

### **Annex III**

#### **Amendments to relevant sections of the summary of product characteristics and package leaflet**

Note:

The summary of product characteristics and package leaflet may need to be subsequently updated by the national competent authorities, in liaison with the reference Member State, if appropriate

## Summary of Product Characteristics (SmPC)

### Section 4.1 Therapeutic indications

*[The currently approved indications should be deleted and replaced by the following:]*

Treatment of moderate to severe acne related to androgen-sensitivity (with or without seborrhoea) and/or hirsutism, in women of reproductive age.

For the treatment of acne, <invented name> should only be used after topical therapy or systemic antibiotic treatments have failed.

Since <invented name> is also a hormonal contraceptive, it should not be used in combination with other hormonal contraceptives (see section 4.3).

### Section 4.2 Posology and method of administration

*[The wording below should be inserted in this section]*

[...]

#### **Duration of Use**

Time to relieve of symptoms is at least three months. The need to continue treatment should be evaluated periodically by the treating physician.

[...]

### Section 4.3 Contraindications

*[The following contraindications related to thromboembolism should be included in this section]*

[...]

- Concomitant use with another hormonal contraceptive (see section 4.1)
- Venous thrombosis present or in history (deep venous thrombosis, pulmonary embolism)
- Arterial thrombosis present or in history (e.g. myocardial infarction) or prodromal conditions (e.g. angina pectoris and transient ischaemic attack).
- Presence or history of cerebrovascular accident
- The presence of a severe or multiple risk factor(s) for venous or arterial thrombosis (see section 4.4) such as:
  - diabetes mellitus with vascular symptoms
  - severe hypertension
  - severe dyslipoproteinaemia
- Hereditary or acquired predisposition for venous or arterial thrombosis, such as activated protein C (APC) resistance, antithrombin-III-deficiency, protein C deficiency, protein S deficiency, hyperhomocysteinaemia and antiphospholipid-antibodies (anticardiolipin-antibodies, lupus anticoagulant)

[...]

### Section 4.4 Special warnings and precautions for use

*[The wording below should be inserted in this section]*

<invented name> is composed of the progestogen cyproterone acetate and the oestrogen ethinylestradiol and is administered for 21 days of a monthly cycle. It has a similar composition to that of a combined oral contraceptive (COC).

## Duration of Use

Time to relief of symptoms is at least three months. The need to continue treatment should be evaluated periodically by the treating physician (see section 4.2).

[...]

If any of the conditions/risk factors mentioned below is present, the benefits of the use of <invented name> should be weighed against the possible risks for each individual woman and discussed with the woman before she decides to start using <invented name>. In the event of aggravation, exacerbation or first appearance of any of these conditions or risk factors, the woman should contact her physician. The physician should then decide on whether the use of <invented name> should be discontinued.

[...]

