SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Duphaston 10, film-coated tablets 10 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 10 mg dydrogesterone.
Excipient with known effect: 111.1 mg lactose monohydrate.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

A round, biconvex, white film-coated tablet, (with a diameter of 7 mm) with a score line, with the inscription '155' on both sides of the score line. The score line is only to make the tablet easier to break so that it is easier to swallow; it is not intended for dividing it into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- To regulate the menstrual cycle
- Endometriosis
- Dysmenorrhoea
- Infertility as a result of corpus luteum insufficiency
- Luteal support as part of an Assisted Reproductive Technology (ART) treatment
- Threatened miscarriage as a result of progesterone deficiency
- Habitual miscarriage as a result of progesterone deficiency

As a cyclical supplement to oestrogen therapy in women with an intact uterus, Duphaston 10 can be used:
- to prevent endometrial hyperplasia in the postmenopausal period
- for dysfunctional uterine bleeding
- for secondary amenorrhoea

4.2 Posology and method of administration

Posology
The following dosage regimens are recommended for treatment with Duphaston 10. The quantities can be adjusted according to the seriousness of the disorder to be treated and the individual patients' responses to the treatment.

Regulation of the cycle
It is possible to achieve a cycle lasting 28 days by giving 1 tablet of Duphaston 10 a day from the 11th to the 25th day of the cycle.

Endometriosis

1 to 3 tablets of Duphaston 10 a day from the 5th to the 25th day of the cycle or for the entire cycle. Dosages of 10 mg several times a day should be spread over the day. It is recommended to start treatment with the highest dosage.

Dysmenorrhoea
1 to 2 tablets of Duphaston 10 a day from the 5th to the 25th day of the cycle. Dosages of 10 mg several times a day should be spread over the day. It is recommended to start the treatment with the highest dosage.

Infertility as a result of corpus luteum insufficiency
1 tablet of Duphaston 10 a day from the 14th to the 25th day of the cycle.
Treatment should be continued for at least 6 consecutive cycles. It is advisable to continue this treatment for the first months of any pregnancy at dosages as indicated for habitual miscarriage.

Luteal support as part of an Assisted Reproductive Technology (ART) treatment
1 tablet of Duphaston 10 three times a day (30 mg daily) starting at the day of oocyte retrieval and continuing for 10 weeks if pregnancy is confirmed.

Threatened miscarriage
Starting dose: 4 tablets of Duphaston 10 at once followed by 1 tablet of Duphaston 10 mg every 8 hours. Dosages of 10 mg several times a day should be spread over the day. It is recommended that treatment should start at the highest dose.
If the symptoms persist or recur during the treatment, the dose should be increased by 1 tablet of Duphaston 10 every 8 hours.
The effective dose should be maintained for one week after symptoms have ceased; it can then be gradually reduced. If the symptoms recur, the treatment should be resumed immediately at the effective dose.

Habitual miscarriage
1 tablet of Duphaston 10 a day up to the 20th week of pregnancy; the dose can then be gradually reduced. Treatment should preferably be started before conception.
If the symptoms of threatened miscarriage occur during treatment, treatment should be continued as described for that indication.

Dysfunctional uterine bleeding
Bleeding is stopped by 2 tablets of Duphaston 10 a day for 5 to 7 days. The blood loss is reduced considerably within a few days. A few days after the end of this treatment, a heavy withdrawal bleed occurs and the patient should be warned about this.
Subsequent heavy bleeding can be prevented by prescribing a prophylactic dose of 1 tablet of Duphaston 10 a day from the 11th to the 25th day of the cycle, if necessary combined with an oestrogen for 2 to 3 cycles. After this the treatment can be discontinued, in order to check that the patient has a normal cycle again.

Secondary amenorrhoea
1 or 2 tablets of Duphaston 10 per day from the 11th to the 25th day of the cycle to give optimum secretion transformation of the endometrium, that is adequately prepared with an endogenous or exogenous oestrogen.

