SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Desorex 75 micrograms film-coated tablets
Desogestrel Somex Pharma 75 micrograms film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 75 micrograms desogestrel.

Excipient:
Each film-coated tablet contains 54.35 mg lactose monohydrate.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

White to off white, circular, biconvex tablets, 5.5mm in diameter, without embossing.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Oral contraception.

4.2 Posology and method of administration

Method of administration
Tablets must be taken every day at about the same time with a small amount of liquid so that the interval between two tablets is always 24 hours. The first tablet should be taken on the first day of menstrual bleeding. Thereafter one tablet each day is to be taken continuously, without taking any notice on possible bleeding. A new blister is started directly the day after the previous one.

How to start Desogestrel
No preceding hormonal contraceptive use (in the past month)

Tablet-taking has to start on day 1 of the woman's natural cycle (day 1 is the first day of her menstrual bleeding). Starting on days 2-5 is allowed, but during the first cycle a barrier method is recommended for the first 7 days of tablet-taking.

Following first-trimester abortion
After first-trimester abortion it is recommended Desogestrel is started immediately. In which case there is no need to use an additional method of contraception.

Following delivery, preterm delivery or second-trimester abortion
Contraceptive treatment with Desogestrel after delivery can be initiated before the menstruations have returned. If more than 21 days have elapsed after delivery, pregnancy ought to be ruled out and an additional method of contraception should be used for the first week. For additional information on breastfeeding women (see section 4.6).

How to start Desogestrel when changing from other contraceptive methods
Changing from a combined hormonal contraceptive (combined oral contraceptive (COC), vaginal ring, or transdermal patch).
The woman should start Desogestrel preferably on the day after the last active tablet (the last tablet containing the active substances) of her previous COC or on the day of removal of her vaginal ring or transdermal patch. In these cases, the use of an additional contraceptive is not necessary. Not all contraceptive methods may be available in all EU countries.

The woman may also start at the latest on the day following the usual tablet-free, patch-free, ring-free, or placebo tablet interval of her previous combined hormonal contraceptive, but during the first 7 days of tablet-taking an additional barrier method is recommended.

Changing from a progestogen-only-method (minipill, injection, implant or from a progestogen-releasing intrauterine system [IUS])
The woman may switch any day from the minipill (from an implant or the IUS on the day of its removal, from an injectable when the next injection would be due). Additional contraceptive method is not necessary.

Management of missed tablet
Contraceptive protection may be reduced if more than 36 hours have elapsed between two tablets. If the user is less than 12 hours late in taking any tablet, the missed tablet should be taken as soon as it is remembered and the next tablet should be taken at the usual time.
If she is more than 12 hours late, she should use an additional method of contraception for the next 7 days. If tablets were missed in the first week and intercourse took place in the week before the tablets were missed, the possibility of a pregnancy should be considered.

Advice in case of gastrointestinal disturbances
In case of severe gastro-intestinal disturbance, absorption may not be complete and additional contraceptive measures should be taken.
If vomiting occurs within 3-4 hours after tablet-taking, absorption may not be complete. In such an event, the advice concerning missed tablets, as given in this section is applicable.

Treatment surveillance

Before prescription, a thorough case history should be taken and a thorough gynaecological examination is recommended to exclude pregnancy. Bleeding disturbances, such as oligomenorrhoea and amenorrhoea should be investigated before prescription.
The interval between check-ups depends on the circumstances in each individual case. If the prescribed product may conceivably influence latent or manifest disease (see section 4.4), the control examinations should be timed accordingly.

Despite the fact that Desogestrel is taken regularly, bleeding disturbances may occur. If bleeding is very frequent and irregular, another contraceptive method should be considered. If the symptoms persist, an organic cause should be ruled out.

Management of amenorrhoea during treatment depends on whether or not the tablets have been taken in accordance with the instructions and may include a pregnancy test.

The treatment should be stopped if a pregnancy occurs.

