

## **VI.2. ELEMENTS FOR A PUBLIC SUMMARY**

### **VI.2.1 Overview of Disease Epidemiology**

COCs containing DRSP-EE are indicated for the prevention of pregnancy in women who elect to use oral contraceptives as a method of contraception.

Target population is comprised of women in fertile age. There are 60 million women of reproductive age in the US, approximately 64% of whom use some method of contraception. COCs are the most popular reversible method of contraception due to their high efficacy, ease of use, minimal side effects and good cycle control (Bachmann and Kopacz, 2009).

### **VI.2.2 Summary of Treatment Benefits (lay language).**

Combined Oral Contraceptives are not intended to treat any disease. Hormonal contraception suppresses menstruation and its use is intended to prevent undesired pregnancies. Hormonal contraception has the characteristic of being both user-controlled and highly effective, with negligible failure rates.

### **VI.2.3. Unknowns Relating to Treatment Benefits**

The safety profile of COCs containing DRSP-EE is well known and similar to that of other COCs. These COCs are well tolerated and a good number of clinical trials have been performed in target population (women in reproductive age).

DRSP-EE COCs are contraindicated in women with severe hepatic or renal diseases. Related to age, COCs are only indicated before menarche and after menopause.

Concerning ethnic groups, no clinically relevant differences in the pharmacokinetics of DRSP-EE COCs between Japanese and Caucasian women have been found therefore differences in efficacy are not expected.

## VI.2.4 Summary of Safety Concerns

### Important Identified Risks

RISK	WHAT IS KNOWN	PREVENTABILITY
<p>- <i>Venous and arterial blood clots (venous and arterial thrombosis)</i></p>	<p>The use of any combination pill increases a woman's risk of developing a <b>venous blood clot (venous thrombosis)</b> compared with women who do not take any contraceptive pill.</p> <ul style="list-style-type: none"> <li>- Of 100,000 women who are not on the Pill and not pregnant, about 5-10 may have a blood clot in a year.</li> <li>- Of 100,000 women taking a Pill, 30-40 may have a blood clot in a year, the exact number is unknown.</li> <li>- Of 100,000 women who are pregnant, around 60 may have a blood clot in a year.</li> </ul> <p>A blood clot in the veins may travel to the lungs and may block blood vessels (called a lung embolus). Formation of blood clots in the veins may be fatal in 1-2% of cases.</p> <p>The risk of venous blood clots increases:</p> <ul style="list-style-type: none"> <li>- with increasing age</li> <li>- if you are overweight</li> <li>- if one of your close relatives ever had a blood clot in the leg, lung (pulmonary embolism), or other organ at a young age</li> <li>- if you have to have surgery, if you have had a serious accident or if you are immobilized for a long time.</li> </ul> <p>The use of combination pills has been connected with an increase of the risk of an <b>arterial blood clot (arterial thrombosis)</b>, for example, in the blood vessels of the heart (heart attack) or the brain (stroke).</p> <p>The risk of an arterial blood clot increases:</p> <ul style="list-style-type: none"> <li>- if you smoke.</li> <li>- if the fat content of your blood is increased (cholesterol or triglycerides)</li> <li>- if you are overweight</li> <li>- if one of your close relatives ever had a heart</li> </ul>	<p>Stop taking pill and contact your doctor immediately if you notice possible signs of a blood clot, such as:</p> <ul style="list-style-type: none"> <li>- severe pain and/or swelling in one of your legs</li> <li>- sudden severe pain in the chest which may reach the left arm</li> <li>- sudden breathlessness</li> <li>- sudden cough without an obvious cause</li> <li>- any unusual, severe or long-lasting headache or worsening of migraine</li> <li>- partial or complete blindness or double vision</li> <li>- difficulty in speaking or inability to speak</li> <li>- giddiness or fainting</li> <li>- weakness, strange feeling, or numbness in any part of the body</li> </ul> <p>Do not take pill and consult your doctor if you have disturbance of blood clotting (for example, protein C deficiency)</p>

RISK	WHAT IS KNOWN	PREVENTABILITY
	attack or stroke at a young age - if you have high blood pressure - if you suffer from migraine - if you have a problem with your heart (valve disorder, a disturbance of the cardiac rhythm)	
<b>- Breast Cancer</b>	There is a slightly increased relative risk (RR = 1.24) in women who are currently using COCs, although there is not provided evidence for causation. The excess risk gradually disappears during the course of the 10 years after cessation of COC use.  This potential increase in risk is especially important in patients with known or suspected sex-steroid influenced malignancies of the genital organs or the breasts.	Do not take the pill if you have (or have ever had) a tumour in the breast.
<b>- Benign and malignant liver Tumours</b>	In rare cases, benign liver tumors, and in even fewer cases malignant liver tumors have been reported in pill users.	Do not take the pill if you have (or have ever had) a tumor in the liver.  Contact your doctor if you have unusually severe abdominal pain.
<b>-Disturbances of liver function</b>	Oreal clearance (CL/F) was decreased approximately 50 % in volunteers with moderate hepatic impairment as compared to those with normal liver function.	Acute or chronic disturbances of liver function may necessitate the discontinuation of COC use until markers of liver function return to normal.
<b>- Pancreatitis</b>	Women with hypertriglyceridemia or uncontrolled dyslipidemia have potential increased risk of pancreatitis when using COCs.	Contact your doctor if you have hypertriglyceridemia or uncontrolled dyslipidemia
<b>- Increases in blood pressure</b>	High blood pressure (hypertension) is a disease that may increase the risk of a clot in the arteries.	Do not take pill and consult your doctor if you have very high blood pressure.
<b>- Effect on hereditary angioedema</b>	These clinical conditions have been reported to occur or deteriorate with both pregnancy and COC use, although evidence of an association with COC use is inconclusive.	Due to the clinical relevance of this disease, the potential risk for worsening when

RISK	WHAT IS KNOWN	PREVENTABILITY
		administering COCs must be taken into account.

### Important Potential Risks

RISK	WHAT IS KNOWN	PREVENTABILITY
<i>- Cervical cancer</i>	<p>An increased risk of cervical cancer in women taking COCs (&gt; 5 years) has been reported in some studies, but there continues to be controversy about the extent to which this finding is attributable to other effects or factors such as infection by human papilloma virus. The relative risk has not been established.</p> <p>This potential increase in risk is especially important in patients with known or suspected sex-steroid influenced malignancies of the genital organs or the breasts.</p>	Do not take the pill if you have (or have ever had) a cervical cancer.
<i>-Worsening of endogenous depression</i>	Depression or emotional swings may be developed or worsened while you are using pill.	Consult your doctor if you suffer from worsening.
<i>-Crohn's disease and ulcerative colitis</i>	Crohn's disease and ulcerative colitis may be developed or worsened while you are using pill	If you have diabetes, consult your doctor
<i>Insulin resistance</i>	Diabetes may be developed or worsened while you are using pill	If you have diabetes, consult your doctor.
<i>- Hyperkalemia</i>	<p>Concomitant use of COCs containing DRSP and potassium-sparing medicinal products may be a potential risk for hyperkalemia, mainly in patient with mild or moderate renal impairment.</p> <p>High serum potassium levels may lead to severe or fatal cardiac events.</p>	Contact your doctor if potassium levels increased.

### Important Missing Information

None identified

### **VI.2.5 Summary of Additional Risk Minimization Measures by Safety Concern**

*Not applicable.*

### **VI.2.6 Planned Post-authorisation Development Plan**

*Not applicable.*

### **VI.2.7 Summary of Changes to the Risk Management Plan over Time**

*Not applicable.*