Summary of the Risk Management Plan for Moniq Gynial mono 75 µg Filmtabletten

VI.1 Elements for summary tables in the EPAR

VI.1.1 Summary table of Safety concerns

Summary of safety concerns	
Important identified risks	**7 Important Identified Risks (listed by SOC)** 1. Known or suspected sex-steroid sensitive malignancies 2. Hypersensitivity to the active substances or to any of the excipients 3. Presence or history of severe hepatic disease as long as liver function values have not returned to normal 4. Chloasma 5. Angioedema 6. Ectopic pregnancy 7. Abnormal genital bleeding
Important potential risks	**3 Important Potential Risks (listed by SOC)** 1. Insulin resistance/decreased glucose tolerance 2. Active venous thromboembolic disorder 3. Hypertension
Missing information	**3 Missing Information** 1. Effect on bone mineral density 2. Renal impairment 3. Paediatric population (below 18 years)

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

N/A

VI.1.3 Summary of Post authorisation efficacy development plan

N/A

VI.1.4 Summary table of Risk Minimisation Measures

Safety concern	**Routine risk minimisation measures**	**Additional risk minimisation measures**
IMPORTANT IDENTIFIED RISKS		
Known or suspected sex-steroid sensitive malignancies	(Proposed) text in SmPC Listed as contraindication in section 4.3. Special warning in section 4.4.	None

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
	Listed in section 4.8. Prescription only medicine • Routine Pharmacovigilance activities • Monitoring of safety profile • Review in signal detection • Discussion of new cases in the PSURs • Heightened surveillance and follow-up of all sex-steroid sensitive malignancy ADRs from spontaneous and study sources	
Hypersensitivity to the active substances or to any of the excipients	(Proposed) text in SmPC Listed as contraindication in section 4.3. Special warning regarding the excipient lactose in section 4.4. Prescription only medicine • Routine Pharmacovigilance activities • Monitoring of safety profile • Review in signal detection • Discussion of new cases in the PSURs • Heightened surveillance and follow-up of all hypersensitivity ADRs from spontaneous and study sources	None
Presence or history of severe hepatic disease as long as liver function values have not returned to normal	(Proposed) text in SmPC Mentioned in section 4.2. Listed as contraindication in section 4.3. Special warning in section 4.4 Warnings due to possible interactions with other medicinal products in section 4.5. Prescription only medicine • Routine Pharmacovigilance activities • Monitoring of safety profile • Review in signal detection • Discussion of new cases in the PSURs • Heightened surveillance and follow-up of all hepatic disease ADRs from spontaneous and	None

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
	study sources	
Chloasma	(Proposed) text in SmPC Special warning in section 4.4. Listed in section 4.8. Prescription only medicine • Routine Pharmacovigilance activities • Monitoring of safety profile • Review in signal detection • Discussion of new cases in the PSURs • Heightened surveillance and follow-up of all chloasma ADRs from spontaneous and study sources	None
Angioedema	(Proposed) text in SmPC Special warning in section 4.4. Listed in section 4.8. Prescription only medicine • Routine Pharmacovigilance activities • Monitoring of safety profile • Review in signal detection • Discussion of new cases in the PSURs • Heightened surveillance and follow-up of all angioedema ADRs from spontaneous and study sources	None
Ectopic pregnancy	(Proposed) text in SmPC Special warning in section 4.4. Listed in section 4.8. Prescription only medicine • Routine Pharmacovigilance activities • Monitoring of safety profile • Review in signal detection • Discussion of new cases in the PSURs • Heightened surveillance and follow-up of all ectopic pregnancy ADRs from spontaneous and study sources	None
Abnormal genital bleeding	(Proposed) text in SmPC Mentioned in section 4.2. Listed as contraindication in	None