Women should be advised that Desogestrel does not protect against HIV (AIDS) and other sexually transmitted diseases.

Paediatric population

There is no relevant indication for use of Desogestrel in children.
The safety and efficacy of desogestrel in adolescents below 18 years has not yet been established. No data are available.

Hepatic impairment
No clinical studies have been performed in patients with hepatic insufficiency. Since the metabolism of steroid hormones might be impaired in patients with severe hepatic disease, the use of Desogestrel in these women is not indicated as long as liver function values have not returned to normal (see section 4.3).

Renal impairment
No clinical studies have been performed in patients with renal impairment.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients.
- Known or suspected pregnancy.
- Active venous thromboembolic disorder.
- Presence or history of severe hepatic disease as long as liver function values have not returned to normal.
- Known or suspected sex-steroid sensitive malignancies.
- Undiagnosed vaginal bleeding.

4.4 Special warnings and precautions for use

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

The risk for breast cancer increases in general with increasing age. During use of combined oral contraceptives (COCs) the risk of having breast cancer diagnosed is slightly increased. This increased risk disappears gradually within 10 years after discontinuation of COC use and is not related to the duration of use, but to the age of the woman when using the COC. The expected number of cases diagnosed per 10,000 women who use COCs (up to 10 years after stopping) relative to never users over the same period has been calculated for the respective age groups and is presented in the table below.

Age Group	Expected Cases COC users	Expected cases COC non-users
16-19 years	4.5	4
20-24 years	17.5	16
25-29 years	48.7	44
30-34 years	110	100
35-39 years	180	160
40-44 years	260	230

The risk in users of progestogen-only contraceptives (POC), such as Desogestrel, is possibly of similar magnitude as that associated with COCs. However, for POCs the evidence is less conclusive.

Compared to the risk of getting breast cancer ever in life, the increased risk associated with COCs is low. The cases of breast cancer diagnosed in COC users tend to be less advanced than in those who have not used COCs. The increased risk in COC users may be due to an earlier diagnosis, biological effects of the pill or a combination of both. Since a biological effect cannot be excluded, an individual benefit/risk assessment should be made in women with pre-existing breast cancer and in women in whom breast cancer is diagnosed while using desogestrel-only pill.

Since a biological effect of progestogens on liver cancer cannot be excluded an individual benefit/risk assessment should be made in women with liver cancer. When acute or chronic disturbances of liver function occur the woman should be referred to a specialist for examination and advice.

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.

Although progestogens may have an effect on peripheral insulin resistance and glucose tolerance, there is no evidence for a need to alter the therapeutic regimen in diabetics using progestogen-only pills. However, diabetic patients should be carefully observed during the first months of use.

If a 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.

Treatment with Desogestrel leads to decreased oestradiol serum levels, to a level corresponding with the early follicular phase. It is as yet unknown whether the decrease has any clinically relevant effect on bone mineral density.

The protection with traditional progestogen-only pills against ectopic pregnancies is not as good as with combined oral contraceptives, which has been associated with the frequent occurrence of ovulations during the use of progestogen-only pills. Despite the fact that Desogestrel consistently inhibits ovulation, ectopic pregnancy should be taken into account in the differential diagnosis if the woman gets amenorrhoea or abdominal pain.

Chloasma may occasionally occur, especially in women with a history of chloasma gravidarum. Women with a tendency to chloasma should avoid exposure to the sun or ultraviolet radiation whilst taking Desogestrel.

Depressed mood and depression are well-known undesirable effects of hormonal contraceptive use (see section 4.8). Depression can be serious and is a well-known risk factor for suicidal behaviour and suicide. Women should be advised to contact their physician in case of mood changes and depressive symptoms, including shortly after initiating the treatment.

The efficacy of Desogestrel may be reduced in the event of missed tablets (section 4.2), gastro-intestinal disturbances (section 4.2), or concomitant medications that decrease the plasma concentration of etonogestrel, the active metabolite of desogestrel (section 4.5).

