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Summary of the risk management plan (RMP) for Eperzan (albiglutide)

This is a summary of the risk management plan (RMP) for Eperzan, which details the measures to be taken in order to ensure that Eperzan is used as safely as possible. For more information on RMP summaries, see here.

This RMP summary should be read in conjunction with the EPAR summary and the product information for Eperzan, which can be found on Eperzan's EPAR page.

Overview of disease epidemiology

Type 2 diabetes happens when the body does not produce enough insulin or does not respond appropriately to insulin. Insulin is a hormone that regulates how the body uses the food a person eats. With type 2 diabetes, the blood sugar level (glucose) gets too high and can lead to complications that affect the eyes, nerves and kidneys. High sugar levels may also contribute to heart attacks and strokes.

Type 2 diabetes is very common and the number of people with this condition is increasing all over the world. It is more likely to develop in people who have family members with the condition, people with an ethnic background known to be associated with a higher risk (for example Asian or African), people aged over 40 years old, or who are overweight or obese, do not exercise, have high blood pressure, or smoke.

Summary of treatment benefits

The goal of treating diabetes is to lower blood glucose to nearly normal levels and thereby decrease possible damage to patients' eyes, nerves and kidneys. Type 2 diabetes patients are usually treated with diet, exercise and medicines. Patients may have different responses to medicines and many need more than one to lower their glucose.

Eperzan (albiglutide) is an injectable medicine that can be used to lower glucose when metformin cannot be used or does not lower glucose enough.

Albiglutide was studied in 8 clinical trials that lasted from 32 weeks to two years or more. In most studies, patients were already taking one or more diabetes medicines (for example, metformin, a sulfonylurea, sitagliptin, pioglitazone, or insulin). In one study, albiglutide was studied in patients who had only been treated with diet and exercise.

Albiglutide was given to 2365 diabetic adults and the outcomes in these patients were compared to treatment outcomes in 2530 patients who were given other diabetes medicines or placebo. Albiglutide showed benefits in glucose control in all of the studies and lower glucose levels were evident within 2 weeks of starting albiglutide and lasted for at least 2 years.

Unknowns relating to treatment benefits

Experience is very limited in patients over 75 years of age and in patients with serious kidney problems (such as those with severe renal impairment or who are on dialysis).

Albiglutide has not been studied in pregnant women, women who are breast-feeding, children, patients with liver disease and patients with moderate to severe heart failure.

Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Inflammation of the pancreas (Acute pancreatitis)	Pancreatitis may affect between 1 and 10 users in 100. Pancreatitis can be severe and life-threatening. Severe stomach (abdominal) pain that does not go away can be a symptom of pancreatitis. The pain may happen with or without vomiting and may be felt going from the abdomen through to the back.	If a patient has had pancreatitis in the past they should talk with their doctor to see if albiglutide is right for them. The doctor should talk to the patient about the symptoms of pancreatitis. If patients have severe stomach pain that does not go away, they are to stop taking albiglutide and talk to their doctor straight away.
Gastrointestinal side effects – diarrhoea, feeling sick (nausea), being sick (vomiting), indigestion (dyspepsia), heartburn (gastro-oesophageal reflux disease), constipation, bowel obstruction	Some gastrointestinal side effects - diarrhoea and nausea - may affect more than 1 in 10 users and others may affect between 1 and 10 users in 100. Bowel obstruction may affect up to 1 in 100 people. Most gastrointestinal side effects occurred in the first 6 months after starting albiglutide and most patients did not stop taking the medicine because of these side effects. If a patient has kidney problems, they may be more likely to have gastrointestinal side effects.	Albiglutide may make the stomach empty more slowly. If a patient has a serious problem with emptying their stomach (gastroparesis) or severe bowel disease (severe gastrointestinal disease) they should talk to a doctor to see if albiglutide is right for them.
Low blood sugar (Hypoglycaemia)	Low blood sugar can be severe and life threatening. Low blood sugar may affect between 1 and 10 users in 100 when taking albiglutide as the only diabetes	If a patient is taking a sulfonylurea medicine or insulin, the doctor may need to change the dose of these medicines to reduce the risk of lowering blood sugar too