Prevention of hyperplasia of the endometrium in the post menopause
For each cycle of 28 days oestrogen therapy for the first 14 days oestrogen only is used and for the following 14 days in addition to oestrogen therapy once a day 1 or 2 tablets of dydrogesterone 10 mg are taken. With a dose of 2 tablets of dydrogesterone 10 mg per day the tablets must be taken in divided doses over the day. Withdrawal bleeding usually occurs while taking dydrogesterone.
Use of combined oestrogen/progesterone therapy in postmenopausal women should be limited to the lowest effective dose and the shortest time compatible with the treatment aims and risks for the individual woman and must be regularly assessed (see section 4.4).

There is no relevant use of dydrogesterone before the menarche. The safety and efficacy of dydrogesterone in adolescents aged from 12 to 18 years has not been established.

Method of administration
For oral use.
For administration of higher doses, the tablets should be taken evenly distributed over the day.

4.3 Contraindications

- Vaginal bleeding, where the cause has not been established.
- Treatment for luteal support as part of an Assisted Reproductive Technology (ART) treatment should be discontinued upon diagnosis of abortion or miscarriage.
- Presence of serious liver disorders, or serious liver disorders in the medical history until the liver function values have returned to normal.
- Contraindications for use of oestrogens in combination with progestogens such as dydrogesterone in combined therapy.
- Hypersensitivity to the active ingredient or to any of the excipients listed in Section 6.1.
- Known or suspected sex hormone dependent malignancies.

4.4 Special warnings and precautions for use

Before starting treatment with dydrogesterone because of disfunctional uterine bleeding an organic cause should be excluded.

Breakthrough bleeding and spotting may occur during the first months of treatment. If breakthrough bleeeding and spotting continue to occur when treatment has already been underway for some time, or continue when treatment is discontinued, the cause of this should be ascertained, if necessary by taking an endometrial biopsy to exclude malignancy of the endometrium.

If one of the following disorders occurs during use for the first time or gets worse, stopping the treatment should be considered.
- exceptionally severe headache, migraine or symptoms that may indicate cerebral ischemia.
- marked increase in blood pressure.
- occurrence of venous thromboembolism.

In cases of threatened or habitual miscarriage, the viability of the foetus should be ascertained, and it is necessary to monitor during treatment whether the pregnancy is still progressing and whether the embryo is still alive.

Conditions for which monitoring is necessary:
It is known that the following rarely occurring conditions may be affected by sex hormones and may arise or get worse during pregnancy or during the use of sex hormones: cholestatic icterus, herpes gestationis, severe pruritus, otosclerosis and porphyria.

Patients with a history of depression must be carefully monitored; if severe depression recurs, treatment with dydrogesterone must be stopped.

Other conditions
Patients with rare hereditary conditions such as galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not use this medicinal product.

Warnings and precautions regarding the use of Duphaston in the indication "to prevent endometrial hyperplasia in the postmenopausal period"
N.B. See also the warnings in the product information for the oestrogen preparation.

To treat postmenopausal symptoms, treatment with hormone replacement therapy (HRT) should only be started if these symptoms have an adverse effect on quality of life. The benefits and disadvantages of HRT should be carefully assessed in any case at least once a year, and the treatment should only be continued if the benefits outweigh the disadvantages.

Medical examination / follow-up
Before hormone replacement therapy (HRT) is started or when it is resumed after a break, a full medical history (including family medical history) must be taken. A physical examination (including a gynaecological and breast examination) must be carried out on the basis of the medical history, the contraindications and the warnings. Regular checks are recommended during treatment, at a frequency and of a type adapted to the individual. Women must be told what changes in their breasts they must consult their doctor about (see paragraph "Breast cancer" below).
Examination of the breasts, including imaging such as mammography, must be carried out in accordance with the current guidelines for screening, taking into account the medical situation of the individual woman.

Endometrial hyperplasia and carcinoma
Long-term use of oestrogens without progestogen supplement increases the risk of endometrial hyperplasia and endometrial carcinoma in women with an uterus. Depending on the duration and oestrogen dose the risk may be 2 to 12 times higher than in women who do not use oestrogen. After stopping oestrogen treatment this risk continues to exist for at least 10 years. This extra risk can be prevented by combining the oestrogen therapy with a progestogen such as dydrogesterone for at least 12 days per month/28 day cycle.

