SUMMARY OF THE CHARACTERISTICS OF THE PRODUCT

1. NAME OF THE MEDICINAL PRODUCT

<INVENTED NAME> 0.150mg/0.020mg, tablets

2. QUALITATIVE AND QUANTATIVE COMPOSITION

Each tablet contains:

Desogestrel .....150 micrograms
Ethinylestradiol .....20 micrograms

Excipient(s) with known effect:
Each tablet contains 30 mg of lactose (as lactose monohydrate).

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet. White to almost white, biconvex, round tablets, with embosse 20 on one side.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Oral contraception.
The decision to prescribe <INVENTED NAME> should take into consideration the individual woman's current risk factors, particularly those for venous thromboembolism (VTE) and how the risk of VTE with <INVENTED NAME> compare with other CHCs (see sections 4.3 and 4.4).

4.2. Posology and method of administration

Posology

One tablet is taken daily for 21 consecutive days.

Paediatric population
The safety and efficacy of desogestrel in adolescents below 18 years has not been established. No data are available.

Method of administration

How to take <INVENTED NAME>
The tablets should be taken in the order of succession stated on the package every day at about the same time of the day. Each subsequent pack is started after a 7-day tablet-free interval; during this tablet-free interval a menstruation- like withdrawal bleeding occurs. This bleeding usually begins on the 2nd or 3rd day after ingestion of the last tablet and it may not have ceased, before the next pack is started.

How to start <INVENTED NAME>

If no preceding hormonal contraceptive use in the past month
The tablet intake should be started on day 1 of the normal menstrual cycle (i.e. on the first day on which the woman has a menstrual bleeding). Tablet intake is also allowed to start on day 2-5, but during the first cycle concurrent use of a barrier method for the first 7 days of tablet intake is recommended.

Changing from a combined hormonal contraceptive (combined oral contraceptive (COC), vaginal ring or transdermal patch)
The woman should start taking <INVENTED NAME> preferably on the day after the last active tablet (the last tablet containing the active substance) of her previous COC, but at the latest on the day following the usual tablet-free interval or following the last placebo tablet of her previous COC. In case a vaginal ring or a transdermal patch has been used, the woman should start using <INVENTED NAME> preferably on the day of removal, but at the latest when the next application would have been due.

Changing from progestogen only products (progetogen-only-pills, injection, implant) or from a progestogen-releasing intrauterine system (IUS)
The woman can change from progestogen-only pills on any day (changing from implant or IUS on the day of its removal; changing from injection when the next injection should have been given) but should in all of these cases be advised to additionally use a barrier method for the first 7 days of tablet-taking.

After an abortion in the first trimester
Tablet intake should start immediately. In this case no further contraceptive measures are necessary.

After delivery or abortion in the second trimester
For breast-feeding women - see section 4.6.
The woman should be advised to start the pill on day 21-28 after delivery or abortion in the 2nd trimester. She should be advised to use a barrier method concurrently during the first 7 days of tablet intake if she starts the pill later. In case she has already had intercourse, pregnancy should be excluded before she starts tablet intake, or she should wait for her first menstrual bleeding.

Forgotten tablets

If the tablet intake is forgotten for less than 12 hours, contraceptive protection is not reduced. The woman should take the forgotten tablet as soon as she remembers, and the remaining tablets are taken as usual.

If the tablet intake is forgotten for more than 12 hours, contraceptive protection may be reduced. The following two basic rules should be considered in case of forgotten tablets: .
1. Continuous tablet intake must not be interrupted for longer than a period of 7 days.
2. 7 days of uninterrupted tablet intake are required to achieve sufficient suppression of the hypothalamus-pituitary-ovarian-axis.

Thus, the following advice can be given in daily practice:
Week 1

The user should take the last forgotten tablet as soon as she remembers, even if this means that she has to take 2 tablets at the same time. Then, she continues taking the tablets at the usual time of the day. She should concurrently use a barrier method, e.g. a condom, for the next 7 days. If intercourse has taken place during the preceding 7 days, the possibility of pregnancy should be considered. The more tablets are forgotten and the closer they are to the regular tablet-free period, the higher the risk of pregnancy is.

Week 2
The user should take the last forgotten tablet as soon as she remembers, even if this means that she has to take 2 tablets at the same time. Then, she continues taking the tablets at the usual time of the day. Provided that the tablets have been taken in a correct manner during the 7 days preceding the forgotten tablet, it is not necessary to take further contraceptive measures. However, if this is not the case, or if more than 1 tablet has been forgotten, the woman should be advised to use another contraceptive method for 7 days.