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
	section 4.3. Warnings due to possible interactions with other medicinal products in section 4.5. Listed in section 4.8. Listed as possible symptom of overdose in section 4.9. Prescription only medicine • Routine Pharmacovigilance activities • Monitoring of safety profile • Review in signal detection • Discussion of new cases in the PSURs • Heightened surveillance and follow-up of all genital bleeding ADRs from spontaneous and study sources	
IMPORTANT POTENTIAL RISKS		
Insulin resistance/decreased glucose tolerance	(Proposed) text in SmPC Special warning in section 4.4. Prescription only medicine • Routine Pharmacovigilance activities • Monitoring of safety profile • Review in signal detection • Discussion of new cases in the PSURs • Heightened surveillance and follow-up of all insulin resistance/decreased glucose tolerance ADRs from spontaneous and study sources	None
Active venous thromboembolic disorder	(Proposed) text in SmPC Listed as contraindication in section 4.3. Warning and description in section 4.4. Listed in section 4.8. Prescription only medicine • Routine Pharmacovigilance activities • Monitoring of safety profile • Review in signal detection • Discussion of new cases in the PSURs	None

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
	• Heightened surveillance and follow-up of all venous thromboembolism ADRs from spontaneous and study sources	
Hypertension	(Proposed) text in SmPC Special warning in section 4.4. Prescription only medicine • Routine Pharmacovigilance activities • Monitoring of safety profile • Review in signal detection • Discussion of new cases in the PSURs • Heightened surveillance and follow-up of all hypertension ADRs from spontaneous and study sources	None
MISSING INFORMATION		
Effect on bone mineral density	(Proposed) text in SmPC Special warning in section 4.4. Prescription only medicine • Routine Pharmacovigilance activities • Monitoring of safety profile • Review in signal detection • Discussion of new cases in the PSURs • Heightened surveillance and follow-up of all decreased bone mineral density ADRs from spontaneous and study sources	None
Renal impairment	(Proposed) text in SmPC Mentioned in section 4.2 and 5.2. Prescription only medicine • Routine Pharmacovigilance activities • Monitoring of safety profile • Review in signal detection • Discussion of new cases in the PSURs • Heightened surveillance and follow-up of all ADRs in patients with renal impairment from spontaneous and study sources	None
Paediatric population	(Proposed) text in SmPC Mentioned in section 4.2 and 5.1.	None

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
(below 18 years)	Prescription only medicine • Routine Pharmacovigilance activities • Monitoring of safety profile • Review in signal detection • Discussion of new cases in the PSURs • Heightened surveillance and follow-up of all ADRs in adolescents below 18 years from spontaneous and study sources	

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Contraception

Moniq Gynial mono is used to prevent pregnancy. It contains a small amount of one type of female sex hormone, the progestogen desogestrel. For this reason Moniq Gynial mono is called a progestogen-only-pill (POP), or a mini-pill. Contrary to the combined pill, a mini-pill does not contain an oestrogen hormone next to the progestogen.

Most POPs or mini-pills work primarily by preventing the sperm cells from entering the womb but do not always prevent the egg cell from ripening, which is the primary action of combined pills. Moniq Gynial mono is distinct from other mini-pills in having a dose that in most cases is high enough to prevent the egg cell from ripening. As a result, Moniq Gynial mono is highly effective in preventing pregnancy.

In contrast to the combined pill, Moniq Gynial mono can be used by women who do not tolerate oestrogens and by women who are breast feeding. A disadvantage is that vaginal bleeding may occur at irregular intervals during the use of Moniq Gynial mono. You also may not have any bleeding at all [4].

VI.2.2 Summary of treatment benefits

When compared with another desogestrel-only pill for 2 cycles (56 days), the frequency with which an egg cell was released from the womb was found to be 1%, or in 1 out of 103 women. The release of the egg cell was successfully prevented from the first cycle of use. In this study, when the women stopped taking the desogestrel-only pill after 2 cycles (56 days), the release of an egg cell from the ovary occurred again on average after 17 days.

In a study that allowed a maximum time of 3 hours for missed pills, comparing a desogestrel-only pill with another mini-pill, the overall Pearl-Index for the desogestrel-only pill (like Moniq Gynial mono) was 0.4, compared to 1.6 for the other mini-pill. This means that the desogestrel-only pill (like Moniq Gynial mono) was more effective in preventing pregnancy than the other mini-pill.

