SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Hana 75 microgram film coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 75 microgram desogestrel.

Excipient(s) with known effect: each tablet contains approximately 51.5 mg of lactose monohydrate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film coated tablets (tablets).

The tablet is white, round and biconvex without a score line.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Hana is indicated as an oral contraceptive in women of childbearing age.

4.2 Posology and method of administration

Posology

To prevent pregnancy, Hana must be used as directed (see 'How to take Hana' and 'How to start Hana').

Special populations

Renal impairment

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

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 Hana in these women is not indicated as long as liver function values have not returned to normal (see section 4.3).

Paediatric population

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

Method of administration

Oral use.

How to take Hana

Tablets must be taken every day at the same time 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 of possible bleeding. When a pack of pills is finished, a new pack should be started directly the day after the previous one.

How to start Hana

The woman should have none of the contraindications listed in section 4.3 and should be advised to consult with her physician if in doubt.

Any pre-existing bleeding abnormalities such as oligomenorrhoea and amenorrhoea should be investigated by a physician before starting Hana in order that any underlying pathology (see section 4.4) can be managed and followed-up appropriately.

No contraceptive use in the past month

It is preferable to start tablet-taking on day 1 of the woman's natural cycle (day 1 is the first day of menstrual bleeding). However, it can be started on days 2-5, but then a barrier method is recommended for the first 7 days of tablet-taking.

Following miscarriage or abortion

It is recommended to start tablet-taking immediately or within 5 days after miscarriage or abortion. In that case there is no need to use an additional method of contraception.

Following childbirth

The woman should start Hana any day between day 1 and day 21 after childbirth. When starting later, she should use a barrier method for the first 7 days of tablet-taking. However, if unprotected intercourse has already occurred, the woman should take a pregnancy test or talk to her physician before the actual start of Hana.

For additional information for breast-feeding women, see section 4.6.

Starting or resuming Hana after emergency contraception use

If a woman wishes to start taking Hana after using emergency hormonal contraception, it is advisable to start tablet-taking on day 1 of the woman's natural cycle.

If it is considered necessary to start sooner, or if Hana is being resumed after inconsistent use, the following advice should be noted:

Levonorgestrel
Hana can be started or restarted on the same day as emergency contraception containing levonorgestrel. Additional contraceptive measures (abstinence or barrier methods) are required for the first 7 days of Hana use.

Ulipristal acetate
Hana should be started or restarted no sooner than 5 days (120 hours) after emergency contraception containing ulipristal acetate, because the effectiveness of ulipristal can be reduced (see section 4.5). Additional contraceptive measures (abstinence or barrier methods) are required during the 5 day delay before starting or restarting Hana and for an additional 7 days after starting or restarting Hana (12 days in total).
Ulipristal acetate may conversely reduce the effectiveness of Hana. Concomitant use is therefore not recommended (see section 4.5).

How to start Hana 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 Hana 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 barrier method is not necessary.

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, patch or ring use, an additional barrier method is recommended.

Changing from a progestogen-only-method (minipill, injection, implant or a progestogen-releasing intrauterine system [IUS]).

The woman may switch any day from a minipill, on the day of removal of an implant or an IUS, or on the day the next contraceptive injection is due.

Management of missed tablets

Contraceptive protection may be reduced if more than 36 hours have elapsed between two tablets.

If the user is less than 12 hours late from her usual time of taking any tablet, she should take the missed tablet as soon as she remembers and take the next tablet at the usual time, even if it leads to taking two tablets in one day.

If she is more than 12 hours late from her usual taking time, the woman should immediately take the forgotten tablet and take the next tablet at the usual time, even if it leads to taking two tablets in one day. If more than one tablet has been missed, only one of the missed tablets should be taken immediately. In addition, she should use an additional barrier method of contraception for the next 7 days. Missed tablets at any time in the cycle can reduce the efficacy of Hana and risk pregnancy, but missing a tablet in the first week after initiation of Hana is an especially vulnerable time. The need for emergency contraception must be considered for any missed pills.

Advice in case of gastrointestinal disturbances

If vomiting occurs within 3-4 hours of tablet-taking, then the pill should be considered ‘missed’ and the advice for a missed tablet should be followed.

In case of severe or persistent gastro-intestinal disturbance (vomiting or diarrhoea), absorption of Hana may not be complete and contraceptive efficacy may be reduced. Additional contraceptive measures will be required for the duration of the illness and for the first 7 days of normal tablet taking.