The following conditions have been reported both during pregnancy and during sex steroid use, but an association with the use of progestogens has not been established:
- jaundice and/or pruritus related to cholestasis;
- gallstone formation; porphyria;
- systemic lupus erythematosus;
- haemolytic uraemic syndrome;
- Sydenham’s chorea;
- herpes gestationis;
- otosclerosis-related hearing loss;
- (hereditary) angioedema.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Maturation of follicles
Follicular development occurs during the use of all low-dose hormonal contraceptives. The follicles may occasionally grow to be larger than their normal size in the menstrual cycle. Generally, the

enlarged follicles (functional cysts) disappear spontaneously. They are often asymptomatic but in some cases mild abdominal pain may occur. Surgical intervention is rarely required.

4.5 Interaction with other medicinal products and other forms of interaction
Interactions between hormonal contraceptives and other medicinal products may lead to breakthrough bleeding and/or contraceptive failure. The following interactions have been reported in the literature (mainly with combined contraceptives but occasionally also with progestogen-only contraceptives).

Hepatic metabolism:
Interactions can occur with medicinal products that induce microsomal enzymes, which can result in increased clearance of sex hormones (such as, hydantoins (e.g. phenytoin), barbiturates (e.g. phenobarbital), primidone, carbamazepine, rifampicin, and possibly also for oxcarbazepine, topiramate, rifabutin, felbamate, ritonavir, nelfinavir, griseofulvin and products containing
St. John's wort (Hypericum perforatum)).

Enzyme induction can occur after a few days of treatment. Maximal enzyme induction is not seen for 2-3 weeks, but may then be sustained for at least 4 weeks after the cessation of drug therapy. Women on treatment with any of these medicinal products should temporarily use a barrier method in addition to Desogestrel. With microsomal enzyme-inducing drugs, the barrier method should be used during the time of concomitant drug administration and for 28 days after their discontinuation. For women on long-term therapy with hepatic enzyme inducers a non-hormonal method contraception should be considered.

Substances with variable effects on the clearance of contraceptive hormones:
When co-administered with hormonal contraceptives, many combinations of HIV protease inhibitors (e.g. ritonavir, nelfinavir) and non-nucleoside reverse transcriptase inhibitors (e.g. nevirapine) and/or combinations with Hepatitis C virus (HCV) medicinal products (e.g. boceprevir, telaprevir), can increase or decrease plasma concentrations of progestins. The net effect of these changes may be clinically relevant in some cases.

Therefore, the prescribing information of concomitant HIV/HCV medications should be consulted to identify potential interactions and any related recommendations. In case of any doubt, an additional barrier contraceptive method should be used by women on protease inhibitor or non-nucleoside reverse transcriptase inhibitor therapy.

Substances decreasing the clearance of contraceptive hormones (enzyme inhibitors)
Concomitant administration of strong (e.g. ketoconazole, itraconazole, clarithromycin) or moderate (e.g. fluconazole, diltiazem, erythromycin) CYP3A4 inhibitors may increase the serum concentrations of progestins, including etonogestrel, the active metabolite of desogestrel.

During treatment with medical charcoal, the absorption of the steroid in the tablet may be reduced and thereby the contraceptive efficacy. Under these circumstances, the advice as given for missed tablets in section 4.2. is applicable.

Hormonal contraceptives may interfere with the metabolism of other drugs. Accordingly, plasma and tissue concentrations of other active substances may either increase (e.g. ciclosporin) or decrease.

Note: The prescribing information of concomitant medications should be consulted to identify potential interactions.

Laboratory tests
Data obtained with COCs have shown that contraceptive steroids may influence the results of certain laboratory tests, including biochemical parameters of liver, thyroid, adrenal and renal function, serum

levels of (carrier) proteins, e.g. corticosteroid binding globulin and lipid/lipoprotein fractions, parameters of carbohydrate metabolism and parameters of coagulation and fibrinolysis. The changes generally remain within the normal range. To what extent this also applies to progestogen-only contraceptives is not known.

