

Rx

VOGLIBOSE DISPERSIBLE TABLETS

VOLICOSE™ - 0.2/0.3

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VOLICOSE™- 0.2

COMPOSITION

Each uncoated dispersible tablet contains:

Voglibose 0.2 mg

Excipients q.s.

VOLICOSE™- 0.3

COMPOSITION

Each uncoated dispersible tablet contains:

Voglibose 0.3 mg

Excipients q.s.

PHARMACEUTICAL FORM

Tablet

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

Pharmacotherapeutic group:

Alpha-glucosidase inhibitors

ATC code: A10BF03

Mechanism of Action

Voglibose is an alpha glucosidase inhibitor which reduces intestinal absorption of starch, dextrin, and disaccharides by inhibiting the action of α -glucosidase in the intestinal brush border. Inhibition of this enzyme catalyzes the decomposition of disaccharides into monosaccharides and slows the digestion and absorption of carbohydrates; the post-prandial rise in plasma glucose is blunted in both normal and diabetic subjects resulting in improvement of post prandial hyperglycemia and various disorders caused by hyperglycemia. α Glucosidase inhibitors do not stimulate insulin release and therefore do not result in hypoglycemia. These agents may be considered as monotherapy in elderly patients or in patients with predominantly post prandial hyperglycemia. α Glucosidase inhibitors are typically used in combination with other oral antidiabetic agents and/or insulin. Voglibose should be administered at the start of a meal as it is poorly absorbed.

Clinical Efficacy:

In a randomized double-blind trial comprising 1780 Japanese individuals with impaired glucose tolerance, who were treated for an average of 48.1 weeks (standard deviation, SD = 36.3), Ryuzo Kawamori et al reported Voglibose to be better than placebo ($p=0.0026$). It was noted that Voglibose, in addition to lifestyle modification, can reduce the development of type 2 diabetes in high-risk Japanese individuals with impaired glucose tolerance.

Kazuhsa Takami et al examined the effects of dietary modification/restriction alone and dietary modification/restriction with Voglibose or glyburide on abdominal adiposity and metabolic abnormalities in 36 Japanese patients with type 2 diabetes. In newly diagnosed patients who were relatively lean but had excess visceral adipose tissue area (VAT), dietary modification/restriction (with or without Voglibose or glyburide) effectively reduced VAT. Decrease in VAT was closely associated with improvement of glycemic control through diet. Additional use of Voglibose or low dose glyburide had no detrimental effects on abdominal adiposity and had beneficial effects on insulin sensitivity and the acute insulin response.

In another trial, treatment with Voglibose in diabetes mellitus patients demonstrated improved post prandial blood glucose levels, a significant decline of triglyceride level, and an elevation of high density lipoprotein (HDL) cholesterol and apolipoprotein A-1. As compared to acarbose, Voglibose was more effective and had fewer side effects.

In a meta analysis comparing miglitol and Voglibose, no significant differences in post prandial glucose were observed between the 2 groups.

Pharmacokinetic Properties

Absorption:

Voglibose is poorly absorbed after oral doses. Plasma concentrations after oral doses have usually been undetectable. After an 80 mg dose (substantially higher than recommended dose), peak plasma levels of about 20 ng/mL were observed in 1 to 1.5 hours.

When Voglibose tablets were repeatedly administered to healthy male adults (6 subjects) in a single dose of 0.2 mg, 3

times a day, for 7 consecutive days, Voglibose was not detected in plasma or urine. Similarly, when Voglibose was administered to healthy male adults (10 subjects) as a single dose of 2 mg, Voglibose was not detected in plasma or urine.

Distribution:

After ingestion of Voglibose (and other glucosidase inhibitors), the majority of active unchanged drug remains in the lumen of the gastrointestinal tract to exert its pharmacological activity.

Metabolism:

Voglibose is metabolized by intestinal enzymes and by the microbial flora.

Elimination:

Voglibose is excreted in the urine and feces.

In a study in which a single dose of 1 mg/kg of C14-Voglibose was administered to rats, the transfer of Voglibose to the fetus and to mother's milk was observed, and the rates of excretion into urine and feces were about 5% and 98%, respectively.