Week 3
The risk of reduced contraceptive protection is imminent due to the next tablet-free period. However, this risk may be prevented by adjusting tablet intake. Thus, it is not necessary to take further contraceptive measures if one of the two alternatives below is followed, provided that all tablets have been taken in a correct manner during the 7 days preceding the forgotten tablet. If this is not the case, the woman should be advised to follow the first of the two alternatives and concurrently use another contraceptive method for the next 7 days.

1 The user should take the last forgotten tablet as soon as she remembers even if it means that she has to take 2 tablets at the same time. Then she continues taking the tablets at the usual time of the day. She will begin taking the next pack immediately after taking the last tablet in the present pack, i.e. there is no break between the packs. It is not very likely that the user will have her menstrual bleeding until the end of the second pack, but she may experience spotting or break-through bleeding on the days she is taking tablets.
2. The woman may also be advised to stop taking tablets from the present pack. In that case she should keep a tablet-free period of up to 7 days, including those days when she forgot tablets, and then continue with the next pack.

In case the woman has forgotten tablets and then does not have her menstrual bleeding in the first normal tablet-free period, the possibility of pregnancy should be considered

Precautions in case of vomiting or severe diarrhoea
If vomiting or severe diarrhoea occur within 3-4 hours after tablet intake, the tablet may not be absorbed completely. Therefore, the precautions concerning forgotten tablets as described in section 4.2. apply. If the woman does not want to change her usual tablet intake, she has to take the necessary extra tablet(s) from another pack.

How to postpone a withdrawal bleed
To delay a period the woman should continue with another blister pack of <INVENTED NAME> without a tablet-free interval. The extension can be carried on for as long as wished until the end of the second pack. During the extension the woman may experience breakthrough-bleeding or spotting. Regular intake of <INVENTED NAME> is then resumed after the usual 7-day tablet-free interval
To shift her periods to another day of the week than the woman is used to with her current scheme, she can be advised to shorten her forthcoming tablet-free interval by as many days as she likes. The

shorter the interval, the higher the risk that she does not have a withdrawal bleed and will experience breakthrough-bleeding and spotting during the subsequent pack (just as when delaying a period).

4.3. Contraindications

Combined hormonal contraceptives (CHCs) should not be used in the following conditions.

- Presence or risk of venous thromboembolism (VTE)
  - Venous thromboembolism – current VTE (on anticoagulants) or history of (e.g. deep venous thrombosis [DVT] or pulmonary embolism [PE])
  - Known hereditary or acquired predisposition for venous thromboembolism such as APC-resistance, (including Factor V Leiden), antithrombin-III-deficiency, protein C deficiency, protein S deficiency
  - Major surgery with prolonged immobilisation (see section 4.4)
  - A high risk of venous thromboembolism due to the presence of multiple risk factors (see section 4.4)
- Presence of risk of arterial thromboembolism (ATE)
  - Arterial thromboembolism – current arterial thromboembolism, history of arterial thromboembolism (e.g. myocardial infarction) or prodromal condition (e.g. angina pectoris)
  - Cerebrovascular disease – current stroke, history of stroke or prodromal condition (e.g. transient ischaemic attack, TIA)
  - Known hereditary or acquired predisposition for arterial thromboembolism, such as hyperhomocysteinaemia and antiphospholipid-antibodies (anticardiolipin-antibodies, lupus anticoagulant)
  - History of migraine with focal neurological symptoms
  - A high risk of arterial thromboembolism due to multiple risk factors (see section 4.4) or to the presence of one serious risk factor such as:
    - diabetes mellitus with vascular symptoms
    - severe hypertension
    - severe dyslipoproteinemia
- Pancreatitis or a history thereof if associated with severe hypertriglyceridemia
- Presence or history of severe hepatic disease as long as liver function values have not returned to normal.
- Presence or history of liver tumours (benign or malignant).
- Known or suspected sex steroid-influenced malignancies (e.g. of the genital organs or the breasts)
- Endometrial hyperplasia
- Undiagnosed vaginal bleeding.
- Hypersensitivity to the active substances or to any of the excipients of <INVENTED NAME> tablets.

4.4. Special warnings and precautions for use

Warnings

If any of the conditions or risk factors mentioned below is present, the suitability of <INVENTED NAME> should be discussed with the woman.

In the event of aggravation, or first appearance of any of these conditions or risks factors, the woman should be advised to contact her doctor to determine whether the use of <INVENTED NAME> should be discontinued.