Risk	What is known	Preventability
	medicine or when taking albiglutide with metformin or pioglitazone. Low blood sugar may affect more than 1 in 10 users if albiglutide is used with a sulfonylurea medicine or with insulin.	much (hypoglycaemia).
Injection site reactions - rash, redness and/or itching at site of injection	Reactions at the injection site may affect more than 1 in 10 users. Most patients with injection site reactions did not stop taking albiglutide. Most injection site reactions were mild in intensity and did not require treatment.	Not known
Lung infection (pneumonia)	Lung infections may affect between 1 and 10 users in 100.	Not known
Irregular heartbeat (atrial fibrillation/flutter)	Irregular heartbeat may affect between 1 and 10 users in 100 Most of the patients with irregular heartbeat in the studies were older men or patients with kidney problems.	Not known
Immunogenicity	Medicines like albiglutide that are “foreign” proteins given by injection can cause the body to react by making antibodies. Sometimes antibodies against medicines can cause the medicines to stop working or cause other side effects such as severe allergic reactions with swelling of the face, tongue or throat, difficulty breathing, or passing out (anaphylaxis and angioedema). In studies, about 1 in 20 patients showed antibodies to albiglutide but this did not seem to cause the medicine to stop working or to cause side effects.	Not known

Important potential risks

Risk	What is known
Cardiovascular safety of antidiabetic therapy	Problems like heart attacks, heart failure and strokes are common in patients with diabetes. Some diabetes medicines are thought to aggravate or cause heart problems. It is important to watch for heart problems in patients taking new diabetes medicines. In clinical studies, there was no sign that patients taking albiglutide had more heart problems or strokes than patients taking other medicines.
Medullary thyroid cancer (thyroid C cell tumours-nonclinical)	In animal studies with some other diabetes medicines that work like albiglutide, an unusual type of thyroid cancer was seen. It is not known if any of these medicines or albiglutide could cause this type of thyroid cancer in humans.
Liver problems (hepatotoxicity)	Patients with diabetes can have problems with their livers. Sometimes medicines can cause damage to the liver. It is important to monitor new medicines for effects on the liver. In clinical studies, some patients had liver problems but it was not clear that albiglutide caused these problems.
Pancreatic cancers	In some animal studies with some other diabetes medicines that work like albiglutide, changes in the pancreas were seen. It is not known if any of these medicines or albiglutide could cause pancreatic cancer in humans.
Malignant neoplasms (cancer) following combination treatment with insulin	People with diabetes are more likely to develop cancer than people who do not have this condition. Whether some diabetes medicines like insulins may increase the risk of developing cancers is under investigation. Concerns have been raised that medicines like albiglutide increase the risk of developing an unusual type of thyroid cancer or cancers in the pancreas (see medullary thyroid cancer and pancreatic cancer). It is not known if taking both insulin and albiglutide has an effect on the risk of developing cancer.
Effects on the development of a baby (foetal & neonatal developmental toxicity-nonclinical)	See below Missing information- Use in pregnancy and lactation.
Early sexual maturation (puberty) in animals (Accelerated sexual maturation-nonclinical)	See below Missing information- Use in patients aged less than 18 years.

Missing information

Risk	What is known
Use in pregnancy and while breast-feeding (lactation)	Side effects on developing offspring in the womb and after birth were noted in animal studies and a potential risk to human babies cannot be ruled out. Albiglutide should not be used during pregnancy. Also albiglutide may be present in human breast milk, and could be transmitted to an infant during breast-feeding. As it is not known what effect this might have, albiglutide should not be used in women who are breastfeeding.
Use in patients aged less than 18 years (paediatric population)	Some other diabetes medicines that work like albiglutide appeared to speed up sexual maturation of juvenile animals. It is not known whether this would happen in human children who have not yet reached puberty. Albiglutide has not been studied in juvenile animals or in humans less than 18 years of age. It is not known if albiglutide is safe and effective in children under 18 years of age with type 2 diabetes.
Use in patients with liver disease / decreased liver function (hepatic impairment)	A study has not been carried out in patients with liver problems (hepatic impairment), but liver problems are not expected to affect the safety or effectiveness of albiglutide or require the dose to be changed.
Use in patients 75 years or older	Only a very small number of patients 75 years or older were included in studies, but age is not expected to affect the safety or effectiveness of albiglutide or require the dose to be changed.
Use in patients with serious kidney problems	Only a small number of patients with serious kidney problems (severe renal impairment or on dialysis) were studied and albiglutide is not recommended in these patients.
Use in patients with heart failure	Albiglutide has not been studied in patients with moderate to severe heart failure (NYHA class III/IV heart failure).

