NEW ZEALAND DATA SHEET

1 CERAZETTE 75 microgram Film-coated tablet

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 75 microgram desogestrel.

Excipient with known effect:

- lactose monohydrate

For the full list of excipients, see **Section 6.1 List of excipients.**

3 PHARMACEUTICAL FORM

Film coated tablet.

The tablet is white, round, biconvex and 5 mm in diameter. On one side it is coded KV above 2 and on the reverse side ORGANON.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Oral contraception.

4.2 Dose and method of administration

How To Take CERAZETTE

Tablets must be taken in the order directed on the package, every day at about the same time, with some liquid as needed. One tablet is to be taken daily for 28 consecutive days. Each subsequent pack is started immediately after finishing the previous pack.

How To Start CERAZETTE

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 in addition for the first 7 days of tablet-taking.

Changing from a combined hormonal contraceptive (combined oral contraceptive (COC), vaginal ring, or transdermal patch)

The woman should start with CERAZETTE preferably on the day after the last active tablet (the last tablet containing the active substances), or on the day of removal of her vaginal ring or patch. In these cases, the use of an additional contraceptive is not necessary.

The women 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). An additional contraceptive method is not necessary.

Following first-trimester abortion

After first trimester abortion it is recommended to start immediately; an additional contraceptive method is not necessary.

Following delivery or second-trimester abortion

For breastfeeding women see **Section 4.6 Fertility, pregnancy and lactation**.

The woman should be advised to start at day 21-28 after delivery or second trimester abortion. When starting later, she should be advised to use a barrier method in addition for the first 7 days of tablet-taking. However, if intercourse has already occurred, pregnancy should be excluded before the actual start of CERAZETTE use or the woman has to wait for her first menstrual period.

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 follow the same advice but also use an additional method of contraception for the next 7 days. If tablets were missed in the very 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 gastrointestinal 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 under **Management of missed tablets** is applicable.

Paediatric population

No data available.

4.3 Contraindications

Progestogen-only contraceptives should not be used in the presence of any of the conditions listed below. Should any of the conditions appear for the first time during the use of CERAZETTE, the product should be stopped immediately.

- Hypersensitivity to the active substance or to any of the excipients listed in **Section 6.1 List of 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 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 using CERAZETTE. 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 CERAZETTE should be discontinued.

- The risk for breast cancer increases in general with increasing age. During the 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 OC 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

combined OCs (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:

Table 1

Age group	Expected cases combined OC-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 POP users is possibly of similar magnitude as that associated with combined OCs. However, for POPs 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.
- If a sustained hypertension develops during the use of CERAZETTE, or if a significant increase in blood pressure does not adequately respond to antihypertensive therapy, discontinuation with the use of CERAZETTE should be considered.
- Epidemiological investigations have associated the use of combined OCs 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, CERAZETTE should be discontinued in the event of a thrombosis. Discontinuation of CERAZETTE should also be considered in case of long-term immobilisation due to surgery or illness. Women with a history of thromboembolic 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.
- Treatment with CERAZETTE 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 CERAZETTE 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 CERAZETTE.
- 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.

- CERAZETTE contains less than 65mg lactose and therefore should not be administered to patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency, or glucose-galactose malabsorption.

Medical Examination/Consultation

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 Special warnings and precautions for use**), the control examinations should be timed accordingly. Despite the fact that CERAZETTE 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 CERAZETTE does not protect against HIV (AIDS) and other sexually transmitted diseases.

Reduced Efficacy

The efficacy of CERAZETTE may be reduced in the event of missed tablets (see **Section 4.2 Dose and method of administration, Management of missed tablets**), gastrointestinal disturbances (see **Advice in case of gastrointestinal disturbances**) or concomitant medications that decrease the plasma concentration of etonogestrel, the active metabolite of desogestrel (see **Section 4.5 Interactions with other medicines and other forms of interactions**).

Changes in Vaginal Bleeding Pattern

During the use of a progestogen-only contraceptive, vaginal bleeding may become more frequent or of longer duration in some women, whereas in others bleeding may become incidental or be totally absent. These changes are often a reason for women to reject the method or to be non-compliant. Acceptance of bleeding pattern can be improved by offering women who have chosen to use CERAZETTE careful counselling on this point. Evaluation of vaginal bleeding should be done on an *ad hoc* basis and may include examination to exclude malignancy or pregnancy.

Follicular Development

With all low-dose hormonal contraceptives, follicular development occurs and occasionally the follicle may continue to grow beyond the size it would attain in a normal cycle. Generally, these enlarged follicles disappear spontaneously. Often, they are asymptomatic; in some cases they are associated with mild abdominal pain. They rarely require surgical intervention.

4.5 Interactions with other medicines and other forms of interactions

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

Interactions between oral contraceptives and other medicinal products may lead to breakthrough bleeding and/or contraceptive failure. No specific interaction studies have been performed with CERAZETTE. 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 or herbal products that induce microsomal enzymes, specifically cytochrome P450 enzymes (CYP), which can result in increased clearance reducing plasma concentrations of sex hormones and may decrease the effectiveness of oral contraceptives, including CERAZETTE. These products include phenytoin, phenobarbital, primidone, bosentan, carbamazepine, rifampicin; and possibly also oxcarbazepine, rifabutin, topiramate, felbamate, griseofulvin, some HIV protease inhibitors (e.g., ritonavir, nelfinavir) and non-nucleoside reverse transcriptase inhibitors (e.g., efavirenz), and the herbal remedy St John's wort.