Risk of venous thromboembolism (VTE)

The use of any combined hormonal contraceptive (CHC) increases the risk of venous thromboembolism (VTE) compared with no use. **Products that contain levonorgestrel, norgestimate or norethisterone are associated with the lowest risk of VTE. Other products such as <INVENTED NAME> may have up to twice this level of risk. The decision to use any product other than one with the lowest VTE risk should be taken only after a discussion with the woman to ensure she understands the risk of VTE with <INVENTED NAME>, how her current risk factors influence this risk, and that her VTE risk is highest in the first ever year of use. There is also some evidence that the risk is increased when a CHC is re-started after a break in use of 4 weeks or more.**

In women who do not use a CHC and are not pregnant about 2 out of 10,000 will develop a VTE over the period of one year. However, in any individual woman the risk may be far higher, depending on her underlying risk factors (see below).

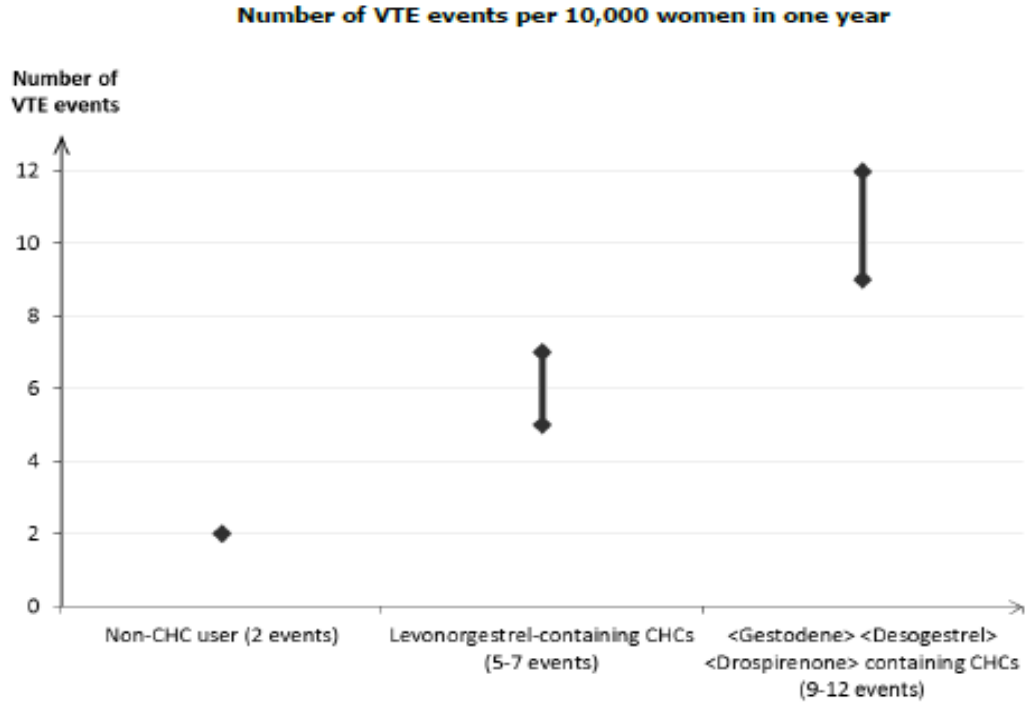
It is estimated[1] that out of 10,000 women who use a CHC containing desogestrel between 9 and 12 women will develop a VTE in one year; this compares with about 6[2] in women who use a levonorgestrel-containing CHC.

In both cases, the number of VTEs per year is fewer than the number expected during pregnancy or in the postpartum period.

VTE may be fatal in 1-2% case.

[1] These incidences were estimated from the totality of the epidemiological study data, using relative risks for the different products compared with levonorgestrel-containing CHCs.

[2] Mid-point of range of 5-7 per 10,000 WY, based on a relative risk for CHCs containing levonorgestrel versus non-use of approximately 2.3 to 3.6



Extremely rarely, thrombosis has been reported to occur in CHC users in other blood vessels, e.g. hepatic, mesenteric, renal, or retinal veins and arteries.

COC-users should be specifically pointed out to contact their physician in case of possible symptoms of thrombosis. In case of suspected thrombosis, COC use should be discontinued.

Risk factors for VTE

The risk for venous thromboembolic complications in CHC users may increase substantially in a woman with additional risk factors, particularly if there are multiple risk factors (see table).

<INVENTED NAME> is contraindicated if a woman has multiple risk factors that put her at high risk of venous thrombosis (see section 4.3). If a woman has more than one risk factor, it is possible that the increase in risk is greater than the sum of the individual factors – in this case her total risk of VTE should be considered. If the balance of benefits and risks is considered to be negative, a CHC should not be prescribed (see section 4.3).