The Pearl-Index for Moniq Gynial mono is comparable to the one historically found for combined pills in the general combined pill-using population [1].

VI.2.3 Unknowns relating to treatment benefits

Bone density

Treatment with desogestrel (the active ingredient in Moniq Gynial mono) leads to decreased oestradiol serum levels, to a level corresponding with the early follicular phase. It is as yet unknown whether the decreased blood level of the hormone oestradiol during treatment with Moniq Gynial mono has any important effect on bone density.

Patients with impaired kidney function

There is no experience with Moniq Gynial mono in patients with impaired kidney function. No studies have been performed in patients with impaired function of the kidneys.

Children and adolescents (below 18 years of age)
There is no data available on the safety and efficacy of desogestrel in adolescents below 18 years of age.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
A cancer that is sensitive to sex-steroids, such as certain types of breast cancer or liver cancer (known or suspected sex-steroid sensitive malignancies)	In women using (combined) pills, a number of undesirable effects have been reported. These include hormone-dependent tumours like liver tumours and breast cancer. Breast cancer has been found slightly more often in women who take the pill than in women of the same age who do not take the pill. If women stop taking the pill, the risk gradually decreases, so that 10 years after stopping the risk is the same as for women who have never taken the pill. Breast cancer is rare under 40 years of age but the risk increases as the woman gets older. Therefore, the extra number of breast cancers diagnosed is higher if the age until which the woman continues to take the pill is higher. How long she takes the pill is less important. The risk of breast cancer in users of progestogen-only pills like Moniq Gynial mono is believed to be similar to that in women who use the combined pill, but the evidence is less conclusive. Breast cancers found in women who take the pill, seem less likely to have spread than breast cancers found in women who do not take the pill. It is not known whether the difference in breast cancer risk is caused by the pill.	Regularly check your breasts and contact your doctor as soon as possible if you feel any lump in your breasts. Do not take Moniq Gynial mono, if you have or are suspected to have a cancer that is sensitive to sex-steroids. Talk to your doctor or pharmacist before taking Moniq Gynial mono if you have liver cancer, since a possible effect of Moniq Gynial mono cannot be excluded.

Risk	What is known	Preventability
	It may be that the women were examined more often, so that the breast cancer is noticed earlier. Since there is a possible effect of the female sex hormone progestogen on liver cancer, the benefits of taking the pill should be higher than the related risks in women who suffer from liver cancer.	
Allergic reaction to the active substance or any of the other ingredients (hypersensitivity)	In rare cases allergic reactions to one of the ingredients of Moniq Gynial mono occur. Since it also contains lactose, Moniq Gynial mono is not suited for people with any type of lactose intolerance.	Do not take Moniq Gynial mono, if you are allergic to desogestrel, lactose or any of the other ingredients of this medicine. If you have been told by your doctor that you are intolerant to some sugars, contact your doctor before taking this medicine.
Presence or history of severe liver disease as long as liver function values have not returned to normal	If your liver does not work properly, it is harder for your body to break down steroid hormones like those contained in Moniq Gynial mono. Therefore, the use of desogestrel is not indicated, as long as liver function values have not returned to normal.	Do not take Moniq Gynial mono if you have or have had jaundice (yellowing of the skin) or severe liver disease and your liver function is still not normal. Contact your doctor as soon as possible if you have a sudden, severe stomach ache or your skin looks yellow (possibly a sign of liver problems).
Yellowish-brown pigmentation patches on the skin, particularly of the face (chloasma)	Chloasma may occasionally occur, especially in women with a history of chloasma during pregnancy. Women with a tendency to develop chloasma should avoid exposure to the sun or ultraviolet radiation whilst taking Moniq Gynial mono.	Talk to your doctor or pharmacist before taking Moniq Gynial mono if you have or have had chloasma (yellowish-brown pigmentation patches on the skin, particularly of the face); if so, avoid too much exposure to the sun or ultraviolet radiation.
Swelling beneath the surface of the skin (angioedema)	During use of Moniq Gynial mono, aggravation of angioedema and/or aggravation of hereditary angioedema may occur. Symptoms of angioedema	You should see your doctor immediately if you experience symptoms of angioedema, such as swollen face, tongue or throat; difficulty to swallow; or