Breakthrough bleeding and spotting may occur during the first months of treatment. If breakthrough bleeding or spotting occur after considerable time on treatment or continue when treatment is discontinued, further investigation is indicated. This may mean taking an endometrial biopsy to exclude malignancy.

Breast cancer
All the available data indicate an increased risk of breast cancer if women take a combination of oestrogen and progestogen as HRT and possibly even if they take oestrogen-only as HRT. This risk depends on the duration of use.

Combined treatment with oestrogen and progestogen:
A randomised, placebo-controlled study (Women's Health Initiative Study (WHI)) and epidemiological studies have conistently shown that there is an increased risk of breast cancer after using for 3 years or longer. After discontinuing treatment this extra risk continues to exist for a maximum of 5 years. As a result of treatment with HRT, in particular combined oestrogen-progestogen treatment, the density of the mammography images increases, which may adversely affect the radiographic detection of breast cancer

Ovarian cancer
Ovarian cancer is much rarer than breast cancer. Epidemiological evidence from a large meta-analysis suggests a slightly increased risk in women taking oestrogen-only or combined oestrogen-progestogen HRT, which becomes apparent within 5 years of use and diminishes over time after stopping. Some other studies, including the WHI trial, suggest that use of combined HRTs may be associated with a similar, or slightly smaller risk (see section 4.8).

Venous thromboembolisms
Hormone replacement therapy is accompanied by a 1.3-3 times higher risk of a venous thromboembolism (VTE) occurring, i.e. of deep-vein thrombosis or pulmonary embolism. The chance of this occurring is greater during the first year of HRT treatment than thereafter.

Patients with known thrombophilia have an increased risk of developing VTE and HRT could further increase that risk. HRT is therefore contraindicated in these patients.

Generally recognised risk factors for the occurrence of VTE are the use of oestrogens, greater age, major surgery, long-term immobilisation, obesity (BMI > 30 kg/m2), pregnancy/postpartum period, systemic lupus erythematosus (SLE) and cancer. There is no consensus regarding the possible role of varicose veins in the occurrence of VTE.

In all post-operative patients, consideration should be given to taking measures after surgery to prevent VTE. If long-term immobilisation will occur after elective surgery it is recommended that HRT be discontinued 4-6 weeks beforehand. The treatment may only be resumed when the woman is fully mobile once again.

Women who themselves have no history of VTE but who have a first degree relative who has had thrombosis at a young age can be offered screening after the limitations of this have been clearly discussed (only a certain number of thrombophilic abnormalities can be determined by screening). If a thrombophilic deviation is found which has led to thrombosis in family members or if it relates to a serious abnormality (e.g. antithrombin, protein S or protein C deficiency, or a combination of defects) HRT is contraindicated.

In women who are already receiving anticoagulant therapy, the benefits and risks of HRT should be carefully assessed.

If a VTE develops after treatment has been started, administration of the medication should be discontinued. Patients must be informed that they should contact their doctor immediately if they experience symptoms that could be the result of thromboembolism (for example, painful swelling of a leg, sudden pain in the chest, shortness of breath).

Coronary heart disease (CHD)
Randomised controlled studies have produced no evidence that women with or without existing CHD who received HRT with oestrogen in combination with progestogen or oestrogen-only were protected against myocardial infarction.

Combined treatment with oestrogen and progestogen:

The relative risk of the occurrence of CHD during HRT with a combination of oestrogen and progestogen is slightly increased. Since the baseline absolute risk of the occurrence of CHD is greatly dependent on age, the number of extra cases of CHD as a result of the use of oestrogen-progestogen in women approaching menopause is very low, but that does increase as they get older.

Ischaemic (CVA)
Use of combined HRT or HRT with oestrogen-only is accompanied by a 1 to 1.5 times higher risk of ischaemic CVA. The relative risk does not change with ageing or with the time that has elapsed since the menopause. However, because the basic risk of CVA is highly dependent on age, the absolute risk will increase with ageing.