Table: Risk factors for VTE

Risk factor	Comment
Obesity (body mass index over 30 kg/m²)	Risk increases substantially as BMI rises Particularly important to consider if other risk factors also present.
Prolonged immobilisation, major surgery, any surgery to the legs or pelvis, neurosurgery, or major trauma	In these situations it is advisable to discontinue use of the patch/pill/ring (in the case of elective surgery at least four weeks in advance) and not resume until two weeks after complete remobilisation. Another method of

Note: temporary immobilization including air travel >4 hours can also be a risk factor for VTE, particularly in women with other risk factors	contraception should be used to avoid unintentional pregnancy. Antithrombotic treatment should be considered if <INVENTED NAME> has not been discontinued in advance.
Positive family history (venous thromboembolism ever in a sibling or parent especially at a relatively early age e.g. before 50).	If a hereditary predisposition is suspected, the woman should be referred to a specialist for advice before deciding about any CHC use
Other medical conditions associated with VTE	Cancer, systemic lupus erythematosus, haemolytic uraemic syndrome, chronic inflammatory bowel disease (Crohn's disease or ulcerative colitis) and sickle cell disease
Increasing age	Particularly above 35 years

There is no consensus about the possible role of varicose veins and superficial thrombophlebitis in the onset or progression of venous thrombosis.

The increased risk of thromboembolism in pregnancy, and particularly the 6 weeks period of the puerperium, must be considered (for information on "Pregnancy and lactation" see section 4.6).

Symptoms of VTE (deep vein thrombosis and pulmonary embolism)

In the event of symptoms women should be advised to seek urgent medical attention and to inform the healthcare professional that she is taking a CHC.

Symptoms of deep vein thrombosis (DVT) can include:
- unilateral swelling of the leg and/or foot or along a vein in the leg;
- pain or tenderness in the leg which may be felt only when standing or walking,
- increased warmth in the affected leg; red or discoloured skin on the leg.

Symptoms of pulmonary embolism (PE) can include:
- sudden onset of unexplained shortness of breath or rapid breathing;
- sudden coughing which may be associated with haemoptysis;
- sharp chest pain;
- severe light headedness or dizziness;
- rapid or irregular heartbeat.

Some of these symptoms (e.g. "shortness of breath", "coughing") are non-specific and might be misinterpreted as more common or less severe events (e.g. respiratory tract infections).
Other signs of vascular occlusion can include: sudden pain, swelling and slight blue discoloration of an extremity.
If the occlusion occurs in the eye symptoms can range from painless blurring of vision which can progress to loss of vision. Sometimes loss of vision can occur almost immediately.

Risk of arterial thromboembolism (ATE)

Epidemiological studies have associated the use of CHCs with an increased risk for arterial thromboembolism (myocardial infarction) or for cerebrovascular accident (e.g. transient ischaemic attack, stroke). Arterial thromboembolic events may be fatal.

Risk factors for ATE

The risk of arterial thromboembolic complications or of a cerebrovascular accident in CHC users increases in women with risk factors (see table). <INVENTED NAME> is contraindicated if a woman has one serious or multiple risk factors for ATE that puts her at high risk of arterial thrombosis (see section 4.3). If a woman has more than one risk factor, it is possible that the increase in risk is greater than the sum of the individual factors - in this case her total risk should be considered. If the balance of benefits and risks is considered to be negative a CHC should not be prescribed (see section 4.3).

Table: Risk factors for ATE

Risk factor	**Comment**
Increasing age	Particularly above 35 years
Smoking	Women should be advised not to smoke if they wish to use a CHC. Women over 35 who continue to smoke should be strongly advised to use a different method of contraception.
Hypertension	
Obesity (body mass index over 30 kg/m2)	Risk increases substantially as BMI increases. Particularly important in women with additional risk factors
Positive family history (arterial thromboembolism ever in a sibling or parent especially at relatively early age e.g. below 50).	If a hereditary predisposition is suspected, the woman should be referred to a specialist for advice before deciding about any CHC use
Migraine	An increase in frequency or severity of migraine during CHC use (which may be prodromal of a cerebrovascular event) may be a reason for immediate discontinuation
Other medical conditions associated with adverse vascular events	Diabetes mellitus, hyperhomocysteinaemia, valvular heart disease and atrial fibrillation, dyslipoproteinaemia and systemic lupus erythematosus.

Symptoms of ATE

In the event of symptoms women should be advised to_seek urgent medical attention and to inform the healthcare professional that she is taking a CHC.

