MIDGEO™
मिडजिओ

1. **Generic Name**

Midodrine

2. **Qualitative and Quantitative composition**

Midodrine 2.5mg

3. **Dosage form and strength**

2.5-mg tablets for oral administration

4. **Clinical particulars**

4.1 Therapeutic indication

MIDGEO is indicated for the treatment of symptomatic orthostatic hypotension and recurrent reflex syncope.

4.2 Posology and method of administration

As directed by Physician.

4.3 Contraindication

- MIDGEO is contraindicated in patients with severe organic heart disease, acute renal disease, urinary retention, pheochromocytoma or thyrotoxicosis.
- MIDGEO should not be used in patients with persistent and excessive supine hypertension.

4.4 Special warnings and precautions for use

- Supine Hypertension: The most potentially serious adverse reaction associated with MIDGEO therapy is marked elevation of supine arterial blood pressure (supine hypertension). It is essential to monitor supine and sitting blood pressures in

patients maintained on MIDGEO. Uncontrolled hypertension increases the risk of cardiovascular events, particularly stroke.

- The potential for supine and sitting hypertension should be evaluated at the beginning of MIDGEO therapy. Supine hypertension can often be controlled by preventing the patient from becoming fully supine, i.e., sleeping with the head of the bed elevated. The patient should be cautioned to report symptoms of supine hypertension immediately. Symptoms may include cardiac awareness, pounding in the ears, headache, blurred vision, etc. The patient should be advised to discontinue the medication immediately if supine hypertension persists.
- Blood pressure should be monitored carefully when MIDGEO is used concomitantly with other agents that cause vasoconstriction, such as phenylephrine, ephedrine, dihydroergotamine, phenylpropanolamine, or pseudoephedrine.
- A slight slowing of the heart rate may occur after administration of MIDGEO, primarily due to vagal reflex. Caution should be exercised when MIDGEO is used concomitantly with cardiac glycosides (such as digitalis), psychopharmacologic agents, beta blockers or other agents that directly or indirectly reduce heart rate. Patients who experience any signs or symptoms suggesting bradycardia (pulse slowing, increased dizziness, syncope, cardiac awareness) should be advised to discontinue MIDGEO and should be re-evaluated.
- MIDGEO should be used cautiously in patients with urinary retention problems, as desglymidodrine acts on the alpha-adrenergic receptors of the bladder neck.
- MIDGEO should be used with caution in orthostatic hypotensive patients who are also diabetic, as well as those with a history of visual problems who are also taking fludrocortisone acetate, which is known to cause an increase in intraocular pressure and glaucoma.
- Patients should be told that certain agents in over-the-counter products, such as cold remedies and diet aids, can elevate blood pressure, and therefore, should be used cautiously with MIDGEO, as they may enhance or potentiate the pressor effects of MIDGEO.

- Patients should also be made aware of the possibility of supine hypertension. They should be told to avoid taking their dose if they are to be supine for any length of time.

4.5 Drug interactions

- When administered concomitantly with MIDGEO, cardiac glycosides may enhance or precipitate bradycardia, A.V. block or arrhythmia.
- The risk of hypertension increases with concomitant administration of drugs that increase blood pressure (phenylephrine, pseudoephedrine, ephedrine, dihydroergotamine, thyroid hormones, or droxidopa). Avoid concomitant use of drugs that increase blood pressure. If concomitant use cannot be avoided, monitor blood pressure closely.
- Avoid use of MAO inhibitors or linezolid with midodrine.
- MIDGEO has been used in patients concomitantly treated with salt-retaining steroid therapy (i.e., fludrocortisone acetate), with or without salt supplementation. The potential for supine hypertension should be carefully monitored in these patients and may be minimized by either reducing the dose of fludrocortisone acetate or decreasing the salt intake prior to initiation of treatment with MIDGEO. Alpha-adrenergic blocking agents, such as prazosin, terazosin, and doxazosin, can antagonize the effects of MIDGEO.
- **Potential for Drug Interaction:** It appears possible, although there is no supporting experimental evidence, that the high renal clearance of desyglymidodrine (a base) is due to active tubular secretion by the base-secreting system also responsible for the secretion of such drugs as metformin, cimetidine, ranitidine, procainamide, triamterene, flecainide, and quinidine. Thus there may be a potential for drug-drug interactions with these drugs.

4.6 Use in special population

- Paediatric: Safety and effectiveness in pediatric patients have not been established.
- Geriatric: Use with caution.

- Liver impairment: MIDGEO use has not been studied in patients with hepatic impairment. MIDGEO should be used with caution in patients with hepatic impairment, as the liver has a role in the metabolism of midodrine.
- Renal failure: MIDGEO use has not been studied in patients with renal impairment. Because desglymidodrine is eliminated via the kidneys, and higher blood levels would be expected in such patients, MIDGEO should be used with caution in patients with renal impairment
- Pregnancy and lactation: Pregnancy Category C. MIDGEO should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

  It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when MIDGEO is administered to a nursing woman.

4.7 Effects on ability to drive and use machine

Patients should be cautioned against engaging in activities requiring complete mental alertness, and motor coordination such as operating machinery until their response to MIDGEO is known.

4.8 Undesirable effects

The most frequent adverse reactions are supine and sitting hypertension; paresthesia and pruritus, mainly of the scalp; goosebumps; chills; urinary urge; urinary retention and urinary frequency.

4.9 Overdose

Symptoms of overdose could include hypertension, piloerection (goosebumps), a sensation of coldness and urinary retention. Desglymidodrine is dialyzable. Recommended general treatment, based on the pharmacology of the drug, includes induced emesis and administration of alpha-sympatholytic drugs (e.g., phentolamine).