## Circulatory disorders

- The use of <invented name> carries an increased risk of venous thromboembolism (VTE) compared with no use. The excess risk of VTE is highest during the first year a woman starts <invented name> or when restarting or switching after a pill-free interval of at least a month. Venous thromboembolism can be fatal in 1-2% of cases.
- Epidemiological studies have shown that the incidence of VTE is 1.5 to 2 times higher in users of <invented name> than in users of levonorgestrel-containing combined oral contraceptives (COCs) and may be similar to the risk for desogestrel / gestodene / drospirenone-containing COCs.
- The user group of <invented name> is likely to include patients that may have an inherently increased cardiovascular risk such as that associated with polycystic ovarian syndrome.
- Epidemiological studies have also associated the use of hormonal contraceptive with an increased risk for arterial (myocardial infarction, transient ischaemic attack) thromboembolism.
- Extremely rarely, thrombosis has been reported to occur in other blood vessels, e.g. hepatic, mesenteric, renal, cerebral or retinal veins and arteries, in hormonal contraceptive users.
- Symptoms of venous or arterial thrombosis or of a cerebrovascular accident can include: unusual unilateral leg pain and / or swelling; sudden severe pain in the chest, whether or not it radiates to the left arm; sudden breathlessness; sudden onset of coughing; any unusual, severe, prolonged headache; sudden partial or complete loss of vision; diplopia; slurred speech or aphasia; vertigo; collapse with or without focal seizure; weakness or very marked numbness suddenly affecting one side or one part of the body; motor disturbances; 'acute' abdomen
- The risk of venous thromboembolic events increases with:
  - increasing age;
  - smoking (with heavier smoking and increasing age the risk further increases, especially in women over 35 years of age. Women over 35 years of age should be strongly advised not to smoke if they wish to use <invented name>);
  - a positive family history (i.e. venous thromboembolism ever in a sibling or parent at a relatively early age). If a hereditary predisposition is suspected, the woman should be referred to a specialist for advice before deciding about any hormonal contraceptive use;
  - prolonged immobilisation, major surgery, any surgery to the legs, or major trauma. In these situations it is advisable to discontinue use (in the case of elective surgery at least four weeks in advance) and not to resume until two weeks after complete remobilisation. Antithrombotic treatment should be considered if the use of <invented name> has not been discontinued in advance.
  - obesity (body mass index over 30 kg/m<sup>2</sup>).
- The risk of arterial thromboembolic complications or of a cerebrovascular accident increases with:
  - increasing age;
  - smoking (with heavier smoking and increasing age the risk further increases, especially in women over 35 years of age. Women over 35 years of age should be strongly advised not to smoke if they wish to use <invented name>);
  - dyslipoproteinemia;
  - obesity (body mass index over 30 kg/m<sup>2</sup>);

- hypertension;
- migraine;
- valvular heart disease;
- atrial fibrillation;
- a positive family history (arterial thrombosis ever in a sibling or parent at a relatively early age). If a hereditary predisposition is suspected, the woman should be referred to a specialist for advice before deciding about any hormonal contraceptive use.
- Other medical conditions, which have been associated with adverse circulatory events, include diabetes mellitus, systemic lupus erythematosus, hemolytic uraemic syndrome, chronic inflammatory bowel disease (e.g. Crohn's disease or ulcerative colitis) and sickle cell disease.
- The increased risk of thromboembolism in the puerperium must be considered (for information on 'Pregnancy and lactation' see section 4.6).
- An increase in frequency or severity of migraine during use of <invented name > (which may be prodromal of a cerebrovascular event) may be a reason for immediate discontinuation of <invented name>.

Women using <invented name> should be specifically pointed out to contact their physician in case of possible symptoms of thrombosis. In case of suspected or confirmed thrombosis, <invented name> use should be discontinued. Adequate contraception should be initiated because of the teratogenicity of anti-coagulant therapy (coumarins).

#### **Section 4.8 - Undesirable effects**

*[The wording below should be inserted in this section]*

*[...]*

- There is an increased risk of thromboembolism for all women who use <invented name> (see section 4.4).

*[The following to be included in the table of adverse reactions]*

- Vascular Disorders Rare ( $\geq 1/10,000$  to  $< 1/1000$ ): Thromboembolism

*[The following to be included below the table of adverse reactions]*

The following serious adverse events have been reported in women using <invented name>, which are discussed in section 4.4 Special warning and precautions for use:

- Venous thromboembolic disorders
- Arterial thromboembolic disorders

*[...]*

## Package Leaflet

### 1. What < invented name > is and what it is used for

*[This section should replace any existing one and should read as follows:]*

<Invented name> is used to treat skin conditions such as acne, very oily skin and excessive hair growth in women of reproductive age. Due to its contraceptive properties it should only be prescribed for you if your doctor considers that treatment with a hormonal contraceptive is appropriate.

You should only take <invented name> if your skin condition has not improved after use of other anti-acne treatments, including topical treatments and antibiotics.