Symptoms of a cerebrovascular accident can include:

- sudden numbness or weakness of the face, arm or leg, especially on one side of the body;

- sudden trouble walking, dizziness, loss of balance or coordination;
- sudden confusion, trouble speaking or understanding
- sudden trouble seeing in one or both eyes;
- sudden, severe or prolonged headache with no known cause;
- loss of consciousness or fainting with or without seizure.

Temporary symptoms suggest the event is a transient ischaemic attack (TIA).

Symptoms of myocardial infarction (MI) can include:
- pain, discomfort, pressure, heaviness, sensation of squeezing or fullness in the chest, arm, or below the breastbone;
- discomfort radiating to the back, jaw, throat, arm, stomach;
- feeling of being full, having indigestion or choking;
- sweating, nausea, vomiting or dizziness;
- extreme weakness, anxiety, or shortness of breath;
- rapid or irregular heartbeats.

Tumours
In some epidemiological studies an increased risk of uterine cervix cancer in long-term users of COCs has been reported, but it has still not been sufficiently clarified to which extent this finding may be influenced by effects of sexual behaviour and other factors like human papillomatous virus (HPV).

A meta-analysis from 54 epidemiological studies has shown that women using COCs have a slightly increased relative risk (RR = 1.24) to be diagnosed with breast cancer. This increased risk gradually declines for 10 years after cessation of COCs. Since breast cancer is a rare condition in women below 40 years of age, the increase in the number of diagnosed cases of breast cancer in present and former users of COCs is low compared to the risk of breast cancer in their entire lifetime. These studies do not put forward evidence of a causal relationship. The observed pattern of an increased risk may be due to an earlier diagnosing of breast cancer in users of COCs, the biological effects of COCs or a combination of both. The diagnosed cases of breast cancer in users of COCs have a tendency to be less clinically advanced compared to the diagnosed cases of breast cancer in never-users.

Benign liver tumours have been reported in rare cases, and even more rarely malignant liver tumours in users of COCs. These tumours have in a few cases led to life-threatening intra-abdominal bleedings. A liver tumour should be taken into consideration as a differential diagnose when severe pain occurs in upper abdomen, in case of hepatomegaly or at signs of intra-abdominal bleeding in women taking COCs.

The size of fibromyomas of uterus can change after administration of oral contraceptive COCs.

Other conditions
Women with hypertriglyceridaemia or hereditary disposition for this condition may have an increased risk of pancreatitis when taking COCs.
In women with hereditary angioedema exogenous estrogens may induce or exacerbate symptoms of angioedema.

Although small increases in blood pressure have been reported in many women taking COCs, clinically relevant increases are rare. Only in these rare cases an immediate discontinuation of COC use is justified. A systematic relationship between COC use and clinical hypertension has not been established. If, during the use of a COC in preexisting hypertension, constantly elevated blood pressure values or a significant increase in blood pressure do not respond adequately to antihypertensive treatment, the COC must be withdrawn. Where considered appropriate, contraceptive pill use may be resumed if normotensive values can be achieved with antihypertensive therapy.

It has been reported that the following conditions may arise or have been aggravated both during pregnancy and use of COCs, but the evidence of a relationship with use of COCs is inconclusive: Jaundice and/or itching in connection with cholestasis; formation of gallstones; porphyria; systemic lupus erythematosus; haemolytic uraemic syndrome; Sydenham's chorea; herpes gestationis; hearing loss due to otosclerosis.

Acute or chronic disturbances of liver function may necessitate discontinuation of COCs until liver function parameters have been normalised. Recurrent cholestatic jaundice and/or cholestasis-related pruritus which previously occurred during pregnancy or during previous use of sexual hormones, requires discontinuation of COCs.

Even though COCs may have an influence on peripheral insulin resistance and glucose tolerance there is no indication that it is necessary to change the therapeutic regime in diabetics using COCs. However, diabetics should be followed closely during use of COCs.

Worsening of endogenous depression, of epilepsy, of Crohn's disease and of ulcerative colitis has been reported during COC use.

Chloasma may occasionally occur, in particular in women with a medical history of chloasma during pregnancy. Women with a tendency to chloasma should avoid exposure to sunlight or ultra-violet radiation while taking COCs.

<INVENTED NAME> contains < 65 mg lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption who are on lactose-free diet should take this amount into consideration. When counseling the choice of contraceptive method(s), all the above information should be taken into account.

Medical examination/consultation

Prior to the initiation or reinstitution of <INVENTED NAME> a complete medical history (including family history) should be taken and pregnancy must be ruled out. Blood pressure should be measured and a physical examination should be performed, guided by the contra-indications (see section 4.3) and warnings (see section 4.4). It is important to draw a woman's attention to the information on venous and arterial thrombosis, including the risk of <INVENTED NAME> compared with other CHCs, the symptoms of VTE and ATE, the known risk factors and what to do in the event of a suspected thrombosis.

