Summary of the Swiss Risk Management Plan (RMP)

Name of the medicinal product:	Zoely, film-coated tablets
Active substance:	estradiolum, nomegestroli acetas
Version number of the current RMP:	13.0
Name of the marketing authorisation holder:	Future Health Pharma GmbH
Data lock point for the RMP:	14. Juli 2022
Date of RMP:	11. August 2022

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 “Zoely, film-coated tablets” 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 “Zoely, film-coated tablets” in Switzerland is the “Arzneimittelinformation/ Information sur le médicament” (see www.swissmedic.ch) approved and authorized by Swissmedic. “Future Health Pharma GmbH” is fully responsible for the accuracy and correctness of the content of the published summary RMP of “Zoely, film-coated tablets”.

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN BY PRODUCT

Summary of risk management plan for Zoely

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

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

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

I. The Medicine and What it is Used For

Zoely is authorised for oral contraception (see SmPC for the full indication). It contains nomegestrol acetate + 17β-estradiol as the active substances and it is given as a film-coated oral tablet.

Further information about the evaluation of Zoely's benefits can be found in Zoely'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/zoely#assessment-history-section

II. Risks Associated With the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Zoely, together with measures to minimise such risks and the proposed studies for learning more about Zoely '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 the case of NOMAC-E2, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

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 Zoely is not yet available, it is listed under 'missing information' below.

II.A List of Important Risks and Missing Information

Important risks of Zoely 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 Zoely. 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 II.A.1: List of Important Risks and Missing Information

List of Important Risks and Missing Information	
Important identified risks	▪ Depression/Depressed mood ▪ Venous thromboembolic events ▪ Arterial thromboembolic events
Important potential risks	▪ Cholelithiasis/Cholecystitis/Elevated hepatic enzymes ▪ Meningioma
Missing information	▪ Safety in post-menarcheal adolescents ▪ Safety in women during pregnancy

II.B Summary of Important Risks

Table II.B.1: Important Identified Risk: Depression/ Depressed Mood

Evidence for linking the risk to the medicine	Clinical trial data Published literature
Risk factors and risk groups	The following factors predispose certain women to OC-related negative changes in mood/affect: A history of depression, other symptoms of psychological distress (eg, anxiety, stress, neuroticism), dysmenorrheal and premenstrual mood symptoms prior to OC use, a history of pregnancy-related mood symptoms, a family history of OC-related mood complaints, being in the postpartum period and age. A number of OC-related variables also mediate mood/affect changes for certain individuals: For women with a history of premenstrual emotional symptoms prior to OC use, OC formulations with higher progesterone to estrogen dosage ratios are associated with less negative mood changes, as are the use of monophasic versus triphasic OCs. For women without a history of premenstrual irritability, formulations with lower ratios of progesterone to estrogen decrease the risk of negative mood change. Finally, monophasic OCs have a greater stabilizing effect than triphasic OCs.
Risk minimisation measures	**Routine risk minimisation measures:** The risk of depression/ depressed mood is described in sections 4.4 Special warnings and precautions for use and 4.8 Undesirable effects of the SmPC.
Additional pharmacovigilance activities	**Additional pharmacovigilance activities:** None

Table II.B.2: Important Identified Risk: Venous Thromboembolic Events

Evidence for linking the risk to the medicine	Clinical trial data Published literature
Risk factors and risk groups	Risk factors for VTE are: Hereditary risk factors: • Antithrombin III deficiency • Protein C deficiency • Protein S deficiency • Activated protein C resistance (Factor V Leiden gene mutation) • Prothrombin gene mutation (G20210A) • Hyperhomocysteinemia Acquired risk factors: • Obesity • Varicose veins • Antiphospholipid antibodies (lupus anticoagulant and anticardiolipin antibodies) • Postpartum period • Pregnancy • Surgery • Trauma • Stasis (eg, due to prolonged immobility) • Increasing age • Positive (family) history • Other diseases (eg, hemolytic uremic syndrome, inflammatory bowel disease, auto-immune states such as systemic lupus erythematosus, HBsAg, hypothyroidism, malignancy, renal disease) • Smoking
Risk minimisation measures	**Routine risk minimisation measures:** The risk of VTEs are described in sections 4.3 Contraindications, 4.4 Special warnings and precautions for use and 4.8 Undesirable effects of the SmPC. **Additional risk minimization measures:** A one-time distributed DHPC was sent in collaboration with other MAHs of CHCs and National Competent Authorities in the first quarter of 2014. Also, educational materials were implemented at the time of DHPC distribution and maintained and distributed on a country-specific level according to local Health Authority requirements.
Additional pharmacovigilance activities	**Additional pharmacovigilance activities:** None