Excipients
This medicinal product contains lactose monohydrate.
Patients with rare hereditary conditions, such as galactose intolerance, Lapp-lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction

In vitro data that the main active metabolite 20α-dihydrodydrogesterone (DHD) and to less extent also dydrogesterone are primarlily metabolized by CYP3A4.

Substances that increase the clearance of progestogens (less efficacy due to enzyme induction) are for example: barbiturates, phenytoin, carbamazepine, primidone, rifampicin and HIV medication like ritonavir, neviparine and efavirenz, and possibly also products containing the herb St. John's Worth (hypericum perforatum).

An increase in the clearance of dydrogesterone may lead to a clinical decrease of effect and changes in the bleeding pattern.

Substances with variable effects on the clearance of progestogens:
Many combinations of HIV protease inhibitors and non-nucleoside reverse-transcriptase inhibitors, including combinations with HCV inhibitors could, if concomitantly administered with progestogens, raise or lower the plasma concentrations of the progestogen. In some cases the net effect of these changes could be clinically relevant.

For this reason the product information of HIV/HCV medicines should be consulted, if they are administered concomitantly, to determine potential interactions and any associated recommendations.

Substances that decrease clearance of progestogens (enzyme inhibitors):
The clinical relevance of possible interactions with enzyme inhibitors is unknown. Concomitant use of strong CYP3A4 inhibitors may raise the plasma concentrations of progestogens.

4.6 Fertility, pregnancy and lactation

Pregnancy
It is estimated that over 9 million women have already been exposed to dydrogesterone during pregnancy. To date there were no indications that the use of dydrogesterone during pregnancy has a harmful effect. In the literature a study is described in which it was found that the use of some progestogens can be accompanied by an increase in the risk of hypospadia occurring. However, because this has not been clearly confirmed to date in other studies, no final conclusion can be drawn about the effect of progestogens on the occurrence of hypospadia.

Clinical trials in which a limited number of women were treated with dydrogesterone in the first stage of pregnancy did not show that the risk is increased. To date no other epidemiological data are available.

The effects that were observed during non-clinical study into embryo-foetal and postnatal development corresponded with the pharmacological profile. Unwanted effects only occurred in case of exposure that was considerably higher than the maximum exposure in humans (see section 5.3).

Dydrogesterone may be administered during pregnancy if there is a clear indication for this.

Lactation
It is not known whether dydrogesterone is excreted in breast milk. No research has been done into the excretion of dydrogesterone in breast milk. Experiences with other progestogens indicate that progestogens and their metabolites are found in small quantities in breast milk. It is not known whether there is a risk for the child. Dydrogesterone should therefore not be used while breastfeeding.

Fertility
There are no data on the effect of dydrogesterone on fertility.

4.7 Effects on ability to drive and use machines

Dydrogesterone has a slight effect on ability to drive and to use machinery.

In rare cases dydrogesterone may cause somnolence and/or dizziness, in particular during the first couple of hours afer taking it. Caution is therefore advised when driving and operating machinery.

4.8 Undesirable effects

The adverse effects of this product most commonly reported in patients who were treated with drydrogesterone during clinical trials into indications without oestrogen treatment were vaginal haemorrhage, metrorraghia, painful/ sensitive breasts, nausea, vomiting, abdominal pain and migraine/headache.

The following adverse effects, with the frequencies indicated, were observed during clinical trials with dydrogesterone (n=3,483) for indications without oestrogen treatment in two company sponsored interventional clinical trials in luteal support as part of an ART treatment using dydrogestrone (n = 1,036) and from spontaneous reporting. Frequencies are based on the most conservative approach.