The woman should also be instructed to carefully read the user leaflet and to adhere to the advice given. The frequency and nature of examinations should be based on established practice guidelines and be adapted to the individual woman.

Women should be advised that hormonal contraceptives do not protect against HIV infections (AIDS) or other sexually transmitted diseases.

Reduced efficacy
The effect of COCs may be reduced in case of forgotten tablets (section 4.2.), vomiting or severe diarrhoea (section 4.2.) or concomitant intake of other medication (section 4.5.).
Herbal preparations containing St. John's wort (Hypericum perforatum) should not be used while taking <INVENTED NAME> due to the risk of decreased plasma concentrations and reduced clinical effects of <INVENTED NAME> (see Section 4.5 Interactions).

Reduced cycle control
In connection with intake of all COCs irregular bleeding (spotting and break-through bleeding) may occur, during the first months in particular. It is therefore only relevant to evaluate the occurrence of irregular bleeding after a period of adaptation of approx. 3 cycles.

If the bleeding irregularities persist or occur after previous regular cycles non-hormonal causes should be considered and adequate, diagnostic precautions should be taken to exclude malignancy or pregnancy. These may include curettage.

Some women do not have a menstrual bleeding during the tablet-free period. If the COCs have been taken according to the instructions described in section 4.2, it is unlikely that the woman is pregnant. If, however, the COCs have not been taken according to the instructions prior to the first missing menstrual bleeding, or in case two menstrual bleedings are missing, pregnancy should be excluded before continuation of intake of the COCs.

4.5. Interaction with other medecinal products and other forms of interaction

Influence of other medical products on <INVENTED NAME>
Drug interactions resulting in an increased clearance of sexual hormones may involve break-through bleeding and contraceptive failure. This has been established with hydantoins, barbiturates, primidone, bosentan, carbamazepine and rifampicine rifabutin; oxcarbazepine, modafinil, topiramate, felbamate, griseofulvine, nelfinavir, efavirenz and nevirapine are also suspected. The mechanism of this interaction seems to be based on the liver enzyme inducing properties of these drugs. Maximal enzyme induction is generally not seen until 2-3 weeks after start of treatment, but may then persist for at least 4 weeks after discontinuation of treatment.

Contraceptive failure has also been reported with antibiotics like ampicillin and tetracyclines. This mechanism of action has not been elucidated.

Women on short term treatment (up to one week) with some of the above mentioned groups of drugs or individual drugs should temporarily use a barrier method concomitantly with the COCs, i.e. in the period of other concomitant drug intake and for 7 days after cessation of this drug. Women taking rifampicine should use a barrier method concomitantly with intake of COCs for the period in which she is treated with rifampicine and for 28 days after cessation of rifampicine. In case other concomitant drug intake exceeds the number of tablets in the COCs pack, she should start the next pack of pills without keeping the usual tablet-free period.

In women on long-term treatment with hepatic enzyme-inducing active substances, another reliable, non-hormonal, method of contraception is recommended.

The herbal preparation St. John's wort (Hypericum perforatum) should not be taken concomitantly with this medicine as this could potentially lead to a loss of contraceptive effect. Break-through

bleeding and unintended pregnancies have been reported. This is due to induction of drug metabolising enzymes by St. John's wort. The inducing effect may persist for at least 2 weeks after cessation of treatment with St. John's wort.

Concomitant administration of ritonavir with a fixed COC resulted in a reduction of the ethinyl oestradiol mean AUC by 41 %, increased doses of COCs containing ethinyl oestradiol, or alternate methods of contraception should be considered.

Influence of <INVENTED NAME> on other medicinal products
Oral contraceptives may affect the metabolism of certain other active substances. Accordingly, plasma and tissue concentrations may either increase (e.g. cyclosporin) or decrease (e.g. lamotrigine).
Laboratory analyses
The use of contraceptive steroids may have an influence on the results of certain laboratory analyses, including biochemical parameters for liver, thyroidea, adrenal and kidney function; the plasma levels of (transport)-proteins, e.g. corticosteroid-binding globulin and lipid/lipoprotein fractions; parameters for carbohydrate metabolism and parameters for coagulation and fibrinolysis. Changes usually remain within the normal laboratory reference values.

