4.2 Part VI.2 Elements for a Public Summary

4.2.1 Part VI.2.1 Overview of disease epidemiology

Globally, 63% of married women or those in union were using some form of contraception in 2008. However, in the WHO African Region, use of contraceptive was below 25% and 43% in the WHO Eastern Mediterranean Region. [1)] In 2012, 70.7% of European married women or those in union were using some form of contraception [2)].

Today, the voluntary control of fertility is of paramount importance to modern society. From a global perspective, countries currently face the crisis of rapid population growth that has begun to threaten human survival. On a smaller scale, effective birth control can be essential to a woman's ability to achieve her individual goals and to contribute to her sense of well-being. [3)]

4.2.2 Part VI.2.2 Summary of treatment benefits

There are several contraceptive methods available. Examples are oral, injectable or implantable hormonal contraceptives, intrauterine devices, condoms, male or female sterilisation, periodic abstinence, or spermicidal agents. A patient's choice of contraceptive method involves factors such as efficacy, safety, non-contraceptive benefits, cost, and personal considerations [3)].

With 30%, oral contraceptives like Ethinylestradiol/ Gestodene are the most widely used method of contraception for women in Europe. This is followed by condom use (20%), reversible long-term contraceptive methods (11%), sterilisation methods (11%), and unreliable methods of contraception (6%). [4)] Failure rates of oral contraceptives are correlated to individual compliance and range from 0.1-0.3% with perfect use to 2.2 – 8% with typical use [3,5)].

4.2.3 Part VI.2.3 Unknowns relating to treatment benefits

None

4.2.4 Part VI.2.4 Summary of safety concerns

Table 4-4 Important identified risks

Risk	What is known	Preventability
Venous thromboembolism (VTE) (blood clots of a vein)	The use of any COC carries an increased risk of VTE compared with no use. The excess risk of VTE is highest during the first year a woman ever uses a combined oral contraceptive. This increased risk is less than the risk of VTE associated with pregnancy, which is estimated as 60 cases per 100,000 pregnancies.	COCs (Combined Oral Contraceptives) should not be used in the presence of venous thrombosis present or in history (deep venous thrombosis, pulmonary embolism). Should venous thrombosis appear for the first time during COC use, the product should be stopped.
Arterial thromboembolism (blood clots of an artery)	Epidemiological studies have associated the use of combined COCs with an increased risk for myocardial infarction (heart attack) and for stroke. Extremely rarely, thrombosis has been reported to occur in hepatic (liver), mesenteric (bowel), renal (kidney) or retinal (eye) arteries, in contraceptive pill users. There is no consensus as to whether the occurrence of these events is associated with the use of hormonal contraceptives.	COCs should not be used in the presence of arterial thrombosis present or in history. Should arterial thrombosis, prodromal conditions or cerebrovascular accident (in the brain) appear for the first time during COC use, the product should be stopped.
Benign and malign liver tumours	In rare cases, benign liver tumours, and even more rarely, malignant liver tumours have been reported in users of COCs.	COCs should not be used in the presence or history of liver tumours (benign or malignant). Should a liver tumour appear for the first time during COC use, the product should be stopped.
Breast cancer Cervical cancer	The frequency of diagnosis of breast cancer is very slightly increased among OC users. An increased risk of cervical cancer in long-term users of COCs has been reported in some epidemiological studies, but there continues to be controversy about the extent to which this finding is attributable to the confounding effects of sexual behavior and other factors such as human papilloma virus.	COCs should not be used in the presence of known or suspected breast cancer. Should breast cancer appear for the first time during COC use, the product should be stopped. COCs should not be used in the presence or history of cervical cancer. Should cervical cancer appear for the first time during COC use, the product should be stopped.

Effect on hereditary angioedema (blood disorder that causes episodic attacks of swelling of parts of the body)	In women with hereditary angioedema exogenous estrogens may induce or exacerbate symptoms of angioedema.	COCs should be used with care in patients with hereditary angioedema.
Disturbances of liver function	Liver function can be impaired by COC, although jaundice (yellowish pigmentation of the skin) is rare[7)].	COCs should not be used in the presence of severe hepatic disease, current or previous, as long as liver function values have not returned to normal. Should severe hepatic disease appear for the first time during COC use, the product should be stopped. Also acute or chronic disturbances of liver function may necessitate discontinuation of COC use until the liver function values return to normal.
Pancreatitis (inflammation of the pancreas)	Women with hypertriglyceridemia, or a family history thereof, may be at an increased risk of pancreatitis when using COCs. Hypertriglyceridemia is one of the known causes of pancreatitis. Estrogen treatment can aggravate hypertriglyceridemia.	COCs should not be used in the presence of pancreatitis or history of such a condition, if associated with severe hypertriglyceridemia. Should pancreatitis appear for the first time during COC use, the product should be stopped.
Increased blood pressure	Even though slight increases in blood pressure have been reported in many women taking COCs, clinically important increases in blood pressure are rare.	If persistent clinical hypertension develops during COC use, intake should be discontinued and the hypertension treated. Use of COCs may be resumed, if appropriate, when normotensive values are reached with antihypertensive therapy.

Table 4-5 Important potential risks

Risk	What is known
Worsening of endogenous depression/depressed mood	Depressive mood has been reported to occur or deteriorate during both pregnancy and COC use, but the evidence of an association with COC use is inconclusive. Depressed mood is observed commonly (> 1/100) with COC use. Worsening of endogenous depression has been reported during COC use.
Crohn's disease and ulcerative colitis (bowel diseases)	Worsening of Crohn's disease and of ulcerative colitis has been reported during COC use. However, the association with COC use is not conclusive. Although an increased risk of relapse of Crohn's disease in women who had taken oral contraceptives in the past was reported in one study, this and another study found no increase in risk in current users. These

Risk	What is known
	results may have been influenced by smoking, or changes in oestrogen dose and progestogen content.[7)]

4.2.5 Part VI.2.5 Summary of additional risk minimisation measures by safety concern

All medicines have a 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 special conditions and restrictions for its safe and effective use (additional risk minimisation measures). These additional risk minimization measures are for the following risks:

Risk minimization measure(s)
Summary description of main additional risk minimisation measures: **Embolic and thrombotic events** Objective and rationale: To remind healthcare professionals of the importance of recognizing the risk of a blood clot occurrence and the need to instruct patients on correct identification of signs and symptoms they need to look out for and what action are needed to be taken. Proposed action: The PRAC requested a DHPC to be communicated, following the changes of the label. This was sent to the Health Care Professionals as requested. *The Patient Information Card* The Patient Information Card is instructing the patients: • In which situations is the risk of a blood clot highest • When to immediately seek medical attention • What symptoms need to be addressed towards the care giver • When should the patients inform the doctor, nurse or surgeon that she is taking Gestodene / Ethinylestradiol. *The Checklist for Prescribers* The Checklist for Prescribers encourages the HCPs to use this tool in conjunction with the Summary of Product Characteristics during every combined hormonal contraceptive (CHC) consultation. The HCPs are advised for which medical conditions the CHC should not be used and the HCPs are advised to discuss the suitability of a CHC with the patient. The patients should be informed about the situations when the blood clot risk is increased.

4.2.6 Part VI.2.6 Planned post authorisation development plan

None

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

N/A