SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product:

IMEG 500MG Tablets

2. Qualitative and quantitative composition

Each film coated contains: Imeglimin hydrochloride 500mg tablets. For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film Coated Tablet.

White capsule shaped film coated tablet plain on both sides

4. Clinical particulars

4.1. Therapeutic indications

Imeglimin is used for treatment of type 2 diabetes

4.2. Posology and method of administration

Imeglimin Hydrochloride 500 mg is typically taken orally, usually once or twice daily with meals. The dosage may vary based on individual patient factors, such as renal function and other medications being taken concurrently. It's crucial to follow the healthcare provider's instructions regarding dosage adjustments and timing of administration.

4.3. Contraindications

Patients with a history of hypersensitivity to the ingredients of this drug
Patients with severe ketosis, diabetic coma or precoma, and type 1 diabetes mellitus (Prompt correction of hyperglycaemia with transfusion and insulin is essential)

Patients with severe infections, pre- and post-surgery, and severe trauma (Because blood sugar control by insulin injection is desired, administration of this drug is not suitable)

4.4. Special warnings and precautions for use

• The use of this drug should be considered only when dietary therapy and exercise therapy, which are the basics of diabetes treatment, are adequately performed in advance and the effect is insufficient.

• In patients with renal dysfunction, renal excretion is delayed and the blood concentration of this drug increases, depending on the degree of renal dysfunction. Efficacy and safety in patients with moderate or severe renal impairment (eGFR less than 45 mL/min/1.73 m2) have not been conducted and administration is not recommended.

• If you have renal dysfunction, it is advisable to have your renal function checked regularly, as the excretion of this drug may be delayed and blood levels may increase.

• Patients should be fully informed of hypoglycemics symptoms and how to deal with them when using this drug.

• Since hypoglycemics symptoms may occur, care should be taken when administering to patients who are engaged in work at heights, driving a car, etc.

• When administering this drug, blood glucose should be checked regularly to confirm the drug's effect, and if the drug's effect is insufficient after 3 months of administration, a change to a more appropriate treatment should be considered.

• The mechanism of action of this drug and biguanides may be partially shared, and the combination of both drugs may cause gastrointestinal symptoms compared to combination therapy with other antidiabetic drugs. Since many cases were observed, care should be taken when selecting concomitant drugs.

4.5. Interaction with other medicinal products and other forms of interaction

This drug is mainly excreted through the kidneys as unchanged drug

Precautions for co-administration

Drug name, etc.	**Clinical symptoms/measures**	**Mechanism/risk factor**
Diabetes medicine • Insulin preparations preparations Sulfonylureas. Fast-acting insulin secretagogues α- glucosidase inhibitors, Thiazolidines DPP-4 inhibitors GLP-1 receptor agonists SGLT2 inhibitors, etc.	Be alert for episodes of hypoglycemia. Especially when used concomitantly with Insulin preparation sulfonylureas or rapid-acting insulin secretagogues, the risk of	Hypoglycemic effect may be enhanced.
Biguanides	Increased. Consider hypoglycemia may be reducing the dose of insulin, sulfonylureas, or fast-acting insulin secretagogues to reduce the risk of hypoglycemia with these agents.	For hypoglycemia, the hypoglycemic effect may be enhanced. Gastrointestinal symptoms tend to occur more frequently, especially in the initial period of concomitant use.
Drugs that enhance hypoglycemic action• β-blockers Salicylates Monoamine oxidase inhibitors, etc. Drugs that attenuate hypoglycemic effects • Adrenaline Adrenal cortical hormone Thyroid hormone, etc	Pay attention to the occurrence of hypoglycemia and gastrointestinal symptoms.	Hypoglycemic effect may be enhanced.
	Patients should be	Hypoglycemic effect may be attenuated

	carefully monitored for blood sugar levels and other conditions before administration Patients should be carefully monitored for blood sugar levels and other conditions before administration.	

4.6. Pregnancy and Lactation

• Do not administer this drug to pregnant women or women who may be pregnant, but use insulin preparations. In animal experiments (rats), transfer to the foetus has been confirmed. In animal experiments in which this drug was administered during foetal organogenesis, rats were orally administered 1500 mg/kg/day (corresponding to an exposure level approximately 17 times higher than the maximum clinical dose of 2000 mg/day), low live foetal weight and delayed ossification2). After oral administration of 200 mg/kg/day (equivalent to approximately 1.4 times the maximum clinical dose of 2000 mg/day) to rabbits, there was a trend toward lower whole embryo resorption and the number of live foetuses after implantation. A trend toward increased mortality and decreased live foetal weight has been observed

• Lactating women**:** Consider the therapeutic benefit and the benefit of breastfeeding and consider continuing or discontinuing breastfeeding. In animal experiments (rats), migration into breast milk has been confirmed.

4.7. Effects on ability to drive and use machines

Patients should be warned of the potential hazards of driving or operating machinery if they experience side effects such as dizziness.