4.6 Fertility, pregnancy and lactation

Desogestrel is contraindicated (see section 4.3) in pregnancy. If pregnancy occurs during treatment with Desogestrel, further intake should be stopped.

Animal studies have shown that very high doses of progestogenic substances might cause masculinisation of female fetuses.

Extensive epidemiological studies have revealed neither an increased risk of birth defects in children born to women who used COCs before pregnancy, nor a teratogenic effect when COCs were taken inadvertently during early pregnancy. Pharmacovigilance data collected with various desogestrelcontaining COCs also do not indicate an increased risk.

Based on clinical study data,desogestrel does not appear to influence the production or the quality (protein, lactose, or fat concentration) of breast milk. However, there have been infrequent postmarketing reports of a decrease in breast milk production while using Desogestrel.Small amounts of etonogestrel are excreted in the breast milk. As a result, 0.01 - 0.05 micrograms etonogestrel per kg body weight per day might be ingested by the child (based on an estimated milk ingestion of 150 millilitre per kg body weight per day). Like other progestogen-only pills, Desogestrel can be used during breast feeding.

Limited long-term follow-up data are available on children, whose mothers started using desogestrel during the 4th to 8th weeks post-partum. They were breast-fed for 7 months and followed up to 1.5 years (n=32) or to 2.5 years (n=14) of age. Evaluation of growth and physical and psychomotor development did not indicate any differences in comparison to nursing infants, whose mother used a copper-IUD. Based on the available data, Desogestrel may be used during lactation. The development and growth of a nursing infant, whose mother uses Desogestrel, should, however, be carefully observed.

4.7 Effects on ability to drive and use machines

Desogestrel has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The most commonly reported undesirable effect in the clinical trials is bleeding irregularity. Some kind of bleeding irregularity has been reported in up to 50% of women using desogestrel. Since desogestrel causes ovulation inhibition close to 100%, in contrast to other progestogen-only-pills, irregular bleeding is more common than with other progestogen-only pills. In 20 -30% of the women, bleeding may become more frequent, whereas in another 20% bleeding may become less frequent or totally absent. Vaginal bleeding may also be of longer duration. After a couple of months of treatment, bleedings tend to become less frequent. Information, counselling and a bleeding diary can improve the woman’s acceptance of the bleeding pattern.

The most commonly reported other undesirable effects in the clinical trials with desogestrel (> 2.5%) were acne, mood changes, breast pain, nausea and weight increase. The undesirable effects

mentioned in the table below have been judged, by the investigators, as having an established, probable or possible link to the treatment. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness:

Very common (1/10)
Common (1/100 to <1/10)
Uncommon (1/1,000 to <1/100)
Rare (1/10,000 to <1/1,000)
Very rare (<1/10,000),
Not known (cannot be estimated from the available data).

System Organ Classes	**Frequency of adverse reactions**			
	Common	**Uncommon**	**Rare**	**Not known**
Immune system disorders				**Hypersensitivity reactions, including angioedema and anaphylaxis**
Infections and infestations		Vaginal infection		
Psychiatric disorders	Mood altered, Depressed mood libido decreased			
Nervous system disorders	Headache			
Eye disorders		Contact lens intolerance		
Gastrointestinal disorders	Nausea	Vomiting		
Skin and subcutaneous tissue disorders	Acne	Alopecia	Rash, urticaria, Erythema nodosum	
Reproductive system and breast disorders	Breast pain, menstruation irregular, amenorrhoea	Dysmenorrhoea, ovarian cyst		
General disorders and administration site conditions		Fatigue		
Investigations	Weight increased			

Breast discharge may occur during use of desogestrel. On rare occasions, ectopic pregnancies have been reported (see section 4.4). In addition, aggravation of hereditary angioedema may occur (see section 4.4).