Preclinical Safety Data

No animal studies of safety pharmacology, repeated-dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development have been conducted with VOLICOSE™ 0.2/0.3 mg.

CLINICAL PARTICULARS

Therapeutic Indications

For improvement of post prandial hyperglycemia in diabetes mellitus, when only diet and/or exercise or oral hypoglycemic drugs or insulin preparation in addition to diet and/or exercise do not result in adequate glycemic control.

Posology and Method of Administration

Normal Adult Dose

Usually, Voglibose tablets are orally administered in a single dose of 0.2 mg, 3 times a day, before each meal. If the effect is not sufficient, the quantity of a single dose may be increased up to 0.3 mg.

Dosage in Renal Failure

Voglibose is poorly absorbed after oral doses and renal excretion is negligible, suggesting that no dose adjustment is required. However, pharmacokinetic studies in patients with renal insufficiency are not available.

Pediatrics

The safety and effectiveness of Voglibose in children has not been established.

Geriatrics

Since elderly patients generally have a physiological hypofunction, it is desirable that such caution be taken as starting the administration at a low dose (eg, 0.1 mg at a time). Furthermore, this drug should be carefully administered under close observation, through the course of the disease condition, with careful attention to the blood sugar level and the onset of gastrointestinal symptoms.

Contraindications

- Hypersensitivity to Voglibose or to any of the excipients.
- Diabetic ketoacidosis, diabetic pre-coma
- Severe infection, before and after operation or with serious trauma.
- Gastrointestinal obstruction or predisposed to it.

Special Warnings and Precautions for Use

Voglibose tablets dissolve in the mouth and need not be swallowed.

The administration of Voglibose tablets should be limited to patients who have established diabetes as there are certain other disease conditions such as abnormal glucose tolerance and positive urinary sugar that represent diabetes-like symptoms (renal glycosuria, senile abnormal glucose tolerance, abnormal thyroid function, etc).

In patients who are being managed with lifestyle modifications (diet and/or exercise), this drug must be given only when the 2-hour post prandial blood glucose levels are ≥ 200 mg/dL.

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ULFESIM Ext-0.2/0.3

During administration of this drug, disease progression should be closely observed with monitoring of blood glucose levels at regular intervals. If the effect on post prandial glucose levels is not satisfactory even after the administration of this drug for 2 to 3 months (post prandial glucose α 200 mg/dL), consider a change to more appropriate treatment. After administration of this drug, if sufficient control of blood glucose is achieved (post prandial glucose α 160 mg/dL) and can satisfactorily be maintained with lifestyle therapy or with additional use of oral hypoglycemic drugs or insulin preparations, the administration of Voglibose tablets should be discontinued, and subsequent progress of disease should be monitored.

Voglibose tablets should be administered with caution to the following patients: patients with history of laparotomy or ileus; patients with chronic intestinal disease accompanied by disturbance in digestion and absorption; patients with aggravating symptoms due to increased generation of intestinal gas (eg, Roemheld syndrome, severe hernia, and stenosis and ulcer of the large intestine); and patients with serious hepatic or renal disorders.

Other Precautions:

- All patients should continue their dietary restriction with a regular distribution of carbohydrate intake during the day. Overweight patients should continue their energy restricted diet.
- The usual laboratory tests for diabetes monitoring should be performed regularly.
- Patients should be instructed and explained to recognize hypoglycemic symptoms and its management.
- When patients with diabetes are exposed to unusual stress such as fever, trauma, infection, or surgery, a temporary loss of control of blood glucose may occur. At such times insulin therapy may be necessary for some time.

Drug Interactions

When Voglibose is used in combination with derivative(s) of sulfonamide, sulfonyleurea or biguanide, or with insulin, hypoglycemic symptoms may occur. Therefore, when used in combination with any of these drugs, care should be taken, such as starting the administration at a low dose.

