Swiss Summary of the Risk Management Plan (RMP) for Vipdomet® (alogliptin/metformin)

Version 1.0, 7-Feb-2023
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The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risk as well as to prevent or minimize them.

The RMP summary of Vipdomet® is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of Vipdomet® in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedicinfo.ch) approved and authorized by Swissmedic. Takeda Pharma AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Vipdomet®.

Summary of risk management plan for Vipdomet® (alogliptin/metformin)

This is a summary of the risk management plan (RMP) for VIPDOMET. The RMP details important risks of VIPDOMET, how these risks can be minimised, and how more information will be obtained about VIPDOMET's risks and uncertainties (missing information).

VIPDOMET's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how VIPDOMET should be used.

This summary of the RMP for VIPDOMET should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of VIPDOMET's RMP.

I. The medicine and what it is used for

VIPDOMET is authorised in the treatment of adult patients aged 18 years and older with type 2 diabetes mellitus:

- As an adjunct to diet and exercise to improve glycaemic control in adult patients, inadequately controlled on their maximal tolerated dose of metformin alone, or those already being treated with the combination of alogliptin and metformin.
- In combination with pioglitazone (i.e. triple combination therapy) as an adjunct to diet and exercise in adult patients inadequately controlled on their maximal tolerated dose of metformin and pioglitazone.
- In combination with insulin (i.e. triple combination therapy) as an adjunct to diet and exercise to improve glycaemic control in patients when insulin at a stable dose and metformin alone do not provide adequate glycaemic control.

It contains alogliptin and metformin as the active substances and it is given orally as 12.5 mg/850 mg, 12.5 mg/1000 mg film-coated tablets.

Further information about the evaluation VIPDOMET's benefits can be found VIPDOMET's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage:

https://www.ema.europa.eu/en/medicines/human/EPAR/vipdomet

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of VIPDOMET, together with measures to minimise such risks and the proposed studies for learning more about VIPDOMET's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute routine risk minimisation measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of VIPDOMET is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of VIPDOMET are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of VIPDOMET's. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g., on the long-term use of the medicine).

List of important risks and missing information	
Important identified risks	Lactic acidosis
Important potential risks	Pancreatic cancer Arthralgia
Missing information	Use in pregnant women and breast feeding

II.B Summary of important risks

Important Identified Risk: Lactic acidosis	
Evidence for linking the risk to the medicine	Harmonised Glucophage SmPC.
Risk factors and risk groups	Risk groups have been identified, including those with acute alcohol intoxication, hepatic insufficiency, severe renal impairment, sepsis, dehydration, and the use of iodinated contrast agents.
Risk minimization measures	**Routine risk minimisation measures:** SmPC Section 4.8 and 4.9 and PL Section 4 (undesirable effects) SmPC Sections 4.2, 4.3 & PL Section 2 and 3 indicated populations in which alogliptin+metformin is contraindicated or monitoring is required. SmPC 4.4, 4.5 and PL Section 2 include special warnings and precautions for patients at risk for lactic acidosis. **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	None

Important Potential Risk: Pancreatic cancer	
Evidence for linking the risk to the medicine	Alogliptin clinical trials OPI-004,305, and 402 and post-marketing database, published literature.
Risk factors and risk groups	There are known risk factors associated with development of pancreatic cancer; among these are gender (men are 30% more at risk), age (70% are age 65 years or older), race (African-Americans are at higher risk), smoking (responsible for 20%-30% of pancreatic cancers), obesity, diabetes, chronic pancreatitis, liver cirrhosis, family history, occupational exposure to pesticides, dyes, chemicals used in metal refining, and genetic syndromes, such as mutations in genes such as BRCA2, p16/CDKN2A (familial melanoma), and PRSSi (familial pancreatitis), Lynch syndrome (also known as hereditary nonpolyposis colorectal cancer), Peutz-Jeghers syndrome, von Hippel-Lindau syndrome, neurofibromatosis type 1 (gene mutation), and multiple endocrine neoplasia type 1.
Risk minimization measures	**Routine risk minimisation measures:** None **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	None

Important Potential Risk: Arthralgia	
Evidence for linking the risk to the medicine	Alogliptin clinical studies, post-marketing safety surveillance database, non-clinical data, and scientific literature.
Risk factors and risk groups	Elderly patients and women. The major cause of musculoskeletal pain is osteoarthritis. Additional causes for joint pain include injuries, mechanical problems, obesity and overweight, types of arthritis and other health problems.
Risk minimization measures	**Routine risk minimisation measures:** None **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	None

Missing Information: Use in pregnant women and breast feeding	
Risk minimization measures	**Routine risk minimisation measures:** SmPC Section 4.6 and PL Section 2 recommends to avoid the use of alogliptin+metformin during pregnancy and considerations related to

Missing Information: Use in pregnant women and breast feeding	
	lactation. **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	None

II.C. Post-authorisation development plan

II.C.1. Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of VIPDOMET.

II.C.2. Other studies in post-authorisation development plan

There are no studies required for VIPDOMET.