4.6. Fertility, pregnancy and lactation

Pregnancy

<INVENTED NAME> is not indicated during pregnancy.
If pregnancy occurs, the treatment with <INVENTED NAME> should be discontinued immediately. However, extensive epidemiological studies have neither showed an increased risk of birth defects in children born to women taking COCs before pregnancy, nor any teratogenic effect at unintentional intake of COCs in early pregnancy.

The increased risk of VTE during the postpartum period should be considered when re-starting <INVENTED NAME> (see section 4.2 and 4.4).

Lactation

Lactation may be influenced by COCs since they may reduce the amount and change the composition of breast milk, thus, the use of COCs should generally not be recommended until the nursing mother has weaned the child completely. Small amounts of contraceptive steroids and/or their metabolites may be excreted with the milk, but there is no evidence that this adversely affects infant health.

4.7. Effects on ability to drive and use machines

<INVENTED NAME> has no influence on the ability to drive and use machines

4.8. Undesirable side effects

For serious adverse experiences in users of COCs see section 4.4.

Description of selected adverse reactions
An increased risk of arterial and venous thrombotic and thrombo-embolic events, including myocardial infarction, stroke, transient ischemic attacks, venous thrombosis and pulmonary

embolism has been observed in women using CHCs, which are discussed in more detail in section 4.4.

As with all CHCs, changes in vaginal bleeding patterns may occur, especially during the first months of use. These may include changes in bleeding frequency (absent, less, more frequent or continuous), intensity (reduced or increased) or duration.
Possibly related undesirable effects that have been reported in users of Desogestrel or CHC users in general are listed in the table below. All ADRs are listed by system organ class and frequencies are defined as:

Very common	≥ 1 /10
Common	≥ 1 /100 - < 1/10
Uncommon	≥ 1/1.000 - < 1/100
Rare	≥ 1/10.000 - < 1/1.000
Very rare	< 1/10.000
Not known	Frequency cannot be estimated from the available data

Organ systems	***Very common*** **≥1/10**	***Common*** **(>1/100)**	***Uncommon*** ***(>1/1000 < 1/100)***	***Rare*** **less than 1/1000**
Infections and infestations				**Vaginal candidiasis**
Immune system disorders				**Hypersensitivity**
Metabolism and nutrition disorders			**Fluid retention**	
Psychiatric disorders		**Depressed mood** **Mood altered**	**Libido decreased**	**Libido increased**
Nervous system disorders		**Headache** **Dizziness** **Nervousness**	**Migraine**	
Eye disorders				**Contact lens intolerance**
Ear and labyrinth disorders				**Otosclerosis**
Vascular disorders		**Hypertension**		**VTE** **ATE**
Gastrointestinal disorders		**Nausea, abdominal pain**	**Vomiting, diarrhoea**	
Skin and subcutaneous tissue disorders		**Acne**	**Rash, urticaria**	**Erythema nodosum** **Erythema multiforme** **Pruritus** **Alopecia**

Reproductive system and breast disorders	**Irregular bleeding**	**Amenorrhea** **Breast tenderness** **Breast pain** **Breast tenderness** **Metrorrhagia**	**Breast enlargement**	**Vaginal discharge** **Breast discharge**
Investigations		**Weight increased**		**Weight decreased**

The following serious adverse events were reported in women using COCs:
- Venous thromboembolic conditions;
- Arterial thromboembolic conditions;
- Hypertension;
- Liver tumours;
- Cervical cancer ;
- Breast cancer ;
- Occurence or deterioriation of conditions for which an association with COC use has not been established: Crohn's disease, ulcerative colitis, epilepsy, migraine, endometriosis, uterine myoma, porphyria, generalised lupus erythematosus, gestational herpes, Sydenham's chorea, haemolytic uraemic syndrome, cholestatic icterus;
- Chloasma
- In women with hereditary angioedema, exogenous estrogens may induce or exacerbate symptoms of angioedema.

For further information, see sections 4.3 and 4.4.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V*.

4.9. Overdose

There have been no reports of serious, harmful effects after overdose. The symptoms which may occur in connection with overdose are: nausea, vomiting and, in young girls, a small vaginal bleeding. There is no antidote, and further treatment should be symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Progestogens and estrogens, fixed combinations
ATC code: G 03 AA 09

The contraceptive action of COCs is based on interaction of different factors, out of which the most important is the inhibition of ovulation and changes in the cervical secretion. Besides protection against pregnancy, COCs have several positive properties which, next to the negative properties (see Warnings, Undesirable effects), can be useful in deciding on the method of birth control. The cycle is more regular and the menstruation is often less painful and bleeding is lighter. The latter may result in a decrease in the occurrence of iron deficiency. In the largest multicenter trial (n=23

258 cycles), the uncorrected Pearl Index is estimated at 0.1 (95% confidence interval 0.0-0.3). Furthermore, 4.5% of the women reported absence of withdrawal bleeding and 9.2% reported occurrence of irregular bleeding after 6 treatment cycles.

