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 + metformin 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 + metformin 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
Transaminase elevation 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 + metformin 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 + metformin should not be taken if allergic to vildagliptin or metformin.
Inflammation of the	Inflammation of the pancreas (pancreatitis):	Patients are advised to talk to

Risk	What is known	Preventability
pancreas *(Acute 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.	the doctor if having or having had a disease of the pancreas.
Lactic acidosis	Vildagliptin + metformin may cause a very rare, but very serious side effect called lactic acidosis, particularly if kidneys are not working properly. The risk of developing lactic acidosis is also increased with uncontrolled diabetes, serious infections, prolonged fasting or alcohol intake, dehydration, liver problems and any medical conditions in which a part of the body has a reduced supply of oxygen (such as acute severe heart disease). Excessive alcohol intake while taking vildagliptin + metformin should be avoided since this may increase the risk of lactic acidosis.	Patients are advised to avoid excessive alcohol intake.
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 + metformin. Should these occur, the doctor should be promptly consulted.
Low blood glucose *(Hypoglycaemia)*	Some patients have had the following side effects while taking vildagliptin +metformin: 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 + metformin 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 heart events in patients with pre-existing heart failure.
Muscle events/muscle pain (*myopathy*)/ breakdown of muscle fibers	Since this product has been marketed, the following side effect has also been reported: muscle pain.

Risk	What is known (Including reason why it is considered a potential risk)
(*rhabdomyolysis*) , in particular with current blood cholesterol lowering medicine (*statin*) use	
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 + metformin 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 + metformin 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.