Table II.B.3: Important Identified Risk: Arterial Thromboembolic Events

Evidence for linking the risk to the medicine	Clinical trial data Published literature
Risk factors and risk groups	Risk factors for ATE are: • Increasing age, particularly above 35 years. • Smoking. • Hypertension • Obesity (body mass index over 30kg/m^2) • Positive family history (arterial thromboembolism ever in a sibling or parent especially at relatively early age, e.g., below 50) • Migraine • Other medical conditions associated with adverse vascular events (e.g., diabetes mellitus, hyperhomocysteinaemia, valvular heart disease and atrial fibrillation, dyslipoproteinemia and systemic lupus erythematosus)
Risk minimisation measures	**Routine risk minimisation measures:** The risk of ATEs are described in sections 4.3 Contraindications, 4.4 Special warnings and precautions for use and 4.8 Undesirable effects of the SmPC. **Additional risk minimization measures:** A one-time distributed DHPC was sent in collaboration with other MAHs of CHCs and National Competent Authorities in the first quarter of 2014. Also, educational materials were implemented at the time of DHPC distribution and maintained and distributed on a country-specific level according to local Health Authority requirements.
Additional pharmacovigilance activities	**Additional pharmacovigilance activities:** None

Table II.B.4: Important Potential Risk: Cholelithiasis/ Cholecystitis/ Elevated Hepatic Enzymes

Evidence for linking the risk to the medicine	Clinical trial data Published literature
Risk factors and risk groups	Some risk factors for gallstones are unalterable, such as advancing age, being female, and genes/ethnicity. Ethnic differences vary from a high prevalence of 60-70% in American Indians to prevalences of 20% in Northern Europe and 6-17% overall in Europe and North American white adults. Very low rates occur in Black Africans. Other factors can be modified such as obesity, rapid weight loss, diet, drugs, and activity. Detrimental are diets with a high caloric intake and refined carbohydrates. Beneficial are diets high in fibre, vegetable protein, nuts, calcium, vitamin C, caffeinated coffee, and alcohol in moderation. Physical activity appears protective, decreasing the possibility of developing cholelithiasis. Reduced physical activity increased the risk. Ceftriaxone is avidly secreted into bile and can precipitate with calcium to form biliary sludge and stones. Estrogen is also thought to promote the formation of gallstones.
Risk minimisation measures	**Routine risk minimisation measures:** The risks of cholelithiasis/ cholecystitis/ elevated hepatic enzymes are described in sections 4.3 Contraindications and 4.8 Undesirable effects of the SmPC.
Additional pharmacovigilance activities	**Additional pharmacovigilance activities:** None

Table II.B.5: Important Potential Risk: Meningioma

Evidence for linking the risk to the medicine	Published literature
Risk factors and risk groups	Established risk factors for meningioma include mutations in the neurofibromatosis gene (NF2) as well as exposure of the brain to high does ionizing radiation.
Risk minimisation measures	**Routine risk minimisation measures:** The risk of meningioma is described in sections 4.3 Contraindications and 4.4 Special warnings and precautions for use of the SmPC. **Additional risk minimization measures:** DHPC will be send in collaboration with other MAHs of chlormadinone and nomegestrol containing products and National Competent Authorities as an obligation of the referral procedure (EMEA/H/A-31/1510).

Table II.B.6: Missing Information: Safety in Post-menarcheal Adolescents

Risk minimisation measures	**Routine risk minimisation measures:** The missing information regarding safety in post-menarcheal adolescents is described in sections 4.4 Special warnings and precautions for use, 5.1 Pharmacodynamic properties, and 5.2 Pharmacokinetic properties.
Additional pharmacovigilance activities	**Additional pharmacovigilance activities:** None

Table II.B.7: Missing Information: Safety in Women During Pregnancy

Risk minimisation measures	**Routine risk minimisation measures:** The missing information regarding safety in women during pregnancy is described in sections 4.2 Posology and method of administration, 4.4 Special warnings and precautions for use, and 4.6 Fertility, pregnancy and lactation.
Additional pharmacovigilance activities	**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 to the marketing authorisation or specific obligation for Zoely at the time of updating the RMP.

II.C.2 Other Studies in Post-Authorisation Development Plan

There are no studies required for NOMAC-E2.