Summary of risk minimisation measures by safety concern

All medicines have a summary of product characteristics (SmPC) which provides physicians, pharmacists and other healthcare professionals with details on how to use the medicine, and also describes the risks and recommendations for minimising them. Information for patients is available in lay language in the package leaflet. The measures listed in these documents are known as ‘routine risk minimisation measures’.

The SmPC and the package leaflet are part of the medicine’s product information. The product information for Eperzan can be found on Eperzan’s EPAR page.

This medicine has no additional risk minimisation measures.

Planned post-authorisation development plan

List of studies in post-authorisation development plan

Study / activity (including study number)	Objectives	Safety concerns / efficacy issue addressed	Status	Planned date for submission of (interim and) final results
V30016 and V70310N In vitro binding study to evaluate GLP-1R distribution in thyroid cells from healthy untreated rodents and monkeys compared to humans (non-clinical, 3)	Determine GLP-1R distribution in thyroid cells from healthy untreated rodents and monkeys compared to humans	Thyroid C-cell tumours (medullary thyroid cancer)	Started	December 2014
Juvenile toxicity study in mice treated with albiglutide (non-clinical, 3)	Determine if albiglutide has effects on sexual maturation and CNS/behaviour in juvenile mice	Use in paediatric population	Planned	December 2014
GLP113121 A Randomised, Double-Blind, Placebo-Controlled, Parallel Group, Multicenter Monotherapy Study to Determine the Efficacy and Safety of 2 Dose Levels of Albiglutide in Subjects With Type 2 Diabetes (clinical interventional)	To determine in Japanese patients how well albiglutide lowers blood glucose and how safe it is compared to a blank injection (placebo), or another diabetes medicine, liraglutide. when these medicines are used for 1 year	Phase III efficacy data out to 52 weeks in Japanese subjects with type 2 diabetes	Started	Final CSR planned for submission May 2016
GLP116170 A 52-Week, Open-label, Multicenter Study to Determine the Long-term Safety and Efficacy of Albiglutide in Combination With Monotherapy of Oral Antihyperglycemic Medications in Japanese Patients with Type 2 Diabetes	To determine in Japanese patients how well albiglutide lowers blood glucose and how safe it is compared to a blank injection (placebo), or several other diabetes medicines (sulphonylureas, glinides, biguinides, thiazolidinedione, or an alpha-glucosidase inhibitor) when these medicines are used for 1	Phase III efficacy data out to 52 weeks in Japanese subjects with type 2 diabetes	Started	Final CSR planned for submission February 2016

Study / activity (including study number)	Objectives	Safety concerns / efficacy issue addressed	Status	Planned date for submission of (interim and) final results
(clinical interventional)	year			
Paediatric study Randomised, double-blind, placebo controlled study of paediatric patients with type 2 diabetes inadequately controlled with diet and exercise or metformin monotherapy (clinical interventional)	To determine whether albiglutide is safe and effective in lowering blood glucose in children (aged ≥ 10 to 18 years) with type 2 diabetes when added to metformin compared to a blank injection (placebo) when used for at least 4 months and up to 8 to 12 months.	Missing information in paediatric population	Planned July 2017	Final report April 2021 as per EMEA-C1-001175-PIP01-11

Studies which are a condition of the marketing authorisation

None of the above studies is a condition of the marketing authorisation.

Summary of changes to the risk management plan over time

Not applicable

This summary was last updated in 02-2014.