Risk	What is known	Preventability
	are a swollen face, tongue or throat, difficulty to swallow, hives and difficulties to breathe.	hives and difficulties to breathe.
Pregnancy outside the womb (ectopic pregnancy)	On rare occasions, ectopic pregnancies, which are pregnancies outside the womb, have been reported. When using progestogen-only pills, ovulation (which is the release of an egg from the ovary towards the womb) happens much more often than during the use of combined pills. Therefore, progestogen-only pills are less effective in protecting you from a pregnancy outside the womb. Despite the fact that Moniq Gynial mono consistently prevents the release of an egg from the ovary, an ectopic pregnancy must be considered if you notice the absence of your menstrual period or experience abdominal pain.	Contact your doctor as soon as possible if you have a sudden or severe pain in the lower abdomen or stomach area, possibly indicating an ectopic pregnancy.
Abnormal genital bleeding	Genital bleeding may occur at irregular intervals during the use of Moniq Gynial mono. This may be just slight staining which may not even require a pad, or heavier bleeding, which looks rather like a scanty period and requires sanitary protection. You may also not have any bleeding at all. The irregular bleedings are not a sign that the contraceptive protection of Moniq Gynial mono is decreased. In general, you need not take any action; just continue to take your tablets as normal. Slight vaginal bleeding may occur as a symptom from taking too many Moniq Gynial mono tablets at one time.	Do not take Moniq Gynial mono if you have any unexplained vaginal bleeding. Contact your doctor as soon as possible if you have unusual, heavy vaginal bleeding.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Low ability to break down blood sugar (insulin resistance / decreased glucose tolerance)	Although the female sex hormone progestogen (like in Moniq Gynial mono) may lower the effectiveness of insulin in your body and lower your ability to break down blood sugar, it is not proven that women who suffer from diabetes necessarily have to change the way they use the progestogen-only pill. However, if you suffer from diabetes, talk to your doctor or pharmacist before taking Moniq Gynial mono.
Formation of a blood clot in a blood vessel (active venous thromboembolic disorder)	Thrombosis is the formation of a blood clot, which may block a blood vessel. A thrombosis sometimes occurs in the deep veins of the legs (deep venous thrombosis). If this clot breaks away from the veins where it is formed, it may reach and block the blood vessels of the lungs, causing a so-called "pulmonary embolism". As a result, fatal situations may occur. Deep venous thrombosis is a rare occurrence. It can develop whether or not you are taking the pill. It can also happen if you become pregnant. The risk is higher in pill-users than in non-users. The risk with progestogen-only pills like Moniq Gynial mono is believed to be lower than in users of pills that also contain oestrogens (combined pills).
High blood pressure (hypertension)	Talk to your doctor or pharmacist before taking Moniq Gynial mono if you have high blood pressure. It is possible that your blood pressure rises during use of Moniq Gynial mono. If your blood pressure remains high, or a strong increase in blood pressure does not subside after corrective blood pressure treatment, you should consider stopping Moniq Gynial mono treatment.

Missing information

Risk	What is known
Reduced bone mineral density	Treatment with desogestrel (the active ingredient in Moniq Gynial mono) leads to decreased oestradiol serum levels, to a level corresponding with the early follicular phase. It is as yet unknown whether the decreased blood level of the hormone oestradiol during treatment with Moniq Gynial mono has any important effect on bone density.
No information on use in patients with impaired kidney function	There is no experience with Moniq Gynial mono in patients with impaired kidney function. No studies have been performed in patients with impaired function of the kidneys.

Risk	What is known
No information on use in children and adolescents below 18 years of age	There is no data available on the safety and efficacy of desogestrel in adolescents below 18 years of age.

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 package leaflet (PL). 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

N/A

VI.2.7 Summary of changes to the Risk Management Plan over time

N/A