### 2. What you need to know before you use < invented name >

*[The wording below should be inserted in the relevant sections]*

*[...]*

#### **Do not take <invented name>**

Tell your doctor if any of the following conditions applies to you before starting to use <invented name>. Your doctor may then advise you to use a different treatment:

- if you are using another hormonal **contraceptive**
- if you have (or have ever had) a **blood clot** in your leg (thrombosis), lung (pulmonary embolism) or other part of your body
- if you have (or have ever had) a disease that may be an indicator of a heart attack in the future (e.g. angina pectoris which causes severe pain in the chest) or '**mini-stroke**' (transient ischaemic attack)
- if you have (or have ever had) a **heart attack or stroke**
- if you have a condition that may increase the risk of a **blood clot** in your arteries. This applies to the following conditions:
  - **diabetes affecting your blood vessels**
  - very high **blood pressure**
  - a very high level of **fat in your blood** (cholesterol or triglycerides)
- if you have problems with **blood clotting** (e.g. protein C deficiency)
- if you have (or have ever had) a **migraine, with visual disturbances**

*[...]*

#### **Warnings and precautions**

*[The wording below should be inserted in this section]*

#### **When should you contact your doctor**

*[...]*

**Stop taking tablets and contact your doctor immediately if you notice possible signs of a blood clot. The symptoms are described in section 2 'Blood clots (Thrombosis)'.**

*[...]*

<invented name> also works as an oral contraceptive. You and your doctor will have to consider all the things that would normally apply to the safe use of oral hormonal contraceptives

### Blood clots (thrombosis)

Taking <invented name> may slightly increase your risk of having a blood clot (called a thrombosis). Your chances of having a blood clot are only increased slightly by taking <invented name> compared with women who do not take <invented name> or any contraceptive pill. A full recovery is not always made and in 1-2% of cases, can be fatal.

### Blood clots in a vein

A blood clot in a vein (known as a 'venous thrombosis') can block the vein. This can happen in veins of the leg, the lung (a lung embolus), or any other organ.

Using a combined pill increases a woman's risk of developing such clots compared with a woman not taking any combined pill. The risk of developing a blood clot in a vein is highest during the first year a woman uses the pill. The risk is not as high as the risk of developing a blood clot during pregnancy.

The risk of blood clots in a vein in users of a combined pill increases further:

- with increasing age;
- **if you smoke.**  
**When using a hormonal contraceptive like <invented name> you are strongly advised to stop smoking, especially if you are older than 35 years;**
- if one of your close relatives has had a blood clot in the leg, lung or other organ at a young age;
- if you are overweight;
- if you must have an operation, or if you are off your feet for a long time because of an injury or illness, or you have your leg in a plaster cast.

If this applies to you, it is important to tell your doctor that you are using <invented name>, as the treatment may have to be stopped. Your doctor may tell you to stop using <invented name> several weeks before surgery or while you are less mobile. Your doctor will also tell you when you can start using <invented name> again after you are back on your feet.

### Blood clots in an artery

A blood clot in an artery can cause serious problems. For example, a blood clot in an artery in the heart may cause a heart attack, or in the brain may cause a stroke.

The use of a combined pill has been connected with an increased risk of clots in the arteries. This risk increases further:

- with increasing age;
- **if you smoke.**  
**When using a hormonal contraceptive like < invented name > you are strongly advised to stop smoking, especially if you are older than 35 years;**
- if you are overweight;
- if you have high blood pressure;
- if a close relative has had a heart attack or stroke at a young age;
- if you have a high level of fat in your blood (cholesterol or triglycerides);
- if you get migraines;
- if you have a problem with your heart (valve disorder, disturbance of the rhythm).

## Symptoms of blood clots

**Stop taking tablets and see your doctor immediately if you notice possible signs of a blood clot, such as:**

- an unusual sudden cough;
- severe pain in the chest which may reach the left arm;
- breathlessness;
- any unusual, severe, or long-lasting headache or worsening of migraine;
- partial or complete loss of vision, or double vision;
- slurring or speech disability;
- sudden changes to your hearing, sense of smell, or taste;
- dizziness or fainting;
- weakness or numbness in any part of your body;
- severe pain in your abdomen;
- severe pain or swelling in either of your legs.

Following a blood clot, recovery is not always complete. Rarely serious permanent disabilities may occur or the blood clot may even be fatal.

Directly after giving birth, women are at an increased risk of blood clots so you should ask your doctor how soon after delivery you can start taking < invented name >.

### **3. How to take < invented name >**

*[the wording below should be inserted in the relevant sections]*

*[...]*

#### **Duration of use**

Your doctor will tell you how long you need to keep taking <invented name>.

### **4. Possible side effects**

*[This wording should be added under 'Rare side effects']*

Venous blood clot.