## VI.2 Elements for a public summary

### VI.2.1 Overview of disease epidemiology

Diabetes type 2 (diabetes mellitus, non-insulin dependent diabetes) consists of an array of dysfunctions that happen when the body does not produce enough insulin, does not react appropriately to insulin and when there is an excessive or inappropriate glucagon secretion. With diabetes type 2, the blood sugar level (glucose) gets too high which leads to microvascular (damage to the small blood vessels, like in the eye or kidneys), macrovascular (affects bigger blood vessels, such as heart arteries or other big blood vessels) and neurophatic complications (damage to the nerves).

Type 2 diabetes is very common and the rates are increasing worldwide. It is more likely to develop in people who are over 40 years of age, are overweight or obese, do not exercise, have high blood pressure, who have family history of type 2 diabetes, or people with a certain ethnic background (for example Asian or African).

### VI.2.2 Summary of treatment benefits

Sitagliptin, is a dipeptidyl-peptidase-4 (DPP-4) inhibitor. It works by blocking the breakdown of 'incretin' hormones in the body. These hormones are released after a meal and stimulate the pancreas to produce insulin. By increasing levels of incretin hormones in the blood, sitagliptin stimulates the pancreas to produce more insulin when blood glucose levels are high. Sitagliptin does not work when the blood glucose is low. Sitagliptin also reduces the amount of glucose made by the liver, by increasing insulin levels and decreasing the levels of the hormone glucagon. Together, these processes reduce blood glucose levels and help to control diabetes type 2.

Sitagliptin was studied in nine studies involving almost 6,000 patients with type 2 diabetes whose blood glucose levels were not adequately controlled. In these studies sitaglipting was compared to placebo (a dummy treatment) and other antidiabetes medicines; combinations of sitagliptin with other medicines were compared to placebo as well. The studies showed that sitagliptin was more effective than placebo when it was taken alone or in combination with other antidiabetes medicines

In the studies comparing sitagliptin with other medicines, the effectiveness of adding sitagliptin to metformin was similar to that of adding glipizide. When taken on their own, sitagliptin and metformin produced similar results, but the effectiveness of sitagliptin seemed to be slightly lower than that of metformin.

### VI.2.3 Unknowns relating to treatment benefits

No studies with sitagliptin have been performed in paediatric patients. There are no adequate data about the use of sitagliptin in pregnant women. It is unknown whether sitagliptin is excreted in human breast milk. Sitaglipin should not be used during pregnancy, breast-feeding and in children below 18 years of age.

### VI.2.4 Summary of safety concerns

**Important identified risks**

| Risk | What is known | Preventability |
|---|---|---|
| Hypersensitivity reactions, including anaphylactic reaction, angioedema, rash, urticaria, cutaneous vasculitis, skin exfoliation and Stevens-Johnson syndrome<br>*(Allergic reactions, including swelling of the face, lips, tongue, and throat that may cause difficulty in breathing or swallowing, rash and hives, which may be severe)* | Allergic reactions, including severe ones, have been reported in patients using sitagliptin. Frequency of these reactions is not known.<br>Usually these reactions occur within the first 3 months of treatment with sitagliptin. | If a serious allergic reaction occurs, patients should stop taking sitagliptin and call their doctor right away. The doctor may prescribe a medicine to treat the allergic reaction and a different medicine for diabetes |
| Hypoglycaemia with concomitant sulfonylurea (*Low blood sugar with concomitant sulfonylurea [a group of antidiabetic medicines])* | Sitagliptin is unlikely to cause low blood sugar because it does not work when patient's blood sugar is low. However, when this medicine is used in combination with a sulphonylurea medicine, low blood sugar (hypoglycaemia) can occur. | Patients should tell their doctor or pharmacist if they are taking, have recently taken or might take any other medicines.<br>The doctor may reduce the dose of sulphonylurea in order to lower the risk of low blood sugar. |
| Hypoglycaemia with concomitant insulin<br>*(Low blood sugar with concomitant insulin)* | This medicine is unlikely to cause low blood sugar because it does not work when patient's blood sugar is low. However, when this medicine is used in combination with insulin, low blood sugar (hypoglycaemia) can occur. | Patients should tell their doctor or pharmacist if they are taking, have recently taken or might take any other medicines.<br>The doctor may reduce the dose of insuling the patient takes in order to lower the risk of low blood sugar. |