Organ class according to MedDRA database	**Very common ≥1/10**	**Common ≥1/100, <1/10**	**Uncommon ≥1/1,000, <1/100**	**Rare ≥1/10,000, <1/1,000**
Neoplasms, benign, malignant and non-specified (including cysts and polyps)				Growth of progestogen-dependent neoplasms (e.g. meningioma)*
Blood and lymphatic system disorders				Haemolytic anaemia*
Psychiatric disorders			Depressed mood	
Immune system disorders				Hypersensitivity
Nervous system disorders		Migraine/ headache	Dizziness	Somnolence

Gastrointestinal disorders		Nausea, vomiting, abdominal pain		
Hepatobiliary disorders			Disturbed liver function (with icterus, asthenia or malaise, and abdominal pain)	
Skin and subcutaneous tissue disorders			Allergic dermatitis (e.g. rash, pruritus, urticaria)	Angioedema*
Reproductive system and breast disorders	Vaginal haemorrhage	Disturbed menstruation (including metrorrhagia, menorrhagia, oligo-/amenorrhoea, dysmenorrhoea and irregular menstruation) Painful/ sensitive breasts		Swelling of the breasts
General disorders and administration site conditions				Oedema
Investigations			Weight gain	

* Adverse effects reported spontaneously but not observed during clincal trials are classified as "rare" in view of the fact that the upper limit of the 95% confidence interval of the estimated frequency is not higher than 3/x, where x=3,483 (the total number of patients in the clinical trials).

Adverse effects that may occur during treatment with oestrogen-progestogen (see also the section 4.4 and the product information for the oestrogen formulation):

- Breast cancer, endometrial hyperplasia, endometrial carcinoma, ovarian cancer
- Ovarian cancer: use of estrogen-only or combined estrogen-progestogen HRT has been associated with a slightly increased risk of having ovarian cancer diagnosed (see section 4.4). A meta-analysis from 52 epidemiological studies reported an increased risk of ovarian cancer in women currently using HRT compared to women who have never used HRT (RR 1.43, 95% CI 1.31-1.56). For women aged 50 to 54 years taking 5 years of HRT, this results in about 1 extra case per 2,000 users. In women aged 50 to 54 who are not taking HRT, about 2 women in 2,000 will be diagnosed with ovarian cancer over a 5-year period.
- Venous thromboembolism
- Myocardial infarction, coronary heart disease, ischemic CVA

Report 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 all suspected adverse reactions via the Netherlands Pharmacovigilance Centre Lareb, website www.lareb.nl.

4.9 Overdose

Symptoms
Dydrogesterone is a substance with very low toxicity. Nausea, vomiting, lethargy and dizziness are symptoms which may theoretically occur in the event of an overdose. There are no known cases in which an overdose of dydrogesterone led to harmful effects.

Treatment
Specific treatment is clearly not necessary. In case of overdose symptomatic treatment may be considered.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic category: urogenital system and sex hormones, ATC code: G03DB01

Mechanism of action
Dydrogesterone is a synthetic progesterone with an oral biological availability that causes a secretory phase of the endometrium in a uterus prepared by oestrogen. It gives protection against the increased risk of endometrial hyperplasia and/or endometrial carcinoma that is induced by oestrogens. Dydrogeserone has no oestrogenic, androgenic, anabolic and corticoid properties.

Dydrogesterone does not suppress ovulation. As a result, conception remains possible if dydrogesterone is used by women of child-bearing age.

In postmenopausal women with a uterus, oestrogen replacement leads to an increase in the risk of endometrial hyperplasia and endometrial carcinoma. The addition of a progestogen prevents this additonal risk.

Clinical efficacy and safety

Luteal support as part of an Assisted Reproductive Technology (ART) treatment:

A Double-Blind, Double-Dummy, Randomized, Multicentre Study Comparing the Efficacy, Safety, and Tolerability of Oral Dydrogesterone 30 mg daily versus Intravaginal Micronized Progesterone Capsules 600 mg daily for Luteal Support in In-Vitro Fertilization (LOTUS I).

A Randomized, Open-Label, Multicenter Study comparing the Efficacy, Safety and Tolerability of Oral Dydrogesterone 30 mg daily versus Crinone 8% intravaginal progesterone gel 90 mg daily for Luteal Support in In Vitro Fertilization (LOTUS II).

In these studies, non-inferiority of oral dydrogesterone compared to intravaginal micronized progesterone was achieved in terms of the presence of foetal heartbeats at 12 weeks' gestation (week 10).

In the studied patient population, the pregnancy rates at 12 weeks' gestation (10 weeks pregnancy) were 37.6% and 33.1% (LOTUS I), and 36.7% and 34.7% (LOTUS II). The difference in the pregnancy rate between the two groups was 4.7 (95% CI, -1.2; 10.6) (LOTUS I) and 2.0 (95% CI, -4.0; 8.0) (LOTUS II).