<u>Regular screening</u>

Women should be advised to continue to have regular smear tests (cervical screening) while taking Hana. Women aged 50 years and above should be advised to attend for regular breast screening while women below 50 years should be advised to report any lump or change in their breast to their physician.

Women should be advised to go for a check-up at a sexual health clinic as soon as they can if they are worried they may have a Sexually Transmitted Infection (STI). Many STIs, including HIV (AIDS), have no symptoms at all. Women can only know for sure that they do not have an STI if they get tested.

4.3 Contraindications

Hana must not be used if any of the conditions listed below are present.

- Known or suspected sex-steroid sensitive malignancies.
- Active venous thromboembolic disorder.
- Presence or history of severe hepatic disease as long as liver function values have not returned to normal.
- Undiagnosed vaginal bleeding.
- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Excluding pregnancy

Excluding pregnancy before starting Hana

Women who have not recently been pregnant	**Women who have recently been pregnant**	
	Following childbirth	Following miscarriage, abortion or ectopic pregnancy
Pregnancy can reasonably be excluded if the woman • has not had unprotected sex since the start of her last menstrual period or • has been correctly and consistently using a reliable method of contraception (including condoms where those have been used correctly for every episode of sexual intercourse) or • has had unprotected sex but only between day 1 and day 5 of her menstrual cycle.	Pregnancy can reasonably be excluded if the woman • has not had unprotected sex since childbirth or • has had unprotected sex but less than 21 days after childbirth or • is fully breastfeeding, amenorrheic and less than 6 months postpartum.	Pregnancy can reasonably be excluded if the woman • has not had unprotected sex since miscarriage, abortion or ectopic pregnancy or • has had unprotected sex but less than 5 days after miscarriage, abortion or ectopic pregnancy.

The woman should use a reliable method of contraception (current contraceptive or a barrier method) until the first day of her next period before starting Hana. She should be advised that if her menstrual period is already late or does not come when she expects it, she may be pregnant and she should do a pregnancy test (at least 3 weeks after the last episode of unprotected sexual intercourse) or see a physician. Provided the pregnancy test is negative she can start Hana on the first day of her next period. If, in the meantime, her menstrual period comes, she can start Hana on the first day of her period.

Excluding pregnancy before starting a new pack of Hana.

Before starting a new pack of Hana, a woman should be reasonably certain that she is not pregnant. If in doubt, particularly if she has not been using Hana correctly and consistently, she should be advised that there is a chance that she may be pregnant and she should do a pregnancy test at least 3 weeks after the last episode of unprotected intercourse. She should continue taking Hana until the result of the pregnancy test is available but if it is positive she should stop immediately and see a physician.

Warnings

If any of the conditions/risk factors mentioned below are present, the woman should be referred to her physician to weigh-up the benefits of progestogen use against the possible risks in her situation before she can start Hana.

In the event of exacerbation, or first appearance of any of these conditions, the woman should be referred to her physician. The physician should then decide on whether the use of Hana should be discontinued.

Breast cancer

Hana is contraindicated in women who have breast cancer because it may increase the risk of recurrence (Section 4.3).

Women with a past history of breast cancer should be referred to a physician before taking Hana.

The risk of breast cancer increases with age. The risk in users of progestogen-only contraceptives (POCs), such as Hana, is possibly of similar magnitude as that associated with combined oral contraceptives (COCs). However, for POCs the evidence is less conclusive.

During use of 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 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

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.

Hepatic disorders and disturbances of liver function

Hana is contraindicated in women who have, or have had, severe hepatic disease as long as liver function values have not returned to normal (Section 4.3).

When acute or chronic disturbances of liver function occur, the woman should be referred to a specialist for examination and advice.

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.

Hypertension

If sustained hypertension develops during the use of Hana, or if a significant increase in blood pressure does not adequately respond to antihypertensive therapy, a physician should decide whether Hana should be discontinued.

Thromboembolic disorders

Hana is contraindicated in women who have an active venous thromboembolic disorder (Section 4.3).

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, Hana should be discontinued in the event of a thrombosis. Discontinuation of Hana should also be considered in case of long-term immobilisation due to surgery or illness.

Women with a history of thromboembolic disorders can take Hana but should be made aware of the possibility of a recurrence.

