Skip to main content

Empagliflozin and Linagliptin Tablets (Glyxambi)

??? ??????: 30 ??????/?????? 2017

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Empagliflozin and Linagliptin

The safety of concomitantly administered empagliflozin (daily dose 10 mg or 25 mg) and linagliptin (daily dose 5 mg) has been evaluated in a total of 1363 patients with type 2 diabetes treated for up to 52 weeks in active-controlled clinical trials. The most common adverse reactions with concomitant administration of empagliflozin and linagliptin based on a pooled analyses of these studies are shown in Table 1.

Table 1 : Adverse Reactions Reported in ? 5% of Patients Treated with Empagliflozin and Linagliptin

GLYXAMBI 25 mg/5 mg n=273 n (%)	GLYXAMBI 10 mg/5 mg n=272 n (%)	
31 (11.4)	34 (12.5)	[a]Urinary tract infection
18 (6.6)	16 (5.9)	Nasopharyngitis
19 (7.0)	19 (7.0)	Upper respiratory tract infection
Predefined adverse event grouping, including, but not limited to, [a] urinary tract infection, asymptomatic bacteriuria, cystitis		

Empagliflozin

Adverse reactions that occurred in ? 2% of patients receiving empagliflozin and more commonly than in patients given placebo included (10 mg, 25 mg, and placebo): urinary tract infection (9.3%, 7.6%, and 7.6%), female genital mycotic infections (5.4%, 6.4%, and 1.5%), upper respiratory tract infection (3.1%, 4.0%, and 3.8%), increased urination (3.4%, 3.2%, and 1.0%), dyslipidemia (3.9%, 2.9%, and 3.4%), arthralgia (2.4%, 2.3%, and 2.2%), male genital mycotic infections (3.1%, 1.6%, and 0.4%), and nausea (2.3%, 1.1%, and 1.4%).

Empagliflozin causes an osmotic diuresis, which may lead to intravascular volume contraction and adverse reactions related to volume depletion.

Linagliptin

Adverse reactions reported in ? 2% of patients treated with linagliptin 5 mg and more commonly than in patients treated with placebo included: nasopharyngitis (7.0% and 6.1%), diarrhea (3.3% and 3.0%), and cough (2.1% and 1.4%).

Other adverse reactions reported in clinical studies with treatment of linagliptin monotherapy were hypersensitivity (e.g., urticaria, angioedema, localized skin exfoliation, or bronchial hyperreactivity) and myalgia.

In the clinical trial program, pancreatitis was reported in 15.2 cases per 10,000 patient year exposure while being treated with linagliptin compared with 3.7 cases per 10,000 patient year exposure while being treated with comparator (placebo and active comparator, sulfonylurea). Three additional cases of pancreatitis were reported following the last administered dose of linagliptin.

Hypoglycemia

Table 2 summarizes the reports of hypoglycemia with empagliflozin and linagliptin over a treatment period of 52 weeks.

Hypoglycemic Adverse Reactions [b]and Severe [a]Table 2 : Incidence of Overall

GLYXAMBI 25 mg/5 mg (n=137)	GLYXAMBI 10 mg/5 mg (n=136)	Add-on to Metformin (52 weeks)
3.6%	2.2%	Overall (%)
0%	0%	Severe (%)
Overall hypoglycemic events: plasma or capillary glucose of less than[a] or equal to 70 mg/dL or requiring assistance		
Severe hypoglycemic events: requiring assistance regardless of [b] blood glucose		

Laboratory Tests

Empagliflozin and Linagliptin

Changes in laboratory findings in patients treated with the combination of empagliflozin and linagliptin included increases in cholesterol and hematocrit compared to baseline.

Empagliflozin

Increase in Low-Density Lipoprotein Cholesterol (LDL-C): Dose-related increases in low-density lipoprotein cholesterol (LDL-C) were observed in patients treated with empagliflozin. LDL-C increased by 2.3%, 4.6%, and 6.5% in patients treated with placebo, empagliflozin 10 mg, and empagliflozin 25 mg, respectively]. The range of mean baseline LDL-C levels was 90.3 to 90.6 mg/dL across treatment groups.**WARNINGS AND PRECAUTIONS**[see

Median hematocrit decreased by 1.3% in placebo and increased by 2.8% in empagliflozin 10 mg and 2.8% in empagliflozin 25 mg treated **:*Increase in Hematocrit*** patients. At the end of treatment, 0.6%, 2.7%, and 3.5% of patients with hematocrits initially within the reference range had values above the upper limit of the reference range with placebo, empagliflozin 10 mg, and empagliflozin 25 mg, respectively.

Linagliptin

Changes in laboratory values that occurred more frequently in the linagliptin group and ? 1% more than in the placebo group were increases in uric acid (1.3% in the placebo group, 2.7% in the linagliptin group).

Postmarketing Experience

Additional adverse reactions have been identified during postapproval use of linagliptin. Because these reactions are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- Acute pancreatitis, including fatal pancreatitis [see **INDICATIONS AND USAGE** and**WARNINGS AND PRECAUTIONS**]
- Hypersensitivity reactions including anaphylaxis, angioedema, and exfoliative skin conditions [see **WARNINGS AND PRECAUTIONS**]
- Rash