SUMMARY OF PRODUCT CHARACTERISTICS
MIGENPRO (Flunarizine Dihydrochloride 10 mg Tablets)

1. NAME OF THE MEDICINAL PRODUCT

MIGENPRO (Flunarizine Dihydrochloride 10 mg Tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains 10 mg Flunarizine Dihydrochloride BP equivalent to flunarizine.

Excipients with known effect:

Each tablet contains 60.0 mg of lactose monohydrate and 0.20 mg sodium benzoate. For warnings, see section 4.4.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.

White, round, flat, bevelled uncoated tablet with a break-line on one side and plain on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

In the prophylaxis of migraine.

The limited information available for periods longer than 12 months has shown flunarizine to continue to be effective. Patients should be regularly reviewed to assess their response to treatment, and if a sustained attack-free period is established, interrupted flunarizine treatment should be considered.

4.2 Posology and method of administration

Adults and elderly (18 years of age and older)

Starting dose: Treatment is started at 10 mg daily (at night) for adult patients aged 18 to 64 years and at 5 mg daily (at night) for elderly patients aged 65 years and older. If, during this treatment, depressive, extrapyramidal or other unacceptable adverse experiences occur, administration should be discontinued. If, after 2 months of this initial treatment, no significant improvement is observed, the patient should be considered a non-responder and administration should be discontinued.

Maintenance treatment: If the patient is responding satisfactorily and a maintenance treatment is needed, the same daily dose should be used, but this time interrupted by two successive drug-free days every week (e.g. Saturday and Sunday). Even if the prophylactic maintenance treatment is successful and well tolerated, it should be interrupted after 6 months and re-initiated only if the patient relapses.

Children, infants and neonates

Not recommended.

Method of administration

Oral. The tablet should be taken at night.

4.3 Contraindications

- Hypersensitivity to flunarizine or to any of the excipients listed in section 6.1.
- Current depressive illness or history of recurrent depression.
- Pre-existing symptoms of Parkinson's disease or other extrapyramidal disorders.

4.4 Special warnings and precautions for use

Extrapyramidal and depressive symptoms

Flunarizine may give rise to extrapyramidal and depressive symptoms and reveal Parkinsonism, especially in elderly patients. Therefore, it should be used with caution in such patients. The recommended dose should not be exceeded. Patients should be seen at regular intervals, especially during maintenance treatment, so

that extrapyramidal or depressive symptoms may be detected early; if detected, treatment should be discontinued.

Female patients with a history of depressive illness may be at particular risk of depression during chronic treatment with flunarizine.

Accumulation

Accumulation may occur if given at dose levels higher than recommended, with an increased incidence of side effects.

Fatigue

In rare cases fatigue may increase progressively during flunarizine therapy. In this event, the therapy should be discontinued and possibly initiated again at a lower dosage.

Lactose content

This medicinal product contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Sodium benzoate content

This medicinal product contains sodium benzoate. Sodium benzoate may increase jaundice (yellowing of the skin and eyes) in newborn babies. Caution is recommended in patients with hepatic impairment.

4.5 Interaction with other medicinal products and other forms of interaction

Antihypertensive drugs:

When used in conjunction with antihypertensive drugs, dosage of the latter may need adjustment.

Oral contraceptives:

Galactorrhoea has been reported in some female patients on oral contraceptives within the first two months of flunarizine treatment.

Alcohol, hypnotics and tranquillisers:

Excessive sedation can occur when alcohol, hypnotics or tranquillisers are taken simultaneously with flunarizine.

Topiramate:

The pharmacokinetics of flunarizine were unaffected by topiramate. After repeated dosing in migraine patients, systemic exposure to flunarizine increased by 14%. When flunarizine was co-administered with topiramate 50 mg every 12 hours, repeated dosing resulted in a 16% increase in systemic exposure to flunarizine. The steady-state pharmacokinetics of topiramate were unaffected by flunarizine.

Anti-epileptic drugs (AEDs):

Chronic administration of flunarizine did not affect the disposition of phenytoin, carbamazepine, valproate or phenobarbital. Plasma concentrations of flunarizine were generally lower in patients with epilepsy taking these AEDs compared to healthy subjects given similar doses. The plasma protein binding of carbamazepine, valproate, and phenytoin is not affected by co-administration with flunarizine.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data from the use of flunarizine in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. As a precautionary measure, it is preferable to avoid the use of flunarizine during pregnancy.

Breast-feeding

It is unknown whether flunarizine is excreted in human milk. Animal studies have shown excretion of flunarizine in breast milk. A decision on whether to discontinue breast-feeding or to continue/discontinue therapy with flunarizine should be made taking into account the benefit of breast-feeding to the child and the benefit of therapy to the woman.

Fertility

No data are available on the effect of flunarizine on human fertility.

4.7 Effects on ability to drive and use machines

Since somnolence may occur, especially at the start of treatment, caution should be exercised during activities such as driving or operating dangerous machinery.

4.8 Undesirable effects

Summary of the safety profile
The safety of flunarizine (5 to 10 mg/day) was evaluated in 247 flunarizine-treated subjects who participated in two placebo-controlled clinical trials in the treatment of vertigo and migraine, and in 476 flunarizine-treated subjects who participated in two comparator-controlled clinical trials in the treatment of vertigo and/or migraine. The most commonly reported (≥4% incidence) adverse reactions were weight increased (11%), somnolence (9%), depression (5%), increased appetite (4%) and rhinitis (4%).

