VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Almost all women are at risk for unintended pregnancy throughout their reproductive years. Reproductive rights embrace certain human rights that are already recognized in national laws and international human rights documents. Contraceptive use and unmet need for family planning are key to understanding profound changes in fertility and to improving reproductive health worldwide.

Contraceptive prevalence is the percentage of women who are currently using, or whose sexual partner is currently using, at least one method of contraception, regardless of the method used. It is usually reported for married or in-union women aged 15 to 49.

The distribution of specific methods used was similar in 1990 and 2011 even though contraceptive prevalence among married or in-union women of reproductive age increased worldwide from 55 per cent in 1990 to 63 per cent in 2011. Women's choices are often imposed or limited by direct or indirect social, economic and cultural factors. From the women's point of view, choices are made in a particular time, societal and cultural context; choices are complex, multifactorial and subject to change. Female sterilization remains common in Asia, Latin America and the Caribbean and Northern America, and the IUD continues to be important in Asia and Europe. The pill has the widest geographic distribution of any method. However, adolescents and women of low socioeconomic status are at greater risk for contraceptive non-use and for contraceptive failure; thus they are also at greater risk for unintended conceptions.

VI.2.2 Summary of treatment benefits

The efficacy of desogestrel has been well documented over many years of widespread clinical use.

The contraceptive effect of Desogestrel tablets is achieved by inhibition of ovulation.
When studied this desogestrel product for 2 cycles in a randomized trial, using a definition of ovulation as a progesterone level greater than 16 nmol/L for 5 consecutive days, the ovulation incidence was found to be 1% in the in the ITT group (that's to say the "*Intention To Treat"* group, that includes all patients entering the study, considering user failures + method failures). Ovulation inhibition was achieved from the first cycle of use. When this desogestrel product was discontinued after 2 cycles ovulation occurred on average after 17 days (range 7-30 days).

Hormonal contraceptives are among the most popular, safe, and effective methods of reversible contraception. Authorities all over the world – including the US Food and Drug Administration and the European Medicines Agency – stipulate assessment of efficacy by the Pearl Index (PI) (11)

The Pearl Index is a formula that allows comparison of the efficacy of contraceptive methods and reflects the number of pregnancies per 100 women-years of exposure, or how many pregnancies will occur in 100 sexually active women in one year.

In a comparative efficacy trial (which allowed a maximum time of 3 hours for missed pills), the Pearl–Index found for this medicinal product in the *Intention To Treat* group (all patients entering the study, including user failures + method failures) was 0.4, compared to 1.6 for 30 µg levonorgestrel.

The Pearl-Index for desogestrel is comparable to the one historically found for combined oral contraceptives in the general combined oral contraceptives-using population. Treatment with desogestrel leads to decreased estradiol levels, to a level corresponding to the early follicular phase, which is the phase after your menstrual flow has ended and your levels of estrogen and progesterone are at their lowest. No clinically relevant effects on carbohydrate metabolism, lipid metabolism and haemostasis have been observed.

VI.2.1 Unknowns relating to treatment benefits

This section is not applicable.

VI.2.2 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Venous thromboembolism	Epidemiological investigations have associated the use of COCs with an increased incidence of venous thromboembolism (VTE, deep venous thrombosis and pulmonary embolism). Although the clinical relevance of this finding for desogestrel used as a contraceptive in the absence of an oestrogenic component is unknown, desogestrel should be discontinued in the event of a thrombosis. Discontinuation of desogestrel should also be considered in case of long-term immobilisation due to surgery or illness. Women with a history of thrombo-embolic disorders should be made aware of the possibility of a recurrence.	Desogestrel should be prescribed with caution in patients with risk factors. Warn patients about signs and symptoms. Early detection and monitoring.
Arterial thromboembolism	The results of epidemiological studies indicate a relationship between the use of an oral contraceptive and an increased risk of arterial and venous thrombotic and thromboembolic diseases such as myocardial infarction, cerebral stroke, deep vein thrombosis and pulmonary embolism. These events are rare. Epidemiological studies have shown that the incidence of venous thromboembolism (VTE) in women with no known risk factors for VTE who use low dose oestrogen (<50 mcg EE) COCs ranges from about 20 cases per 100000 woman-years (for levonorgestrel- containing COCs) to 40 cases per 100000 woman-years (for desogestrel/gestodene-containing COCs). This compares with 5 to 10 cases per 100000 woman-years for non-users and 60 cases per 100000 pregnancies. VTE is fatal in 1-2% of cases. Extremely rarely, thrombosis has been	Desogestrel should be prescribed with caution in patients with risk factors. Warn patients about signs and symptoms. Early detection and monitoring.

Risk	What is known	Preventability
	reported to occur in other blood vessels, e.g. hepatic, mesenteric, renal, cerebral or retinal veins and 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.	

Hypertension	If sustained hypertension develops during the use of desogestrel, or if a significant increase in blood pressure does not adequately respond to antihypertensive therapy, the discontinuation of desogestrel should be considered.	Desogestrel should be prescribed with caution in patients with risk factors. Early detection and monitoring.
Disturbances of liver function	Disturbances of liver function have been reported in COC users. COCs should not be used in case of presence or history of severe hepatic disease, as long as liver function values have not returned to normal. Acute or chronic liver function disorders require discontinuation of COC use until liver function markers return to normal. Recurrence of liver function disorders requires discontinuation of COCs.	Desogestrel should be prescribed with caution in patients with predisposing factors. Early detection and monitoring.

Important potential risks

Risk	What is known
Breast Cancer	Numerous epidemiologic studies have been performed on the incidence of breast, endometrial, ovarian, and cervical cancer in women using oral contraceptives. In spite of many studies of the relationship between oral contraceptive use and breast and cervical cancers, a cause-and-effect relationship has not been established.
Cervical cancer	Numerous epidemiologic studies have been performed on the incidence of breast, endometrial, ovarian, and cervical cancer in women using oral contraceptives. In spite of many studies of the relationship between oral contraceptive use and breast and cervical cancers, a cause-and-effect relationship has not been established.

Risk	What is known
Benign or malign liver tumours	In rare cases, benign, and even more rarely, malignant liver tumours have been reported during oral contraceptive use. Contraceptives should not be used in case of presence or history of liver tumours (benign or malignant).

VI.2.3 Summary of additional risk minimisation measures by safety concern

N/A

VI.2.4 Planned post authorisation development plan

N/A

VI.2.5 Summary of changes to risk management plan over time

Version	Date	Safety Concerns	Comment
01	Nov 2015	*Identified Risks* - Venous thromboembolism - Arterial thromboembolism - Hypertension - Disturbances of liver function *Potential Risks* - Breast cancer - Cervical cancer - Benign and malignant liver tumours *Missing information* - Not applicable	
02	Apr 2016	No changes in safety concerns.	-Added estimated patient exposure in PartII -SV.2.1. Non-study post-authorisation exposure. - Reworded in layman language section VI.2.2 Summary of treatment benefits