Changes in bleeding patterns

Hana is contraindicated in women who have undiagnosed vaginal bleeding before they first start taking the tablets (Section 4.3).

Women taking Hana will have bleeding patterns which differ from those associated with their natural cycle. If bleeding is not acceptable to the women (e.g. the frequency of the period is not acceptable), another contraceptive method should be considered. If the bleeding disturbances persist after stopping Hana, the women should be referred to her physician to rule out any pathological cause.

If the bleeding differs from that which would be expected with Hana or is unusually heavy, she should be referred to her physician to rule out any underlying pathology.

Women who repeatedly have post-coital bleeding should be investigated for underlying gynecological pathology, especially cervical cancer. Other causes of post-coital bleeding include benign growths (endometrial and cervical polyps, cervical ectropion); infection (cervicitis, pelvic inflammatory disease, endometritis, vaginitis due to STIs); genital/vulvar lesions (Herpes simplex virus, genital warts); benign conditions usually occurring in postmenopausal women such as vaginal atrophy and uterine prolapse; endometriosis; vaginal and endometrial cancer; and trauma (sexual abuse, foreign bodies).

It is usual that some women may experience amenorrhea because Hana primarily acts by inhibiting ovulation. However, because amenorrhea may indicate pregnancy, if use of Hana has been imperfect, women should be advised to do a pregnancy test. The treatment should be stopped if pregnancy occurs.

Diabetes

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, in the case of any change in insulin requirements during the first months of use, diabetic patients should be referred to their physician.

Psychiatric disorders

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.

Ectopic pregnancy

Hana consistently inhibits ovulation and so reduces the risk of ectopic pregnancy (see section 5.1). However, as with all women of reproductive age, ectopic pregnancy should be considered in the differential diagnosis if the woman has pelvic pain with either vaginal bleeding/spotting or with amenorrhoea, particularly if Hana has been used inconsistently or incorrectly rendering pregnancy more likely.

Effect on bone mineral density

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

Conditions reported during pregnancy or during sex steroid use

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.

Chloasma

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 Hana or consider using another contraceptive.

Reduced efficacy

The efficacy of Hana 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).

Lactose intolerance

Hana contains lactose and therefore should not be used by women with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency, or glucose-galactose malabsorption.

Sexually transmitted infections

Hana does not protect against HIV (AIDS) and other sexually transmitted infections.

4.5 Interaction with other medicinal products and other forms of interaction

Interactions

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

Effect of other medicinal products on Hana

Interactions can occur with medicinal products that induce microsomal enzymes, which can result in increased clearance of sex hormones and may lead to breakthrough bleeding and/or contraceptive failure. Enzyme induction can occur after a few days of treatment. Maximum enzyme induction is generally observed within a few weeks. After drug therapy is discontinued, enzyme induction can last for about 4 weeks.

Short-term treatment

Women on treatment with hepatic enzyme-inducing medicinal or herbal products should be advised that the efficacy of Hana may be reduced. A barrier contraceptive method should be used in addition to Hana. The barrier method must be used during the whole time of concomitant drug therapy and for 28 days after discontinuation of the hepatic enzyme-inducing medicinal product.

Chronic and long-term treatment

If enzyme-inducing medicinal products are used chronically or long-term, Hana may not be the most appropriate method of contraception and the woman should be referred to her physician for further advice.

Substances increasing the clearance of contraceptive hormones (diminished contraceptive efficacy by enzyme induction) e.g.:

Barbiturates (e.g. phenobarbital), bosentan, carbamazepine, hydantoins (e.g. phenytoin), primidone, rifampicin, efavirenz and possibly also felbamate, griseofulvin, oxcarbazepine, topiramate, rifabutin and products containing the herbal remedy St. John's Wort (Hypericum perforatum).

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.

The clinical relevance of potential interactions with enzyme inhibitors remains unknown.

Hana and emergency contraception containing ulipristal acetate:

Hana and the emergency contraceptive containing ulipristal acetate both bind to the progesterone receptor. Concomitant use may result in reduced efficacy of both Hana and ulipristal acetate and is therefore not recommended. Hana should be started or restarted no sooner than 5 days (120 hours) after emergency contraception with ulipristal acetate (see section 4.2).

