Part VI: Summary of the risk management plan by product

VI.1 Elements for summary tables in the EPAR

VI.1.1 Summary table of Safety concerns

Summary of safety concerns	
Important identified risks	• Transaminase elevated and Drug-induced liver injury (DILI) • Angioedema • Acute pancreatitis • Skin lesions • Hypoglycaemia
Important potential risks	• Serious infections • Cardiac events in congestive heart failure (*NYHA Functional Class III*) patients • Muscle events/myopathy/rhabdomyolysis, in particular with current statin use • Neuropsychiatric events • Breast cancer • Pancreatic cancer
Missing information	• Gender incidence/frequency differences • Patients with severe hepatic impairment • Patients with compromised cardiac function *(NYHA functional class IV)* • Pregnancy

VI.1.2 Table of on-going and planned studies in the Post-authorisation Pharmacovigilance Development Plan

Not applicable.

VI.1.3 Summary of Post authorisation efficacy development plan

Not applicable.

VI.1.4 Summary table of risk minimisation measures

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
IMPORTANT IDENTIFIED RISKS		
Transaminase elevated and Drug-induced liver injury (DILI)	Recommendation in section 4.4 to assess the hepatic function regularly. Warning regarding hepatic impairment and liver enzyme monitoring included in section 4.4.	None proposed

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
	Listed in section 4.8 of the SmPC. Prescription only medicine.	
Angioedema	Information on interaction possibly leading to angioedema is presented in section 4.5 of the SmPC. Information regarding angioedema presented in section 4.8 of the SmPC. Prescription only medicine.	None proposed
Acute pancreatitis	Warning in section 4.4 on the risk of acute pancreatitis. Listed in section 4.8 of the SmPC. Prescription only medicine.	None proposed
Skin lesions	Warning in section 4.4 on the risk of skin disorders. Listed in section 4.8 of the SmPC. Described in section 5.3 of the SmPC. Prescription only medicine.	None proposed
Hypoglycaemia	Warning in section 4.4 on the risk of hypoglycaemia. Listed in section 4.8 of the SmPC. Prescription only medicine.	None proposed
IMPORTANT POTENTIAL RISKS		
Serious infections	Prescription only medicine.	None proposed.
Cardiac events in congestive heart failure *(NYHA Functional Class III)* patients	Warning in section 4.4 of the SmPC. Prescription only medicine.	None proposed.
Muscle events/myopathy /rhabdomyolysis, in particular with current statin use	Myalgia is listed in section 4.8 of the SmPC. Muscle pain and increases in creatine phosphokinase (CPK) listed for overdose in section 4.9 of the SmPC. Prescription only medicine.	None proposed
Neuropsychiatric events	Prescription only medicine.	None proposed
Breast cancer	Prescription only medicine.	None proposed.
Pancreatic cancer	Prescription only medicine.	None proposed.
MISSING INFORMATION		
Gender incidence/ frequency differences	Prescription only medicine.	None proposed.
Patients with	Wording regarding posology in hepatic	None proposed.

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
severe hepatic impairment	impairment in SmPC section 4.2. Warning in SmPC section 4.4. Prescription only medicine.	
Patients with compromised cardiac function *(NYHA functional class IV)*	Warning in section 4.4 on the risk of use in patients with compromised cardiac function. Prescription only medicine.	None proposed
Pregnancy	Information on use in pregnancy is presented in section 4.6 of the SmPC. Prescription only medicine.	None proposed

VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Diabetes mellitus type 2

Type 2 diabetes mellitus consists of an array of dysfunctions characterized by hyperglycaemia and resulting from the combination of resistance to insulin action, inadequate insulin secretion, and excessive or inappropriate glucagon secretion.

Microvascular complications of diabetes include retinal, renal, and possibly neuropathic disease. Macrovascular complications include coronary artery and peripheral vascular disease. Diabetic neuropathy affects autonomic and peripheral nerves.

Rates of diabetes are increasing worldwide. The International Diabetes Federation predicts that the number of people living with diabetes will to rise from 366 million in 2011 to 552 million by 2030. Type 2 diabetes mellitus is less common in non-Western countries where the diet contains fewer calories and daily caloric expenditure is higher. However, as people in these countries adopt Western lifestyles, weight gain and type 2 diabetes mellitus are becoming virtually epidemic.

VI.2.2 Summary of treatment benefits

Based on the available data from clinical studies and clinical experience of several years, vildagliptin represents an effective drug in the treatment of diabetes mellitus type 2.

If administered as indicated in the Summary of Product Characteristics and taking into account the contraindications, the warnings and precautions, vildagliptin can be considered effective in the approved indications and generally well tolerated.

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
Liver enzyme values increased (*Transaminase elevated*) and Drug-induced liver injury (DILI)	Liver disease (hepatitis): symptoms include yellow skin and eyes, nausea, loss of appetite or dark-coloured urine, which may indicate liver disease (hepatitis).	A test to determine liver function should be performed before the start of vildagliptin treatment, at three-month intervals for the first year and periodically thereafter. This is so that signs of increased liver enzymes can be detected as early as possible.
Serious allergic reaction which causes swelling of the face or throat *(Angioedema)*	Angioedema: symptoms include swollen face, tongue or throat, difficulty swallowing, difficulties breathing, sudden onset rash or hives, which may indicate a reaction called “angioedema”.	Vildagliptin should not be taken if allergic to vildagliptin.

Risk	What is known	Preventability
Inflammation of the pancreas *(Acute pancreatitis)*	Inflammation of the pancreas (pancreatitis): Symptoms include severe and persistent pain in the abdomen (stomach area), which might reach through to your back, as well as nausea and vomiting.	Patients are advised to talk to the doctor if having or having had a disease of the pancreas.
Skin lesions	Since this product has been marketed, the following side effects have also been reported: localised peeling of skin or blisters.	Patients are advised to pay particular attention to new onset of blisters or ulcers while taking vildagliptin. Should these occur, the doctor should be promptly consulted.
Low blood glucose *(Hypoglycaemia)*	Some patients have had the following side effects while taking vildagliptin alone: low blood glucose.	Patients are advised to talk to the doctor if taking an anti-diabetic medicine known as a sulphonylurea (doctor may want to reduce the dose of the sulphonylurea when taken together with vildagliptin in order to avoid low blood glucose [hypoglycaemia]).

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Serious infections	Limited information is available on serious infections.
Heart events in patients with pre-existing heart failure (*Cardiac events in congestive heart failure (NYHA Functional Class III) patients*)	Limited information is available on patients with compromised cardiac function (*NYHA functional class III*)
Muscle events/ muscle pain (*myopathy*)/ breakdown of muscle fibers (*rhabdomyolysis*), in particular with current blood cholesterol lowering medicine (*statin*) use	Since this product has been marketed, the following side effect has also been reported: muscle pain.
Neuropsychiatric events	Limited information is available on neuropsychiatric events.
Breast cancer	Limited information is available on breast cancer.
Pancreatic cancer	Limited information is available on pancreatic cancer.

Missing information

Risk	What is known
Gender incidence/ frequency differences	Limited information is available on gender incidence/frequency differences.
Patients with severe hepatic impairment	Vildagliptin should not be used in patients with hepatic impairment.
Patients with compromised cardiac function *(NYHA functional class IV)*	Limited information is available on patients with compromised cardiac function (NYHA functional class IV).
Pregnancy	If a woman is pregnant, thinks that may be pregnant or is planning to have a baby, she should ask the doctor or pharmacist for advice before taking this medicine. Vildagliptin should not be used during pregnancy.

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 Patient Information Leaflet (PIL). 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.