<INVENTED NAME> is a COC with ethinylestradiol and the progestogen desogestrel.
Ethinylestradiol is a well known synthetic estrogen.
Desogestrel is a synthetic progestogen. After oral administration it has a strong ovulation-inhibiting activity.
With the use of the higher-dosed COCs (50 µg ethinylestradiol) the risk of endometrial and ovarian cancer is reduced. Whether this also applies to lower-dosed COCs remains to be confirmed.

Paediatric population
No clinical data on efficacy and safety are available in adolescents below 18 years.

5.2. Pharmacokinetic properties

Desogestrel

Absorption
After oral administration of <INVENTED NAME>, desogestrel is rapidly absorbed and converted into 3-keto-desogestrel. Peak plasma levels are reached after 1.5 hours. The absolute bioavailability of 3-keto-desogestrel is 62-81%.

Distribution
3-keto-desogestrel is 95.5-99% bound to the plasma proteins, mainly albumin and SHBG. The ethinyl-oestradiol-induced increase in SHBG influences both the amount of bindings and distribution of 3-keto-desogestrel in the plasma proteins. As a consequence the concentration of 3-keto-desogestrel rises slowly during treatment until steady state is reached within 3-13 days.

Metabolism
The phase-I metabolism of desogestrel includes cytochrom P-450 catalysed hydroxylation and subsequent dehydrogenation at C3. The active metabolite of 3-keto-desogestrel is further reduced, the degradation products are conjugated to sulphate and glucuronides. Animal studies indicate that the enterohepatic circulation has no relevance for the gestagenic activity of desogestrel.

Elimination
3-keto-desogestrel is eliminated with a mean half-life of approx. 31 hours (24-38 hours), plasma clearance varies from 5.0-9.5 l/hour. Desogestrel and its metabolites are eliminated via the urine and in the faeces, either as free steroids or conjugates. Ratio for elimination in urine or faeces is 1.5:1.

Steady-State Conditions
In steady-state conditions the serum level of 3-keto-desogestrel is elevated by two- to three-fold.

Ethinylestradiol

Absorption

Ethinyl oestradiol is rapidly absorbed and peak plasma levels are reached after 1.5 hours. As a consequence of presystemic conjugation and first-pass metabolism the absolute bioavailability is 60%. The area under the curve and Cmax may be expected to rise slightly over time.

Distribution
Ethinyl oestradiol is 98.8% bound to the plasma proteins, almost exclusively to albumin.

Metabolism
Ethinyl oestradiol undergoes presystemic conjugation both in the mucosa of the small intestine and in the liver. Hydrolysis of the direct conjugates of ethinyl oestradiol with the aid of the intestinal flora gives ethinyl oestradiol, which can be re-absorbed, and an enterohepatic circulation is hereby set up. The primary pathway of ethinyl oestradiol metabolism is cytochrom P-450-mediated hydroxylation in which the primary metabolites are 2-OH-EE and 2-methoxy-EE. 2-OH-EE is further metabolised to chemically reactive metabolites.

Elimination
Ethinyl oestradiol disappears from plasma with a half-life of approx. 29 hours (26-33 hours), plasma clearance varies from 10-30 l/hour. The conjugates of ethinyl oestradiol and its metabolites are excreted via urine and faeces (ratio 1:1).

Steady-state conditions
Steady-state conditions are obtained after 3 to 4 days, when the serum drug level is approx. 30 to 40% higher than after the administration of a single dose.

5.3. Preclinical safety data

Toxicological studies have not revealed other effects than those, which can be explained, based on the hormone profile of <INVENTED NAME>.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Pregelatinised maize starch
Lactose monohydrated
Microcrystalline cellulose
α-tocopheryl acetate concentrate (powder form, containing hydrolysed gelatin and silicon dioxide)
Colloidal silicon dioxide
Magnesium stearate
Stearic acid
Povidone 30

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

24 months

6.4. Special precautions for storage

Do not store above 25°C.

6.5. Nature and contents of container

White opaque PVC /Aluminium blisters of 21 tablets per calendar blister strip available in packs containing 1x21, 3x21

6.6. Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTORIZATION HOLDER

<[To be completed nationally]>

8. MARKETING AUTORISATION NUMBER

<[To be completed nationally]>

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

<[To be completed nationally]>

10. DATE OF REVISION OF THE TEXT

<[To be completed nationally]>