Summary of Product Characteristics:

1. Name of the medicinal product

Mitar 2.5mg tablets

2. Qualitative and quantitative composition

Each film coated tablet contains:Mirogabalin 2.5mg

Excipient of known effect

Lactose

3. Pharmaceutical form

Film-coated tablet.

Yellow to light yellow colored round shaped biconvex film coated tablets plain on both sides.

4. Clinical particulars

4.1 Therapeutic indications

Mirogabalin is indicated for: Diabetic peripheral neuropathic pain and postherpetic neuralgia.

4.2 Posology and method of administration

Posology

The initial oral dose for adults is 5 mg twice daily, and then gradually increases to 10 mg twice daily with an interval of at least 1 week. Based on individual patient response and tolerability, the dose can be increased up to the maximum dose of 15 mg twice daily with an interval of at least 1 week.

Method of administration

Orally with a glass of water.

4.3 Contraindications

Mirogabalin is contraindicated in:

Mirogabalin is contraindicated in: patients with hypersensitive to Mirogabalin. Patients to moderate Hepatic & Renal impairment.

4.4 Special warnings and precautions for use

This medicine may cause dizziness, somnolence, or loss of consciousness. Avoid operating dangerous machinery, such as driving a car. Especially for elderly patients, careful attention should be taken. This medicine may cause weight gain. This medicine may cause blurred vision and double vision.

Mitar 2.5mg tablets contains Lactose.Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Mirogabalin may interact with drugs that are metabolized by the same hepatic enzymes, such as CYP3A4 and CYP2D6 inhibitors or inducers. These interactions can affect the plasma concentrations and efficacy of Mirogabalin or co-administered drugs. Co-administrated with OAT1, OAT3, OCT2, MATE1, MATE2-K or UGT inhibitors may increase Mirogabalin exposure, should be used with caution.

4.6 Fertility, pregnancy and lactation

Fertility: There are no specific studies evaluating the effects of Mirogabalin on fertility in humans. Animal studies may provide some insights, but their relevance to humans is limited. If fertility is a concern, patients should discuss this with their healthcare provider.

Pregnancy: Mirogabalin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. There are no adequate and well-controlled studies in pregnant women. Animal reproduction studies have shown some adverse effects on embryo-fetal development at high doses. Therefore, Mirogabalin should be avoided during pregnancy unless the benefits outweigh the risks.

Lactation: It is not known whether Mirogabalin is excreted in human breast milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Mirogabalin, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. Women who are pregnant, planning to become pregnant, or breastfeeding should consult their healthcare provider before taking Mirogabalin. Healthcare providers can provide individualized guidance

based on the patient's medical history and the specific circumstances of their pregnancy or lactation. In some cases, alternative treatment options may be considered that have a better-established safety profile during pregnancy and lactation.

4.7 Effects on ability to drive and use machines

Effects on ability to drive and use machines: Mirogabalin may cause event(s) (e.g., dizziness, somnolence, loss of consciousness)

4.8 Undesirable effects

The most commonly reported adverse drug reactions, mirogabalin-treated patients, the most frequent adverse effects were mild to moderate dizziness (9.4%), somnolence (6.1%), and headache (6.1%). Our patients reported mild somnolence (15.0%), mild dizziness (6.7%), edema and weight gain (6.7%), and dry mouth (3.3%).

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org.

4.9 Overdose

Repeated-dose toxicity studies showed that the dose-limiting toxicity was considered abnormal clinical signs associated with CNS depression, resulting from exaggerated pharmacological action. Mirogabalin can potentially lead to symptoms of central nervous system depression, including drowsiness, dizziness, confusion, sedation, and in severe cases, respiratory depression, coma, and death. If an overdose is suspected, immediate medical attention should be sought.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diabetic peripheral neuropathic pain - Gabapentinoids
ATC code: N02BF03.

Mechanism of action

Mirogabalin is an analog of the neurotransmitter, gamma-aminobutyric acid (GABA). It is a potent and specific ligand of the α2δ subunit of voltage-dependent Ca2+channels, which reduces calcium (Ca2+) influx and neurotransmission in dorsal root ganglia (DRGs), inhibiting neurotransmitter release in presynaptic neuron endings. Mirogabalin acts as a ligand for α2δ subunits of voltage-gated calcium channels (VGCCs). These channels are located in the central nervous system and play a crucial role in transmitting pain signals from peripheral nerves to the spinal cord and brain. By binding to the α2δ subunits, Mirogabalin inhibits the influx of calcium ions into neurons, thereby reducing the release of neurotransmitters involved in pain transmission.

5.2 Pharmacokinetic properties

After oral administration, mirogabalin was rapidly absorbed (time to maximum concentration,1 hour) and eliminated through urine unchanged (61%- 72% urinary excretion). Exposure increased in a dose- proportional manner after single or multiple mirogabalin doses. Absorption
Mirogabalin is orally administered and is rapidly absorbed from the gastrointestinal tract after ingestion. It reaches peak plasma concentrations within a few hours after oral administration. Single-dose mirogabalin was rapidly absorbed (median time to maximum plasma concentration, 1.00 h) and eliminated (mean terminal elimination half-life, 2.57-3.08 h). The exposure was approximately dose-proportional.

