Summary of the Risk Management Plan (RMP)
for Onivyde Pegylated Liposomal

Product concerned (brand name): Onivyde Pegylated Liposomal

Active substance: Liposomal irinotecan

Strength: 4.3 mg/mL

Pharmaceutical form: Concentrate for dispersion for infusion

Version number: 3.1

Manufacturing Authorization Holder: Servier (Suisse) SA

Date of final sign off: 23/12/2021

Disclaimer:

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 risks as well as to prevent or minimise them.

The RMP summary of Onivyde 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 Onivyde in Switzerland is the “Arzneimittelinformation / Information sur le médicament” (see www.swissmedic.ch) approved and authorized by Swissmedic.

Servier Suisse S.A. is fully responsible for the accuracy and correctness of the content of the published summary RMP of Onivyde.

Summary of risk management plan for ONIVYDE (liposomal irinotecan)

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

ONIVYDE's summary of product characteristics (SmPC) and its package leaflet give essential

information to healthcare professionals and patients on how ONIVYDE should be used.

This summary of the RMP for ONIVYDE 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 ONIVYDE's RMP.

I. The medicine and what it is used for

ONIVYDE is authorised for the treatment of metastatic adenocarcinoma of the pancreas (see SmPC for the full indication). It contains irinotecan encapsulated in a lipid bilayer vesicle or liposome as the active substance and it is given intravenously.

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

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

Important risks of ONIVYDE, together with measures to minimise such risks and the proposed studies for learning more about ONIVYDE'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 ONIVYDE is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of ONIVYDE are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. 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 ONIVYDE. 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).

Table 17. List of Important Risks and Missing Information

Important identified risks	Thromboembolic events
Important potential risks	None
Missing information	None

II.B Summary of important risks

Table 18. Important Identified Risk – Thromboembolic Events

Evidence for linking the risk to the medicine	Thromboembolic events have been reported in clinical trials and medical literature.
Risk factors and risk groups	Risk of thromboembolism in cancer patients depends on the tumour type, stage of the disease, surgical intervention, presence of an indwelling central venous catheter, age, and a previous history of thromboembolism. There are no risk factors specific to non-liposomal irinotecan. Risk of venous thromboembolism was found to be highest among patients with cancers of the pancreas, brain, and lung. However, this can vary widely by cancer type and time since diagnosis. Altered liver function may contribute to impaired coagulation or coagulation complications. As such, patients with liver disease maybe at greater risk for thromboembolic events.
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Section 4.2 – Table 1, Recommended dose modifications for ONIVYDE.

Table 18. Important Identified Risk – Thromboembolic Events

	SmPC Section 4.4: Patients should be informed about the signs and symptoms of thromboembolism and advised to contact their physician or nurse immediately if any such signs or symptoms should occur. SmPC Section 4.8 PL Section 4 – Patients should notify their doctor immediately if they have any blood clots. **Additional risk minimisation measures:** No risk minimisation measures.

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 ONIVYDE.

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

There are no studies required for ONIVYDE.