| Risk | What is known | Preventability |
|---|---|---|
| Gastrointestinal disorders: nausea, vomiting, constipation, diarrhoea, abdominal pain, flatulence, abdominal pain upper and related terms (dyspepsia and gastritis) | Mainly when sitagliptin is used together with metformin, nausea, flatulence and vomiting are common side effects (may affect up to 1 in 10 people).<br>Abdominal pain (pain in the stomach area), diarrhoea, constipation, drowsiness are uncommon side effects which may affect up to 1 in 100 people.<br>Constipation is a common side effect when sitagliptin is used together with sulphonylurea and metformin.<br>Constipation is an uncommon side effect when sitagliptin is used alone or with insulin | Patients should talk to their doctor or pharmacist if they get any side effects. |
| Musculoskeletal disorders: osteoarthritis, pain in extremity, and related terms (e.g. arthralgia, myalgia, myopathy)<br>*(Muscle, joint and bone disorders: osteoarthritis, pain in arm or leg, and related terms, e.g. joint pain, muscle pain)* | Joint pain, muscle pain and back pain can be side effects of the use of sitagliptin. The frequency of these side effects is not known.<br>Osteoarthritis is a common side effect when sitagliptin is used alone and/or is used in combination with other diabetes medicines. | Patients should talk to their doctor or pharmacist if they get any side effects. |
| Pancreatitis<br>*(inflammation of the pancreas)* | Cases of inflammation of the pancreas (pancreatitis) have been reported in patients receiving sitagliptin.<br>Symptoms of pancreatitis are severe and persistent pain in the abdomen (stomach area) which might reach through to the back with or without nausea and vomiting.<br>Improvement of condition of patients with pancreatitis has been observed when sitagliptin is discontinued, but very rare severe cases and/or death have been reported. | Patients should tell their doctor if they have or have had:<br>- a disease of the pancreas (such as pancreatitis)<br>- gallstones, alcoholism or very high triglycerides. These medical conditions can increase the chance of getting pancreatitis, or getting it again.<br>- If pancreatitis is suspected, the use of sitagliptin and other potentially suspect medicinal products should be stopped; if acute pancreatitis is confirmed, sitagliptin should not be restarted. |

**Important potential risks**

| Risk | What is known (Including reason why it is considered a potential risk) |
|---|---|
| Infections: Upper respiratory tract infection, nasopharyngitis and related terms (bronchitis, acute bronchitis, pharyngitis, sinusitis, and rhinitis) | Upper respiratory infection, stuffy or runny nose and sore throat may affect between 1 in 100 and 1 in 10 people who are taking sitagliptin. |
| Neurotoxicity: tremor, ataxia, and balance disorders<br>(*Damage to nervous tissue: tremor, problems with coordination and balance)* | There is lack of information regarding the risk of damage to nervous tissue (neurotoxicity) in humans. |
| Suicidal ideation, suicide and depression | There is lack of information regarding this risk. |
| Impaired renal function, including acute renal failure (sometimes requiring dialysis)<br>*(Worsened kidney function, including kidney failure which sometimes requires dialysis)* | Kidney problems, sometimes requiring dialisys can occur with an unknown frequency in patients taking sitagliptin.<br>If patients have kidney problems, their doctor may prescribe lower doses.<br>Patients should tell their doctor if they have or have ever had kidney problems. |
| Pancreatic cancer | There is lack of information regarding this risk. |
| Rhabdomyolysis *(Abnormal muscle breakdown which can lead to kidney problems)* | There is lack of information regarding this risk. |

**Missing information**

| Risk | What is known |
|---|---|
| Patients below18 years of age | Children and adolescents below 18 years should not use this medicine. It is not known if this medicine is safe and effective when used in children and adolescents under 18 years of age. |
| Exposure during pregnancy and lactation | There is a lack of information regarding use of sitagliptin during pregnancy.<br>If a patient thinks she is pregnant, thinks she may be pregnant or is planning to have a baby, the patient should talk to her doctor or pharmacist for advice before taking this medicine.<br>This medicine should not be taken. during pregnancy.<br>It is not known if this medicine passes into breast milk. This medicine should not be taken if the patient is breast-feeding or plan to breast-feed. |
| Theoretic carcinogenic potential | There is lack of information regarding this risk. |

### 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

Not applicable. This is the first RMP.