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 28 days.

When co-administered with hormonal contraceptives, many combinations of HIV protease inhibitors (e.g., 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, including etonogestrel, the active metabolite of desogestrel. The net effect of these changes may be clinically relevant in some cases.

Women receiving any of the above mentioned hepatic enzyme-inducing medicinal or herbal products should be advised that the efficacy of CERAZETTE may be reduced. A barrier contraceptive method should be used in addition to CERAZETTE during administration of the hepatic enzyme-inducing medicinal product, and for 28 days after discontinuation of the hepatic enzyme-inducing medicinal product.

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.

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. In such an event, the advice concerning missed tablets, as given under **Management of missed tablets** is applicable.

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

Interference with serological testing

Data obtained with combined oral contraceptives 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 relates to progestogen-only contraceptives is not known.

4.6 Fertility, pregnancy and lactation

Pregnancy

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 OCs prior to pregnancy, nor a teratogenic effect when OCs were taken inadvertently during early pregnancy.

Pharmacovigilance data collected with various desogestrel-containing combined OCs also do not indicate an increased risk.

Breast-feeding

CERAZETTE does not influence the production or the quality (protein, lactose, or fat concentrations) of breast milk. However 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).

Limited long-term follow-up data are available on children, whose mothers started using CERAZETTE during the 4th to 8th week post-partum. They were breast-fed for 7 months and followed up to 2.5 years 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 CERAZETTE may be used during lactation. The development and growth of a nursing infant, whose mother uses CERAZETTE, should be carefully observed.

Fertility

See **Section 5.1 Pharmacodynamic Properties, Mechanism of Action.**

4.7 Effects on ability to drive and use machines

On the basis of the pharmacodynamic profile, CERAZETTE is expected to have no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The most commonly reported undesirable effects in the clinical trials with CERAZETTE (>2.5%) were bleeding irregularities, acne, mood alterations, 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.

Table 2

System Organ Class (MedDRA)*	**Frequency of adverse reactions**		
	Common ≥ 1/100	**Uncommon < 1/100, ≥ 1/1000**	**Rare (< 1/1000)**
Infections and infestations		Vaginal infection	
Psychiatric disorders	Mood altered 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	Dysmenorrhoea, Ovarian cyst	

	irregular, Amenorrhoea		
General disorders and administration site condition		Fatigue	
Investigations	Weight increase		

*MedDRA version 9.0

Breast discharge and, on rare occasions, ectopic pregnancies have been reported with the use of CERAZETTE during post-marketing surveillance (see **Section 4.4 Special warnings and precautions for use)**. In addition, hypersensitivity reactions (including angioedema and anaphylaxis) have been reported during post-marketing surveillance.

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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

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.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Hormonal contraceptives for systemic use, ATC code: G03AC09

Mechanism of action

CERAZETTE is a progestogen-only pill, which contains the progestogen desogestrel. Like other progestogen-only pills, CERAZETTE is best suited for use during breast feeding and for women who may not or do not want to use oestrogens. In contrast to traditional progestogen-only pills, the contraceptive effect of CERAZETTE 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 CERAZETTE 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 CERAZETTE 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 CERAZETTE is comparable to the one historically found for combined OCs in the general OC-using population. Treatment with CERAZETTE leads to decreased oestradiol levels, to a level corresponding to the early follicular phase. No clinically relevant effects on carbohydrate metabolism, lipid metabolism and haemostasis have been observed.

5.2 Pharmacokinetic properties

Absorption

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

Distribution

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

Biotransformation

Desogestrel is metabolised via hydroxylation and dehydrogenation to the active metabolite etonogestrel. Etonogestrel is metabolised via sulphate and glucuronide conjugation.

Elimination

Etonogestrel 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 etonogestrel is approximately 10 litres per hour. Excretion of etonogestrel and its metabolites either as free steroid or as conjugates, is with urine and faeces (ratio 1.5:1). In lactating women, etonogestrel is excreted in breast milk with a milk/serum ratio of 0.37-0.55. Based on these data and on an estimated milk intake of 150 mL/kg/day, 0.01-0.05 microgram etonogestrel per kg bodyweight per day may be ingested by the infant.

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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core

Silica, colloidal anhydrous; dl-α-tocopherol, lactose monohydrate, maize starch, povidone, stearic acid.

Film Coating

Hypromellose, macrogol 400, purified talc, titanium dioxide (E 171).

6.2 Incompatibilities

None known.

6.3 Shelf life

The shelf-life of CERAZETTE is 36 months.

6.4 Special precautions for storage

Store at 2°C-30°C, protected from light and moisture.

6.5 Nature and contents of container

Each strip contains 28 tablets.

Cartons contain 1, 3 or 6 strips.

6.6 Special precautions for disposal and other handling

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

7 MEDICINE SCHEDULE

Prescription Medicine.

8 SPONSOR

Organon New Zealand Limited
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Auckland 1149
New Zealand
Tel: 0800 111 700

9 DATE OF FIRST APPROVAL

13 May 1997

10 DATE OF REVISION OF THE TEXT

1 December 2020

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
8	Amend sponsor details due to transfer of sponsorship