Tabulated list of adverse reactions
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); not known (cannot be estimated from the available data).

System Organ Class	Very Common ≥1/10	Common ≥1/100 to <1/10	Uncommon ≥1/1,000 to <1/100	Not Known
Immune system disorders			Hypersensitivity	
Infections and infestations		Rhinitis		
Metabolism and nutrition disorders		Increased appetite		
Psychiatric disorders		Depression, insomnia	Depressive symptom, sleep disorder, apathy, anxiety	
Nervous system disorders		Somnolence	Coordination abnormal, disorientation, lethargy, paraesthesia, restlessness, tinnitus, torticollis	Akathisia, bradykinesia, cogwheel rigidity, dyskinesia, essential tremor, extrapyramidal disorder, parkinsonism, gait disturbance, sedation, tremor
Cardiac disorders			Palpitations	
Vascular disorders			Hypotension, flushing	
Gastrointestinal disorders		Constipation, abdominal pain upper, nausea	Intestinal obstruction, dry mouth, dyspepsia, vomiting	
Hepatobiliary disorders				Hepatic transaminases increased
Skin and subcutaneous tissue disorders			Hyperhidrosis, urticaria, rash	Erythema, angioedema, pruritus
Musculoskeletal disorders		Myalgia	Muscle spasms, muscle twitching	Muscle rigidity
Reproductive system disorders		Menstruation irregular, breast pain	Menorrhagia, menstrual disorder, oligomenorrhoea, breast hypertrophy, libido decreased	Galactorrhoea
General disorders		Fatigue	Generalised oedema, peripheral oedema, asthenia	
Investigations	Weight increased			

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 National Regulatory Authority.

4.9 Overdose

Symptoms and signs: On the basis of the pharmacological properties of the drug, sedation and asthenia may be expected to occur. Cases of acute overdosage (up to 600 mg in one intake) have been reported and the observed symptoms were sedation, agitation and tachycardia.

Treatment: Treatment of acute overdosage consists of charcoal administration, if considered appropriate, and supportive measures. No specific antidote is known.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-vertigo preparations. ATC Code: N07CA03.

Flunarizine is a selective calcium entry blocker (Class IV) which reduces arterial and arteriolar smooth muscle spasm. It selectively blocks the influx of calcium ions into cells during depolarisation without affecting the normal physiological calcium ion movement. Its anti-migraine prophylactic effect is attributed to inhibition of the vasoconstriction associated with the headache phase of migraine, with little or no effect on vascular tone at rest.

5.2 Pharmacokinetic properties

Absorption

Flunarizine is well absorbed (>80%) from the gastrointestinal tract, reaching peak plasma concentrations within 2 to 4 hours after oral dosing. Under conditions of reduced gastric acidity (higher gastric pH), bioavailability may be moderately lower.

Distribution

Flunarizine is >99% bound to plasma proteins. It has a large volume of distribution of approximately 78 L/kg in healthy subjects and approximately 207 L/kg in epileptic patients, indicating extensive distribution into extravascular tissue. The drug quickly crosses the blood-brain barrier; concentrations in the brain are approximately 10 times higher than those in plasma.

Metabolism

Flunarizine is metabolised in the liver into at least 15 metabolites. The primary metabolic pathway is CYP2D6.

Elimination

Flunarizine is primarily eliminated as parent drug and metabolites through the faeces via bile. Plasma concentrations of flunarizine remain detectable (>0.5 ng/mL) for a prolonged period (up to 30 days) after discontinuation, possibly due to redistribution from other tissues. Plasma concentrations reach steady state after approximately 8 weeks of once-daily multiple dosing and are approximately 3-fold higher than those observed after a single dose. Steady-state flunarizine concentrations are proportional over a dose range of 5 to 30 mg.

5.3 Preclinical safety data

Preclinical effects of a CNS nature (e.g. sedation, salivation, ataxia) were observed only at exposures considered sufficiently in excess of the maximum human exposure, indicating little relevance to clinical use.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

The following excipients are present in the tablet:

No.	Ingredient
1	Maize starch
2	Lactose monohydrate (excipient with known effect)
3	Microcrystalline cellulose
4	Povidone (PVP K-30)
5	Sodium benzoate (excipient with known effect)

No.	Ingredient
6	Purified water
7	Purified talc
8	Magnesium stearate
9	Colloidal anhydrous silica
10	Crospovidone

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 months.

6.4 Special precautions for storage
Store in a dry place, below 30°C. Protect from light. Keep out of the reach and sight of children.

6.5 Nature and contents of container
10 tablets packed in one ALU-ALU blister; 3 such blisters packed in one carton with package insert. Pack size: 30 tablets.

6.6 Special precautions for disposal and other handling
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER
PRO MED PHARMACEUTICALS LTD
P.O. Box 22953-00100, Nairobi, Kenya.

8. MARKETING AUTHORISATION NUMBER (PPB REGISTRATION NUMBER)
H2025/CTD12247/26496

9. DATE OF FIRST AUTHORISATION / RENEWAL OF AUTHORISATION
11.12. 2025

10. DATE OF REVISION OF THE TEXT
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