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ALBIGLUTIDE

▼EPERZAN® FOR TYPE 2 DIABETES MELLITUS

dtbn
DRUG ASSESSMENT REPORT
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DTB_Navarre

No weight loss, no use

Indications

Adults with type 2 diabetes mellitus (Type 2 DM):

- Monotherapy with albiglutide is indicated when diet and exercise alone do not provide adequate glycaemic control in patients for whom use of metformin is considered inappropriate due to contraindications or intolerance.
- In combination with other glucose-lowering medicinal products including basal insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.

Mechanism of action and pharmacokinetics

Albiglutide is a glucagon-like peptide 1 (GLP-1) receptor agonist that produces a glucose-dependent stimulation of insulin secretion and delays gastric emptying. Maximum concentration is reached 3-5h after administration and its elimination half-life is 5 days approximately.

Posology and method of administration

The recommended dose is 30mg once weekly administered subcutaneously. The dose may be increased to 50mg based on individual glycaemic response. It is available in the form of pen injectors pre-filled with powder and solvent which require previous reconstitution.

Clinical efficacy

The clinical efficacy of albiglutide has been tested in eight phase III clinical trials, as monotherapy, as add-on therapy to metformin to two glucose-lowering agents, three glucose-lowering agents, to insulin glargine, and also in a study in patients with renal failure. Albiglutide has been compared with sitagliptin, glimepiride, insulin glargine, insulin lispro, liraglutide and placebo.

The primary endpoint was change in HbA1c levels with respect to baseline level at different time points according to the study considered (from week 26 to 104). The main studies included a total of 6,043 patients, of whom 3,358 were treated with albiglutide.

Statistically significant reductions were achieved in HbA1c as compared to placebo alone (-0.84 and -1.04 for doses of 30mg and 50mg, respectively) and as add-on to other oral antidiabetic drugs (-0.75 to -0.91), without any significant weight loss.

In studies with an active comparator, albiglutide was proven to be statistically superior to sitagliptin and glimepiride and non-inferior to insulin lispro and insulin glargine. In contrast, albiglutide was found to be statistically inferior to liraglutide and pioglitazone.

Another antidiabetic drug with no morbi-mortality data. Unlike other analogs, it does not help lose weight

A relevant effect of GLP-1 analogs is weight loss. However, albiglutide is not effective for weight loss and has not been proven to have different effects from placebo.

Safety

Adverse reactions

The incidence of pancreatitis in the clinical studies was 0.3% for albiglutide compared to 0.1% for comparators with or without antidiabetic therapy at baseline.

Gastrointestinal events occurred with a higher frequency for albiglutide compared to all comparators (38% vs 32%). The most frequent gastrointestinal events were diarrhea, nausea, vomiting and constipation. The majority occurred within the first 6 months. The frequency of nausea and vomiting was lower with albuglutide compared to liraglutide (7% vs 35%). The frequency of bowel obstruction was slightly higher in the group receiving albiglutide with respect to comparators (0.3% vs 0.2%).

Injection site reactions (typically including rash, erythema, or itching at the injection site) occurred in 15% of patients treated with albiglutide and led to discontinuation in 2%.

The frequency of hypoglycemia was low and similar to that observed with the comparators. It increased when administered as add-on therapy to sulfonylureas or insulin.

A higher incidence of atrial fibrillation/flutter was observed in the group receiving albiglu-

ABSTRACT

Albiglutide is a once-weekly GLP-1 analog. In Spain, it is only reimbursed when administered in combination with other glucose-lowering medicinal products and weight loss is not required.

Studies have not proven non-inferiority vs liraglutide in reducing HbA1c. No comparative studies have been performed with exenatide once weekly.

Effectiveness data in terms of morbi-mortality are not available.

It has a neutral effect on weight, in contrast with other drugs of the same family that help lose weight.

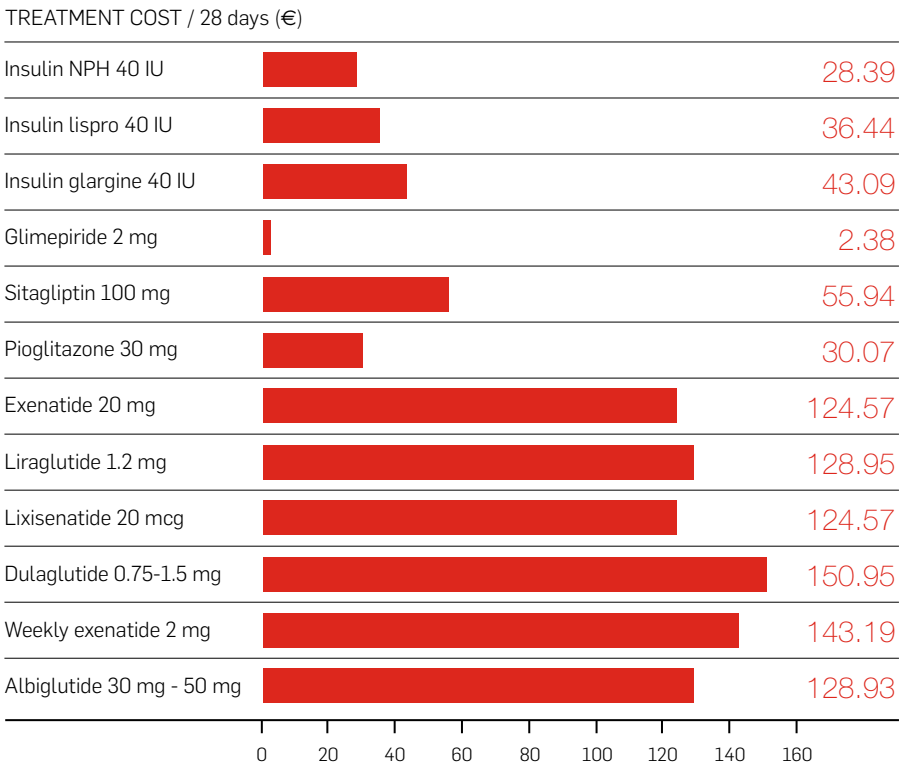
The profile of adverse effects of albiglutide seems to be similar to that of other GLP-1 analogs. The incidence of nausea and vomiting is lower in albiglutide than in liraglutide.

