/2023