VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Secondary hyperparathyroidism in chronic kidney disease

Hyperparathyroidism is a condition in which the parathyroid glands in the neck produce too much parathyroid hormone, which can lead to bone and joint pain and deformities of the arms and legs. 'Secondary' means that it is caused by another condition. cinacalcet can be used as part of treatment including phosphate binders or vitamin D sterols The prevalence of patients in the EU with chronic kidney disease that are on dialysis ranges from approximately 500 per million population to over 1000 per million.

Reduction of hypercalcaemia (high blood calcium levels) in patients with:

- **Parathyroid carcinoma** (cancer of the parathyroid glands). Parathyroid carcinoma is extremely rare and accounts for 0.5% of all primary hyperparathyroidism cases, with an estimated

prevalence of 2 /1,000000. Most patients with parathyroid carcinoma have markedly elevated serum calcium concentrations (> 14 mg/dL) and complications of hypercalcaemia.

- **Primary hyperparathyroidism** who cannot have their parathyroid glands removed or when the doctor thinks that removal of the parathyroid glands is not appropriate. 'Primary' means that the hyperparathyroidism is not caused by any other condition.

VI.2.2 Summary of treatment benefits

Cinacalcet has been compared with placebo (a dummy treatment) in three main studies involving 1,136 dialysis patients with serious kidney disease. The studies lasted for six months. In dialysis patients with serious kidney disease, about 40% of the patients taking cinacalcet had parathyroid hormone levels below 250 micrograms/l at the end of the study, compared with about 6% of those taking placebo. Cinacalcet brought about a 42% reduction in parathyroid hormone levels compared with an increase of 8% in patients taking placebo.

Cinacalcet has also been studied in a study involving 46 patients with hypercalcaemia, including 29 with parathyroid carcinoma, and 17 with primary hyperparathyroidism who could not have their parathyroid glands removed or in whom surgery to remove the parathyroid glands was not effective. The study continued for over three years. A further three studies compared cinacalcet with placebo in a total of 136 patients with primary hyperparathyroidism over up to a year. Of these, 45 went on to a fourth, long-term study looking at the effectiveness of cinacalcet over a total of almost six years Cinacalcet produced a decrease in blood calcium of more than 1 mg/dl in 62% of the cancer patients (18 out of 29) and in 88% of the patients with primary hyperparathyroidism (15 out of 17). The results of the additional studies supported the use of cinacalcet for hypercalcaemia in patients with primary hyperparathyroidism.

VI.2.3 Unknowns relating to treatment benefits

Not applicable.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Low blood calcium levels (Hypocalcaemia)	Cinacalcet may cause low calcium in the blood which can cause numbness, muscle pain, cramping, spasms, twitches and convulsion. Generally patients recover when the low calcium level in their blood is treated.	Patients' whose serum calcium is below the lower limit of normal should not receive cinacalcet. Those receiving cinacalcet should have their calcium levels monitored carefully. Those CKD patients receiving dialysis can be given calcium-containing phosphate binders, vitamin D and/or their dialysate adjusted to manage their blood calcium levels.

Fits (Convulsions/seizures)	Convulsions or seizures can potentially happen when blood calcium levels are low; they are most likely to occur in cases where the blood calcium levels fall dramatically.	Blood calcium levels should be monitored carefully.
Allergic reactions (including rash, hives and swelling of the face, lips, mouth, tongue or throat) [Hypersensitivity reactions (including rash, urticaria, and angioedema)]	Cinacalcet may cause alergic reactions, eg, rash, itching or hives, swelling of the face, lips, mouth, tongue, or throat which may cause breathing difficulty.	Patients who are allergic to cinacalcet or any of the other ingredients of the medicine should not take cinacalcet.
Low blood pressure (hypotension) and/or worsening heart failure	A very small number of patients with heart failure had a worsening of their condition after taking cinacalcet and a very small number of those patients also had low blood pressure.	Patients who experience a worsening of their heart failure or low blood pressure (dizziness, fainting) should notify their doctor as soon as possible.
Effect on heart rhythm because of low blood calcium levels (QT prolongation and ventricular arrhythmias secondary to hypocalcemia)	Low blood calcium can affect heart rhythm. Cases of QT prolongation and ventricular arrhythmia have been reported in patients taking cinacalcet	Patients who have other risk factors such as those with heart rhythm problems since birth or patients taking other medicines that are known to cause heart rhythm effects should notify their doctor.

Important potential risks

Risk	**What is known (Including reason why it is considered a potential risk)**
Fractures	Cinacalcet acts to reduce PTH concentrations in the blood. Patients whose PTH levels are too low for too long may be at greater risk of developing bone disease, which could lead to bone fractures.
Inflammation of the pancreas (Acute pancreatitis)	Patients with ESRD on dialysis are at a greater risk of experiencing sudden inflammation of the pancreas; those undergoing peritoneal dialysis appear to have a higher risk than those who receive haemodialysis treatments.
Possible drug-related liver (hepatic) disorders	A mechanism by which cinacalcet can cause fiver damage is not known. So far in the clinical trials drug-related liver injuries caused directly by cinacalcet have not thought to have occurred; however this potential risk will continue to be monitored.
Decreased blood flow to the heart (myocardial ischemia),	Low blood calcium can theoretically affect blood flow and the heart's ability to pump blood, changes which could cause tightening, or blockage, of the blood vessels leading to the heart muscle. Such an effect is of particular concern for patients who have significant coronary artery atherosclerosis.
Nervous system disorders (excluding seizure)	Patients with CKD undergoing dialysis have a higher risk for a variety of central nervous system events, including disorder or disease of the brain (encephalopathy) and convulsions.
Occurrence of tumours (Neoplastic events)	In a large, long-term study, patients who received cinacalcet had a higher rate of abnormal changes in body tissues (neoplasms) than patients who received placebo.

Missing information

Risk	What is known
Pregnant women	Cinacalcet has not been given to women who are pregnant or breastfeeding. In an animal study in which the mother received very high doses of cinacalcet while pregnant, decreased body weight was seen in the unborn offspring.
Lactating women	Cinacalcet has not been given to women who are pregnant or breastfeeding. In an animal study in which the mother received very high doses of cinacalcet while pregnant, decreased body weight was seen in the unborn offspring.
Paediatric patients	It is not known whether cinacalcet is safe and effective in children. Studies in humans are being conducted to determine if cinacalcet is safe and effective in children; however, results are not available yet.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

Not applicable.

VI.2.7 Summary of changes to the risk management plan over time

Table 2. Major changes to the Risk Management Plan over time

Not applicable.