Effects of Hana on other medicinal products

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

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

Pregnancy

Hana is not indicated during pregnancy. If pregnancy occurs during treatment with Hana, further intake should be stopped.

Animal studies have shown that very high doses of progestogenic substances may 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 prior to pregnancy, nor a teratogenic effect when COCs were taken inadvertently during early pregnancy. Pharmacovigilance data collected with various desogestrel-containing COCs also do not indicate an increased risk.

Breastfeeding

Based on clinical study data, Hana does not appear to influence the production or the quality (protein, lactose, or fat concentrations) 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 microgram etonogestrel per kg body weight per day may be ingested by the child (based on an estimated milk ingestion of 150 ml/kg/day). Like other progestogen-only pills, Hana 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 week post-partum. They were breastfed 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 Hana may be used during lactation. The development and growth of a nursing infant, whose mother uses Hana, should, however, be carefully observed.

Fertility

Hana is indicated for the prevention of pregnancy. For information on return to fertility (ovulation), see section 5.1. There is no evidence suggesting a delay in return of fertility following discontinuation of desogestrel (see section 5.1); therefore if pregnancy is not desired, other contraceptive methods should be used immediately following discontinuation of Hana.

4.7 Effects on ability to drive and use machines

Hana 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. Bleeding irregularity of some kind has been reported in up to 50% of women using desogestrel. Since desogestrel causes ovulation inhibition in close to 100% of cycles, 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, bleeding episodes 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 are listed in the table below by system organ class and frequency.

System Organ Class (MedDRA)*	**Frequency of adverse reactions**		
	Common	**Uncommon**	**Rare**
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 condition		Fatigue	
Investigations	Weight increase		

* MedDRA version 22.0

Breast discharge may occur during use of Hana. On rare occasions, ectopic pregnancies have been reported. Hypersensitivity reactions (including angioedema and anaphylaxis) have also been reported. In addition, aggravation of angioedema and/or 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 or vomiting and, in young girls, slight vaginal bleeding. There are no antidotes and further treatment should be symptomatic.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Mechanism of action

Hana is a progestogen-only pill, which contains the progestogen desogestrel. In contrast to second generation progestogen-only pills, the contraceptive effect of Hana is achieved primarily by inhibition of ovulation. Other effects include increased viscosity of the cervical mucus.

Clinical efficacy and safety

Like other progestogen-only pills, Hana can be used during breast-feeding and by women who may not or do not want to use oestrogens.

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 Hana 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 Hana was 0.4 (95% confidence interval 0.09 - 1.20), compared to 1.6 (95% confidence interval 0.42 - 3.96) for 30 microgram levonorgestrel.

The Pearl-Index for Hana is comparable to that reported for COCs in clinical studies.

Treatment with Hana 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 Hana, 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.

Biotransformation

DSG is metabolised via hydroxylation and dehydrogenation to the active metabolite ENG. ENG is primarily metabolised by the cytochrome P450 3A (CYP3A) isoenzyme and subsequently conjugated with sulphate and glucuronide.

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 microgram etonogestrel maybe ingested by the infant.

Special populations

Effect of renal impairment

No studies have been performed to evaluate the effect of renal disease on the pharmacokinetics of DSG.

Effect of hepatic impairment

No studies have been conducted to evaluate the effect of hepatic disease on the pharmacokinetics of DSG. However, steroid hormones may be poorly metabolized in women with impaired liver function.

Ethnic groups

No studies have been performed to assess pharmacokinetics in ethnic groups.

5.3 Preclinical safety data

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

Environmental Risk Assessment (ERA)

The active substance etonogestrel shows an environmental risk to fish.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Alpha-tocopherol
Lactose monohydrate
Maize starch
Povidone K25
Stearic acid

Film coating

Hypromellose
Macrogol 400
Titanium dioxide (E 171)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years.

Shelf-life after first opening of the sachet: 3 months.

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

PVC/Aluminium blister.

Each blister contains 28 tablets. Each carton contains 1 or 3 blisters.

Blisters are packed in sachets.

6.6 Special precautions for disposal

The active substance etonogestrel shows an environmental risk to fish.

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

7 MARKETING AUTHORISATION HOLDER

Laboratoire HRA Pharma
200 avenue de Paris
92320 Chatillon
France

8 MARKETING AUTHORISATION NUMBER(S)

PL 17836/0015

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 DATE OF REVISION OF THE TEXT