Distribution

Mirogabalin distributes throughout the body, including crossing the blood-brain barrier to reach the central nervous system, where it exerts its therapeutic effects. It binds extensively to plasma proteins, primarily albumin. Following the administration of mirogabalin labeled with 14C under a single-dose regimen (30 mg) in healthy male adults, 14C-mirogabalin was distributed into red blood cells, with a ratio of whole blood concentration to plasma concentration of 0.85 to 0.87 in human (in vitro).

Metabolism

Mirogabalin undergoes hepatic metabolism primarily via cytochrome P450 (CYP) enzymes, particularly CYP3A4 and CYP2D6. The primary metabolite formed through metabolism is not as pharmacologically active as the parent compound. Mirogabalin administered orally was almost completely eliminated via urinary excretion. A small part of the orally administered dose of mirogabalin was metabolised via glucuronidation at the amine and carboxylic acid moiety and oxidation as the primary metabolic pathway. Mirogabalin is rapidly absorbed, and clearance is through renal excretion (approximately 80%) with approximately 20% being metabolized.

Elimination

The elimination half-life of Mirogabalin is relatively long, allowing for once-daily dosing. It is primarily eliminated through renal excretion, with a small portion eliminated through feces. Mirogabalin is rapidly absorbed, and clearance is through renal excretion (approximately 80%) with approximately 20% being metabolized.Eliminated primarily as the parent drug through renal excretion. Mirogabalin was rapidly eliminated via urinary excretion (61%-72%), the majority during the first 0-to-4-hour collection interval for all doses. The mean elimination half-life of mirogabalin observed in clinical trials was 2–3 h [25], 3.5 h [26], and 3–4.9 h.

Special Populations

Pharmacokinetic parameters of Mirogabalin may vary in special populations such as elderly patients, patients with hepatic impairment, or patients with renal impairment. Dose adjustments may be necessary in these populations to optimize therapy and minimize the risk of adverse effects.

5.3 Preclinical safety data

Preclinical safety data for Mirogabalin provide important insights into its potential toxicity and adverse effects observed in animal studies conducted before human trials. While specific preclinical safety data for Mirogabalin may vary depending on the studies conducted by the manufacturer and regulatory agencies, here are some common findings observed in preclinical studies:

Acute Toxicity: Studies typically evaluate the acute toxicity of Mirogabalin by administering high doses to animals and observing for signs of toxicity or adverse effects. This helps determine the maximum tolerated dose and provides initial insights into potential organ toxicity.

Repeated Dose Toxicity: Chronic toxicity studies involve administering Mirogabalin to animals over an extended period to evaluate its effects on various organs and systems. These studies assess the potential for cumulative toxicity and help establish safe dosing regimens for human use.

Genotoxicity: Genotoxicity studies investigate whether Mirogabalin has the potential to damage genetic material, such as DNA, which could increase the risk of cancer or hereditary disorders. These studies include assays for mutagenicity, chromosomal aberrations, and DNA damage.

Carcinogenicity: Carcinogenicity studies assess whether long-term exposure to Mirogabalin is associated with an increased incidence of tumors in animals. These studies are typically conducted over two years in rodent species, such as mice and rats.

Reproductive and Developmental Toxicity: Studies evaluate the effects of Mirogabalin on reproductive function and fetal development. This includes assessing fertility, embryo-fetal development, and postnatal development in pregnant animals exposed to the drug.

Cardiovascular Safety: Preclinical studies may investigate the potential effects of Mirogabalin on the cardiovascular system, including blood pressure, heart rate, and cardiac function.

Central Nervous System Effects: Studies assess the potential for central nervous system effects, such as sedation, cognitive impairment, or changes in locomotors activity.

Local Tolerance: Local tolerance studies evaluate the irritancy or sensitization potential of Mirogabalin when administered via different routes, such as oral, dermal, or ocular administration.

Preclinical safety data are essential for assessing the overall safety profile of Mirogabalin and guiding the design of clinical trials in humans. However, it's important to note that results from preclinical studies may not always directly translate to human outcomes, and additional safety assessments are conducted during clinical development to further evaluate the drug's safety and tolerability in humans.

6. Pharmaceutical particulars

6.1 List of excipients

Microcrystalline Cellulose (PH 101)
Mannitol
Lactose Monohydrate
Pregelatinized starch
Purified Water
Magnesium stearate
Purified Talc
Sodium Lauryl Sulfate
Colloidal Anhydrous Silica (Aerosil)
Microcrystalline Cellulose (PH 102)
Readycoat Film AQ Yellow (AY-517)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

3 X 10 Alu.Alu Tablets

6.6 Special precautions for disposal and other handling

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorisation holder

Dawa limited

Baba Dogo Road, Ruaraka, P.O. Box 16633- 00620 Nairobi,

Country: Kenya.

8. Marketing authorisation number(s)
CTD12726

9. Name of Manufacturing site of the FPP:
Cubit Lifesciences LLP
Plot No. 39-40, Ozone Industrial Park,
At. & post: Kerala- Bhayla Near. Kerala G.I.D.C,
Taluka: Bavla, Dist.: Ahmedabad–382220 Gujarat India.

10. Date of first authorization/renewal of the authorization

Not Applicable

11. Date of revision of the text
Not Applicable