PART VI: Summary of the risk management plan

The content of this part is the same for all invented names of drospirenone 4 mg film-coated tablets.

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

I. The medicine and what it is used for

SLINDA is indicated for oral contraception. It contains drospirenone as the active substance and it is given orally.

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

Important risks of drospirenone, together with measures to minimise such 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.
If important information that may affect the safe use of SLINDA is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of SLINDA are risks that need special risk minimisation 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 SLINDA. 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	• Hyperkalemia
Important Potential Risks	• Venous Thromboembolism • Bone fracture/Decrease in bone mineral density • Disturbances of liver function • Benign and malignant liver tumours • Ectopic pregnancy • Breast cancer
Missing Information	• Not applicable

II.B Summary of important risks

Important identified risk: Hyperkalemia	
Evidence for linking the risk to the medicine	Findings from non-clinical trials; few case reports of hyperkalemia from clinical trials.
Risk factors and risk groups	*Impaired renal function,* concomitant treatments (diuretics, other drugs associated with hyperkalemia as cyclosporine).
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3, 4.4 and 4.8 PIL section 3 Additional risk minimisation measures: Not applicable.

Important potential risk: Venous Thromboembolism	
Evidence for linking the risk to the medicine	Suspicion of an association with the medicinal product of interest but this association has not been confirmed.
Risk factors and risk groups	History of VTE, Prolonged immobilisation

Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3 and 4.4 PIL section 2 Additional risk minimisation measures: Not applicable.

Important potential risk: Bone fracture/Decrease in bone mineral density	
Evidence for linking the risk to the medicine	Suspicion of an association with the medicinal product of interest but this association has not been confirmed.
Risk factors and risk groups	Menopause is associated with an increased risk of decrease in BMD. However, these patients will not be using SLINDA®. Adolescence is a critical period of bone accretion. It is unknown if the use of contraceptives during adolescence and early adulthood could reduce peak bone mass and increase the risk for fracture in later life.
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 PIL section 2 Additional risk minimisation measures: Not applicable.

Important potential risk: Disturbances of liver function	
Evidence for linking the risk to the medicine	Suspicion of an association with the medicinal product of interest but this association has not been confirmed.
Risk factors and risk groups	Subjects with pre-existing severe liver disease.
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3, 4.4 and 4.8 PIL section 2 Additional risk minimisation measures: Not applicable.

Important potential risk: Benign and malignant liver tumours	
Evidence for linking the risk to the medicine	Suspicion of an association with the medicinal product of interest but this association has not been confirmed.

Risk factors and risk groups	Unknown.
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 and 4.8 PIL section 2 Additional risk minimisation measures: Not applicable.

Important potential risk: Ectopic pregnancy	
Evidence for linking the risk to the medicine	Suspicion of an association with the medicinal product of interest but this association has not been confirmed.
Risk factors and risk groups	History of previous ectopic pregnancy, pelvic inflammatory disease, Chlamydia trachomatis infection, smoking, tubal surgery, induced conception cycle, and endometriosis [Rana 2013] Contraceptive methods lead to an overall lower risk of pregnancy and therefore to an overall lower risk of ectopic pregnancy. However, among cases of contraceptive failure, women at increased risk of ectopic pregnancy compared with pregnant controls included those using POPs, progestin-only implants, or IUDs and those with a history of tubal ligation. [Furlong 2002]
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 PIL section 2 Additional risk minimisation measures: Not applicable.

Important potential risk: Breast cancer	
Evidence for linking the risk to the medicine	Suspicion of an association with the medicinal product of interest but this association has not been confirmed.
Risk factors and risk groups	Advancing age is the biggest risk factor for breast cancer. Reproductive factors that increase exposure to endogenous estrogen, such as early menarche and late menopause, increase risk, as does the use of combination estrogen-progesterone hormones after menopause. Nulliparity and alcohol consumption also are associated with increased risk.

	Women with a family history or personal history of invasive breast cancer, ductal carcinoma *in situ* or lobular carcinoma *in situ*, or a history of breast biopsies that show benign proliferative disease have an increased risk of breast cancer. Exposure to ionizing radiation, especially during puberty or young adulthood, and the inheritance of detrimental genetic mutations increase breast cancer risk. [National Cancer Institute: PDQ® Breast Cancer Prevention. Bethesda, MD, 2015]
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3 and 4.4 PIL section 2 Additional risk minimisation measures: Not applicable.

Important missing information: Not applicable

II.C Post-authorisation development plan

There is not post authorisation development program planned.

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

There are no studies, which are conditions of the marketing authorisation.

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

PASS study for VTE.

Summary of risk management plan for Stelista (drospirenone)

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

I. The medicine and what it is used for

Stelista is indicated for oral contraception. It contains drospirenone as the active substance and it is given orally.

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

Important risks of drospirenone, together with measures to minimise such 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.

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

II.A List of important risks and missing information

Important risks of Stelista are risks that need special risk minimisation 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 Stelista. 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	• Hyperkalemia