SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Desogestrel Rowex 75 microgram Film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 75 micrograms desogestrel

Excipient(s) with known effects:
51.3 mg lactose (as mononhydrate)
0.03 mg soya-bean oil.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet

Round, plain, white film-coated tablets with a diameter of 5 mm approximately and a thickness of 2.9 mm approximately.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Contraception.

4.2 Posology and method of administration

Posology

To achieve contraceptive effectiveness, Desogestrel Rowex must be used as directed (see 'How to take Desogestrel Rowex and 'How to start Desogestrel Rowex).

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 Desogestrel Rowex 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 desogestrel in adolescents below 18 years has not been established. No data are available.

Method of administration

Oral use

How to take Desogestrel Rowex

Tablets must be taken every day at about the same time so that the interval between two tablets always is 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 Rowex

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 to start immediately. In that case there is no need to use an additional method of contraception.

Following delivery or second-trimester abortion:
The woman should be advised to start any day between day 21 to 28 after delivery or second-trimester abortion. When starting later, she should be advised to additionally use a barrier method until completion of the first 7 days of tablet-taking. However, if intercourse has already occurred, pregnancy should be excluded before the actual start of Desogestrel Rowex use or the woman has to wait for her first menstrual period.

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

How to start Desogestrel Rowex 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 Rowex 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).

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 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 after initiation of Desogestrel Rowex 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 section 4.2 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 Rowex 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 Rowex does not protect against HIV (AIDS) and other sexually transmitted diseases.

4.3 Contraindications

- 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.
- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- If you are allergic to peanut or soya.

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 Rowex. 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 Rowex 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 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 Rowex, 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 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 Rowex should be discontinued in the event of a thrombosis. Discontinuation of Desogestrel Rowex 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.

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.

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 Rowex, or if a significant increase in blood pressure does not adequately respond to antihypertensive therapy, the discontinuation of Desogestrel Rowex should be considered.

Treatment with Desogestrel Rowex leads to decreased estradiol 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 Rowex 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 Rowex.

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.

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

Desogestrel Rowex contains lactose and therefore should not be administered to patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency, or glucose-galactose malabsorption.

Each tablet of this medicinal product contains maximally 0.03 mg of soya-bean oil and therefore should not be administered to patients who are allergic to peanut or soya.

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.

4.5 Interaction with other medicinal products and other forms of interaction

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

Effect of other medicinal products on Desogestrel Rowex

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.

Management

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 Desogestrel Rowex may be reduced. A barrier contraceptive method should be used in addition to Desogestrel Rowex. 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.

Long-term treatment

For women on long-term therapy with enzyme-inducing medicinal products, an alternative method of contraception unaffected by enzyme-inducing medicinal products should be considered.
Substances increasing the clearance of contraceptive hormones (diminished contraceptive efficacy by enzyme induction) e.g.:

Barbiturates, bosentan, carbamazepine, 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.

Effects of Desogestrel Rowex 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).

4.6 Fertility, pregnancy and lactation

Pregnancy

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

Animal studies have shown that very high doses of progestogenic substances may cause masculinisation of female foetuses.

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.

Breast-feeding

Based on clinical study data, desogestrel 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, Desogestrel Rowex can be used during breast feeding.

Limited long-term follow-up data are available on children, whose mothers started using desogestrel during the 4^{th} to 8^{th} week 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 Rowex may be used during lactation. The development and growth of a nursing infant, whose mother uses Desogestrel Rowex should however, be carefully observed.

Fertility

Desogestrel Rowex is indicated for the prevention of pregnancy. For information on return to fertility (ovulation), see section 5.1.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Summary of the safety profile

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 Rowex 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 are mentioned in the table below.

Tabulated list of adverse reactions

All undesirable effects are listed by system organ class and frequency; common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100) and rare (≥1/10,000 to <1/1,000).

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 increased		

* MedDRA version 12.0

Breast discharge may occur during use of Desogestrel Rowex. On rare occasions, ectopic pregnancies have been reported (see section 4.4). 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 national reporting system at http://www.medicinesauthority.gov.mt/adrportal

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. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Mechanism of action

Desogestrel Rowex is a progestogen-only pill, which contains the progestogen desogestrel. Like other progestogen-only pills, Desogestrel Rowex 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 Rowex is achieved primarily by inhibition of ovulation. Other effects include increased viscosity of the cervical mucus.

Clinical efficacy and safety

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 µg 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 Rowex, 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 sex hormone binding globulin (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 may be ingested by the infant.

Special populations

Renal impairment

No studies were performed to evaluate the effect of renal disease on the pharmacokinetics of desogestrel.

Hepatic impairment
No studies were conducted to evaluate the effect of hepatic disease on the pharmacokinetics of desogestrel. However, steroid hormones may be poorly metabolized in women with impaired liver function.

Ethnic groups
No studies were 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:
Lactose monohydrate
Maize starch
Povidone K30
Silica colloidal hydrated
Silica colloidal anhydrous
RRR-α-tocopherol
Stearic acid
Soya-bean oil, refined

Coating:
Hypromellose 2910
Macrogol 400
Titanium Dioxide (E171)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 30ºC. Store in the original package in order to protect from light.

6.5 Nature and contents of container

PVC-PVDC/Al Blisters with pack sizes 1x28, 3x28, 6x28 and 13x28.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Rowex Ltd
Bantry
Co. Cork, Ireland

8. MARKETING AUTHORISATION NUMBER(S)

MA1122/03301

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11th March 2024

10. DATE OF REVISION OF THE TEXT