5. Pharmacological properties

5.1 Mechanism of action

MIDGEO forms an active metabolite, desglymidodrine, that is an alpha1-agonist, and exerts its actions via activation of the alpha-adrenergic receptors of the arteriolar and venous vasculature, producing an increase in vascular tone and elevation of blood pressure. Desglymidodrine does not stimulate cardiac beta-adrenergic. Desglymidodrine diffuses poorly across the blood-brain barrier and is therefore not associated with effects on the central nervous system. Administration of MIDGEO results in a rise in standing, sitting, and supine systolic and diastolic blood pressure in patients with orthostatic hypotension of various etiologies. Standing systolic blood pressure is elevated by approximately 15 to 30 mmHg at 1 hour after a 10-mg dose of midodrine, with some effect persisting for 2 to 3 hours. MIDGEO has no clinically significant effect on standing or supine pulse rates in patients with autonomic failure.

5.2 Pharmacodynamic properties

Midodrine is a prodrug, i.e., the therapeutic effect of orally administered midodrine is due to the major metabolite desglymidodrine formed by deglycination of midodrine. Administration of midodrine results in a rise in standing, sitting, and supine systolic and diastolic blood pressure in patients with orthostatic hypotension of various etiologies. Standing systolic blood pressure is elevated by approximately 15 to 30 mmHg at 1 hour after a 10-mg dose of midodrine, with some effect persisting for 2 to 3 hours. Midodrine has no clinically significant effect on standing or supine pulse rates in patients with autonomic failure.

5.3 Pharmacokinetic properties

MIDGEO is a prodrug, i.e., the therapeutic effect of orally administered midodrine is due to the major metabolite desglymidodrine, formed by deglycination of midodrine. After oral administration, MIDGEO is rapidly absorbed. The plasma levels of the prodrug peak after about half an hour, and decline with a half-life of approximately 25 minutes, while the metabolite reaches peak blood concentrations about 1 to 2 hours after a dose of midodrine and has a half-life of about 3 to 4 hours. The absolute bioavailability of midodrine (measured as desglymidodrine) is 93%. The bioavailability of desglymidodrine is not affected by food. Approximately the same amount of desglymidodrine is formed after intravenous and oral administration of midodrine. Neither midodrine nor desglymidodrine is bound to

plasma proteins to any significant extent. Metabolism and Excretion: Thorough metabolic studies have not been conducted, but it appears that deglycination of midodrine to desglymidodrine takes place in many tissues, and both compounds are metabolized in part by the liver. Neither midodrine nor desglymidodrine is a substrate for monoamine oxidase. Renal elimination of midodrine is insignificant. The renal clearance of desglymidodrine is of the order of 385 mL/minute, most, about 80%, by active renal secretion. The actual mechanism of active secretion has not been studied, but it is possible that it occurs by the base-secreting pathway responsible for the secretion of several other drugs that are bases

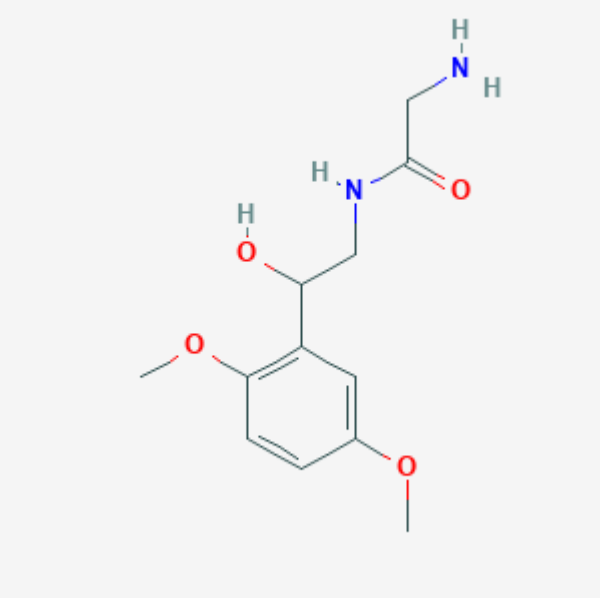
6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

NA.

7. Description

Midodrine is a direct-acting prodrug and sympathomimetic agent with antihypotensive properties. Its chemical name is 2-amino-*N*-[2-(2,5-dimethoxyphenyl)-2-hydroxyethyl]acetamide. The molecular formula and weight is. $C_{12}H_{18}N_2O_4$ and 254.28 g/mol.



8. Pharmaceutical particulars

8.1 Incompatibilities

There are no known incompatibilities.

8.2 Shelf-life

24 months.

8.3 Packaging Information

MIDGEO is available in the strip of 10 tablets.

8.4 Storage and handling instructions

Store in a cool and dry place.

9. Patient Counselling Information

9.1 Adverse Reactions

Refer part 4.8

9.2 Drug Interactions

Refer part 4.5

9.3 Dosage

Refer part 4.2

9.4 Storage

Refer part 8.4

9.5 Risk Factors

Refer part 4.4

9.6 Self-monitoring information

NA

9.7 Information on when to contact a health care provider or seek emergency help

Patients are advised to be alert for the emergence or worsening of the adverse reactions and contact the prescribing physician.

9.8 Contraindications

Refer part 4.3

10. Manufactured by AEON FORMULATIONS PVT. LTD.

11. Details of permission or license number with date

LIC.NO. 12 13 3242 DATED 12.03.2012

12. Date of revision: January 2021