Long-term safety is unknown. There is concern about the associated risk of pancreatitis, pneumonia, cardiovascular disease, and pancreatic and thyroid tumors.

CLASSIFICATION

4	IMPORTANT THERAPEUTIC INNOVATION
3	MODEST THERAPEUTIC INNOVATION
2	SOME ADDED VALUE IN SPECIFIC SITUATIONS
1	**NO THERAPEUTIC INNOVATION**
0	INSUFFICIENT EVIDENCE

The qualification assigned to the drug was agreed by the Drug Assessment Committees of Andalusia, Basque Country, Catalonia Institute of Health, Aragon and Navarre. The current report is based on the available information and is susceptible to be updated according to the latest evidence. Let us remind the reader about the importance of notifying the Pharmacovigilance Centre when there are suspicions of adverse reactions to drugs.



de (1.3%) with respect to the comparators group (0.5%) Small increases in heart rate (1 to 2 bpm) were also observed. Transient ischemic attacks occurred more frequently in patients receiving albiglutide (0.6% vs 0.2%). A meta-analysis conducted to assess major adverse cardiac events of albiglutide (acute myocardial infarction, stroke and CV death) showed no differences with active comparators.
Pneumonia occurred in 2% of patients receiving albiglutide compared to 0.8% in the comparators group.
Two cases of pancreatic cancer and another two cases of thyroid cancer were reported in different phase III clinical trials in patients receiving albiglutide.

Contraindications

Hypersensitivity to the active substance or to any of its excipients.

Special warnings and precautions for use

- Do not use in patients with type 1 DM or diabetic ketoacidosis.
- Patients should be informed of the characteristic symptoms of acute pancreatitis. If pancreatitis is suspected, albiglutide should be discontinued.
- Patients may require a lower dose of sylphonylureas or insulin as add-on therapy to albiglutide to reduce the risk of hypoglycaemia.
- Do not use albiglutide in patients with severe gastrointestinal disease, including gastroparesis.
- After discontinuation, the effect of albiglutide may continue over 3 to 4 weeks. This should be taken into account when prescribing another drug.

There is no experience in patients with heart failure (NYHA III-IV) administered alone or in combination with prandial insulin, dypeptidyl peptidase-4 (DPP-4) inhibitors or sodium/glucose cotransporter inhibitors.

Usage in special situations

Albiglutide should not be used during pregnancy nor in child-bearing age women who do not use contraception. There are no adequate data to support the use of albiglutide during breast-feeding.
Dose adjustment is not required in patients with mild or moderate renal impairment. Albiglutide is not recommended in patients with severe renal impairment or under hemodialysis.
Dose adjustment is not recommended in patients with liver impairment. No studies have been conducted in this population.
There are no data on the safety and effectiveness of albiglutide in patients aged < 18 years.
Similar results have been obtained in patients aged 65 years as compared to the general population. However, there are limited clinical data on patients 75 years.

Drug interactions

Albiglutide delays gastric emptying and may impact the absorption of medicinal products.

EMA's Risk Management Plan

Important risks identified: acute pancreatitis, gastrointestinal events, hypoglycemia, injection site reactions, immunogenecity, pneumonia and atrial fibrillation/flutter.
Potentially important risks: cardiovascular disease, medullary thyroid carcinoma, hepatotoxicity, pancreatic cancer, bowel obstruction, non-clinical fetal and neonatal development toxicity and accelerated sexual maturation.

Place in therapeutics

Albiglutide is the only GLP-1 analog indicated as monotherapy. However, since it has not been proven to be superior to other options, it should not be administered alone.
When adequate glycaemic control is not achieved despite the administration of a combination therapy, the third option consists of starting insulin therapy or using an oral glucose-lowering drug instead if the patient is reluctant to use insulin or correct insulin administration cannot be guaranteed.
Considering that there are no sufficient data on the long-term safety and effectiveness of albiglutide in terms of morbi-mortality, GLP-1 analogs can be used as add-on to a combination therapy replacing insulin in obese patients with a BMI >30-35 kg/m^2 or with important problems in insulinization, or in case of ineffectiveness or intolerance in previous therapies. Albiglutide therapy should be revised at six months and continued only if HbA1c is reduced by at least 1.0 and 3% weight loss at minimum is achieved with respect to baseline values.
In combination therapy, albiglutide has been observed to be less effective in reducing HbA1c as compared to other GLP-1 analogs (liraglutide) and has no effect on body weight. The potential improvement in treatment adherence associated with its weekly administration is not supported by evidence, and albiglutide has not been compared with exenatide administered once weekly. Its safety profile seems to be similar to that of other GLP-1 analogs. Therefore, it is difficult to find a place for albiglutide in the treatment of type 2 DM.

Presentation

Eperzan® (GlaxoSmithKline) 30 mg 4 pens (128.93 €); 50 mg 4 pens (128.93 €).

References

Based on the Therapeutic Positioning Report.

Servicio Navarro de Salud
Osasunbidea

INTERNATIONAL SOCIETY OF DRUG BULLETINS

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