In women using (combined) oral contraceptives a number of (serious) undesirable effects have been reported. These include venous thromboembolic disorders, arterial thromboembolic disorders, hormone-dependent tumours (e.g. liver tumours, breast cancer) and chloasma, some of which are discussed in more detail in section 4.4.

Breakthrough bleeding and/or contraceptive failure may result from interactions of other drugs (enzyme inducers) with hormonal contraceptives (see section 4.5)

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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

There have been no reports of serious deleterious effects from overdose. Symptoms that may occur in this case are nausea, vomiting and, in young girls, slight vaginal bleeding. There are no antidotes and further treatment should be symptomatic.

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: hormonal contraceptives for systemic use,
ATC code: G03AC09.

Desogestrel is a progestogen-only pill, which contains the progestogen desogestrel. Like other progestogen-only pills, Desogestrel can be used for women who may not or do not want to use oestrogens. In contrast to traditional progestogen-only pills, the contraceptive effect of Desogestrel is achieved primarily by inhibition of ovulation. Other effects include increased viscosity of the cervical mucus.

When studied for 2 cycles, 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% (1/103) with a 95% confidence interval of 0.02% - 5.29% in the ITT group (user and method failures). Ovulation inhibition was achieved from the first cycle of use. In this study, when desogestrel was discontinued after 2 cycles (56 continuous days) ovulation occurred on average after 17 days (range 7-30 days).

In a comparative efficacy trial (which allowed a maximum time of 3 hours for missed pills), the overall ITT Pearl-Index found for desogestrel was 0.4 (95% confidence interval 0.09 - 1.20), compared to 1.6 (95% confidence interval 0.42 - 3.96) for 30 g levonorgestrel.

The Pearl-Index for Desogestrel is comparable to the one historically found for COCs in the general COC-using population Treatment with Desogestrel leads to decreased estradiol levels, to a level corresponding to the early follicular phase. No clinically relevant effects on carbohydrate metabolism, lipid metabolism and haemostasis have been observed.

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

5.2 Pharmacokinetic properties

Absorption

After oral dosing of desogestrel (DSG) is rapidly absorbed and converted into etonogestrel (ENG). Under steady-state conditions, peak serum levels are reached 1.8 hours after tablet-intake and the absolute bioavailability of ENG is approximately 70%.

Distribution

ENG is 95.5-99% bound to serum proteins, predominantly to albumin and to a lesser extent to SHBG.

Metabolism

DSG is metabolised via hydroxylation and dehydrogenation to the active metabolite ENG. ENG is metabolised via sulphate and glucuronide conjugation.

Elimination

ENG is eliminated with a mean half-life of approximately 30 hours, with no difference between single and multiple dosing. Steady-state levels in plasma are reached after 4-5 days. The serum clearance after i.v. administration of ENG is approximately 10 l per hour. Excretion of ENG and its metabolites either as free steroid or as conjugates, is with urine and faeces (ratio 1.5:1).

In lactating women, ENG is excreted in breast milk with a milk/serum ratio of 0.37-0.55. Based on these data and an estimated milk intake of 150 ml/kg/day, 0.01 - 0.05 micrograms etonogestrel may be ingested by the infant.

5.3 Preclinical safety data

Toxicological studies did not reveal any effects other than those, that can be explained from the hormonal properties of desogestrel.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Lactose monohydrate

Maize starch

Povidone PVP K-30

Stearic acid

All-rac-alpha-tocopherol

Silica, colloidal anydrous

Film coating:

Tabcoat TC-white-IHS

Hydroxypropyl Methyl Cellulose
Polyethylene Glycol
Talc
Titanium Dioxide

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 Years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PVC/PVDC aluminium blister packs containing 1x28 film-coated tablets.

PVC/PVDC aluminium blister packs containing 3x28 film-coated tablets.

PVC/PVDC aluminium blister packs containing 6x28 film-coated tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

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IG3 8BS

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8 MARKETING AUTHORISATION NUMBER(S)

PL 15764/0044

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