4.8. Undesirable effects

Hypoglycaemia may occur. In particular, hypoglycaemia may occur when used in combination with insulin preparations, sulfonylureas, or rapid-acting insulin secretagogues. If hypoglycemics symptoms (initial symptoms: weakness, severe hunger, sweating, etc.) are observed, take appropriate measures such as ingesting food containing carbohydrates. However, if hypoglycemics symptoms are observed due to concomitant use with an α-glucosidase inhibitor, glucose should be administered

Others that may occur include;

	1% to less than 5%	Less than 1%
Infectious diseases and parasitic diseases		cystitis
Metabolic and nutritional disorders		Loss of appetite

Eye disorder		Diabetic retinopathy, diabetic retinal edema/ macular edema
Gastrointestinal disorders	Nausea, diarrhea, constipation	Vomiting, Abdominal discomfort, Indigestion, Upper abdominal pain, Loose stools, Abdominal distension, Gastroesophageal reflux disease
Clinical examination		Blood lactate increase, lipase increase, weight loss

Reporting of suspected adverse reactions:

Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS)

https://pv.pharmacyboardkenya.org

4.9. Overdose

Clinically significant hypotension requires active cardiovascular support including frequent monitoring of cardiac and respiratory function, elevation of extremities and attention to circulating fluid volume and urine output.

5. Pharmacological properties

5.1. Pharmacodynamic properties

• Mechanism of Action

ATC code A10BX15

Imeglimin is a drug that exerts a hypoglycemic effect through a glucose level-dependent insulin secretagogue effect and an insulin resistance-improving effect, and its mechanism of action is presumed to be via action on mitochondria.

Hypoglycemic effect: Imeglimin showed a hypoglycemic effect in GotoKakizaki (GK) rats, and the effect lasted for 8 weeks from the start of administration.

Glucose Level-Dependent Insulin Secretagogue: Imeglimin stimulated insulin secretion in the presence of high glucose in an in vitro test using pancreatic islets derived from GK rats). In streptozotocininduced diabetic model rats, GK rats, and high-fat diet-loaded rats, it increased blood insulin levels in glucose tolerance tests, and also in glucose clamp tests under hyperglycemic conditions. increased concentration). Patients with type 2 diabetes were orally administered 1500 mg of this drug Note) or placebo twice daily for 7 days, and a high glucose clamp test was performed 2 hours after the last dose.

AUC 0-45min of post-treatment blood insulin concentration increased compared to the placebo group) (foreign subject data). Patients with type 2 diabetes were administered 1500 mg of this drug or placebo twice daily for 18

weeks, and an oral glucose tolerance test was performed 2 hours after the last dose. increased compared to the group) (foreign data).

Improving insulin resistance: Imeglimin showed gluconeogenesissuppressing effects and glucose uptakeincreasing effects) in in vitro tests using primary cultured hepatocytes and in vitro tests using muscle cell lines. It also increased the steady-state glucose infusion rate in a normoglycemic hyperinsulinum clamp test in a streptozotocin-induced diabetic model animal). Patients with type 2 diabetes were administered 1500 mg of this drug Note) or placebo twice daily for 18 weeks, and an oral glucose tolerance test was performed 2 hours after the last dose. The Stumvoll index, which is one of the subjects, improved compared to the placebo group) (foreign data). Note) The approved dosage and administration of this drug is 1000 mg twice daily.

5.2. Pharmacokinetic properties

Absorption:

Imeglimin is a small cationic compound with an intermediate intestinal permeability. Its absorption mechanism involves an active transport process in addition to passive paracellular absorption. Absorption was good (50-80%) in vivo across several species but decreased with increasing dose probably due to a saturation of active transport.

Distribution:

After absorption, imeglimin was rapidly and largely distributed to internal organs. Plasma protein binding was low which can explain the rapid distribution to organs observed in all species.

Biotransformation

In animals and humans, imeglimin was largely excreted unchanged in urine, indicating a low extent of metabolism.

Unchanged drug was the main circulating entity in plasma and none of the identified metabolites were unique to human.

Elimination

Imeglimin renal clearance (CLR) was higher than creatinine clearance indicating that it was actively secreted into urine.

There was no evidence that it had the potential to cause cytochrome P450 (CYP450) inhibition or induction. It was shown to be a substrate of Organic Cation Transporter 1 (OCT1), OCT2, Multidrug and toxin extrusion 1 (MATE1) and

MATE2-K and an inhibitor of OCT1, OCT2 and MATE1; as a consequence, corresponding clinical drug-drug interaction studies were performed and confirmed the absence of relevant interactions with substrates or inhibitors of these transporters.

5.3. Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, fertility and embryo-fetal development and juvenile toxicity.

6. Pharmaceutical Particulars

6.1. List of Excipients

o Microcrystalline cellulose pH 102 BP

o Croscarmellose sodium BP

o Aerosil 200 BP

o Hydroxypropyl cellulose BP

o Magnesium stearate BP

o Tab coat TC 580118 White

6.2. Incompatibilities

Not applicable

6.3. Shelf-Life

24 months

6.4. Special Precautions for storage

Do not store above 30°C.Protected from direct sunlight Keep all medicines out of reach of children.

Store below 30°C.

6.5. Nature and Content of container

PVC /Aluminium foil blister packs of 3 x10's in unit box with literature insert

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

Dawa Limited

8. MARKETING AUTHORISATION NUMBER(S)

H2022/CTD10896/24350

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 21.11.2023

10. DATE OF REVISION OF THE TEXT

21.11.2023