When Voglibose is administered concomitantly with drugs that enhance or diminish the hypoglycemic action of antidiabetic drugs, caution should be taken as this might additionally delay the action of Voglibose on the absorption of carbohydrates. Examples of drugs enhancing the hypoglycemic action of antidiabetic drugs: α blockers, salicylic acid preparations, monoamine oxidase inhibitors, and fibrate derivatives. Examples of drugs diminishing the hypoglycemic action of antidiabetic drugs: epinephrine, adrenocortical hormone, and thyroid hormone.

Voglibose does not affect the pharmacokinetics of warfarin; hence it can be safely administered along with warfarin.

Pregnancy and Lactation

To date, no relevant epidemiological data are available. Animal studies do not indicate harmful effects with respect to pregnancy, embryonal or fetal development, parturition or post natal development, therefore the drug should be given to pregnant women or women suspected of being pregnant only when the potential benefits outweigh the possible hazards.

Animal studies (rats) have revealed a suppressive action of Voglibose on body weight increase in newborns presumably due to suppression of milk production in mother animals resulting from suppression of carbohydrate absorption. Therefore, it is desirable not to give Voglibose tablets to women during lactation. When the administration is unavoidable, nursing should be avoided.

Effects on Ability to Drive and Use Machines

None reported.

Undesirable Effects

Gastrointestinal adverse effects such as diarrhoea, loose stools, abdominal pain, constipation, anorexia, nausea, vomiting, or heartburn may occur with the use of Voglibose. Also abdominal distention, increased flatus, and intestinal obstruction like symptoms due to an increase in intestinal gas, may occur with use of Voglibose.

When Voglibose is administered to patients with serious liver cirrhosis, hyperammonia may worsen with the development of constipation followed by disturbance of consciousness. Elevation of GOT (glutamate oxaloacetate), GPT (glutamate pyruvate transaminase), LDH (lactate dehydrogenase), α GPT (α glutamate pyruvate) or alkaline phosphatase may infrequently occur.

When Voglibose is used in combination with other antidiabetic drugs, hypoglycemia may occur (0.1% to <5%).

Hypersensitivity: Rash and pruritus may rarely occur. In such a case, Voglibose tablets should be discontinued.

Psychoneurologic: Headache may rarely occur.

Hematologic: Anemia; thrombocytopenia, and leucopenia may rarely occur.

Others: Numbness, edema of face, blurred vision, hot flushes, malaise, weakness, hyperkalemia, increased serum amylase, decreased HDL cholesterol, diaphoresis or alopecia, and perspiration.

Overdose

Voglibose competitively and reversibly inhibits the α -glucosidase enzymes (glucoamylase, sucrase, maltase, and isomaltase) in the brush border of the small intestine, which delays the hydrolysis of complex carbohydrates. It is unlikely to produce hypoglycemia in overdose, but abdominal discomfort and diarrhoea may occur.

PHARMACEUTICAL PARTICULARS

List of Excipients

- Microcrystalline cellulose (Grade 101)
- Sodium starch glycolate
- Povidone K-30
- Starch
- Purified talc
- Microcrystalline cellulose (Grade 102)
- Magnesium stearate
- Yellow Oxide of Iron (VOLICOSE™ 0.2 mg)
- Quinoline Yellow WS (VOLICOSE™ 0.3 mg)
- Isopropyl alcohol

Incompatibilities

None reported.

Shelf Life: 24 months.

Storage and Precautions

Store in a cool, dry & dark place.

Special Precautions for Disposal and Other Handling

No special requirements.

Dissolves in Mouth. No need to swallow.

Nature and Contents of Container

Pack of 3x10 tablets.

Manufactured by:

Biocon Limited
at 40/1, Mohabewala Industrial Area,
SBI Road, Dehradun – 248110.

Marketed by:

Biocon Limited
20th KM Hosur Road, Electronics City
Bangalore – 560100.
TM - Trade Mark of Biocon Limited..

For further details, please contact:

Medical Advisor
Biocon Limited,
20th K.M, Hosur Road,
Electronics City,
Bangalore 560 100.

To report adverse events and/or product complaints visit our website www.biocon.com or call the Toll Free Number: 1800 102 9465 or e-mail us at drugsafety@biocon.com.

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