Within the safety sample of 1,029 women (LOTUS I) and 1.030 women (LOTUS II) with at least one dose of study medication administered, the incidence of the most frequently reported TEAEs was similar between the two treatment groups.

Due to the nature of the indication and the studied patient population, a number of early abortions and miscarriages can be expected. Especially until 12 weeks' gestation (pregnancy week 10), the expected pregnancy rate is about 35%.

The safety profile observed in both LOTUS studies is in line with the profile as known for dydrogesterone for the treatment target population and indication.

5.2 Pharmacokinetic properties

Absorption

After oral administration dydrogesterone is rapidly absorbed with a T_{max} of between 0.5 and 2.5 hours. The absolute biological availability of dydrogesterone (20 mg oral dose versus 7.8 mg intravenous infusion) is 28%.

The following tables gives the pharmacokinetic parameters of dydrogesterone (D) and 20α-dihydrodydrogesterone (DHD) after administration of a single dose of 10 mg dydrogesterone:

	D	DHD
C_{max} (ng/mL)	2.1	53.0
AUC_{inf} (ng·h/mL)	7.7	322.0

Distribution

After intravenous administration of dydrogesterone the steady-state distribution volume is around 1400 l. More than 90% of dydrogesterone and DHD are bound to plasma-proteins.

Metabolism

After oral administration dydrgesterone is metabolized quickly to DHD. In vitro data show that the main route of metabolism, the one that generates DHD, is catalyzed in human cytosol by aldo-keto reductase 1C (AKR 1C). Next to this cystolic metabolism, other metabolic routes by cytochrome P450 iso enzymes (CYPs) exist, this is nearly exclusively CYP 3A4, in which less important metabolites are formed. The concentration of the main active metabolite DHD shows a peak concentration approximately 1.5 hours after administration. The plasma concentrations of DHD are substantially higher than the related drug. The AUC and Cmax ratios of DHD and dydrogesterone are approximately 40 and 25. The mean terminal half-life of dydrogesterone and DHD varies from 5-7 and 14-17 hours respectively. A common feature of all characterized metabolites is the maintenance of the 4,6-diene-3-on configuration of the initial drug and the missing 17a-hydroxylation. This clarifies the lack of estrogen and androgen effects of dydrogesterone.

Elimination

After oral administration of labelled dydrogesterone on average 63% of the dose is excreted in the urine. The total plasma clearance is 6.4 l/minute. Within 72 hours the excretion is complete, DHD is present in the urine, mainly as the conjugated glucuronic acid.

Dependence of dose and time
The pharmacokinetics of single and multiple doses are linear in the oral dosage range from 2.5 to 10 mg. Comparison of the kinetics of single and multiple doses shows that the pharmacokinetics of dydrogesterone and DHD do not change as a result of repeated dosing. Steady state is reached after 3 days of treatment.

5.3 Preclinical safety data

Non-clinical data obtained during conventional investigation into the toxixcity of single and repeated doses, genotoxicity and the carcinogenic potential do not show any special risks for humans.
Research into the toxic effects on the reproduction of rats shows for high doses (>80 times the human exposure) an increased incidence of erect nipples (during days 11-19 of the lactation period) and of hypospadia in male rats. The clinical relevance of these observations is not known.

The limited data on safety in animals indicate that dydrogesterone has an extending effect on delivery, which corresponds with the progestogenic action.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Composition of the tablet:
Lactose monohydrate
Hypromellose
Maize starch
Silicon dioxide
Magnesium stearate

Composition of the coating:
Hypromellose
Macrogol 400
Titanium dioxide (E171)

6.2 Cases of incompatibility

None

6.3 Shelf life

5 years

6.4 Special precautions for storage

There are no special storage conditions for this medicinal product.

6.5 Nature and contents of container

The tablets are packaged in blister strips of aluminium foil and PVC.
Duphaston 10 is available in cartons with 1, 2 or 3 blister strips each with 10 tablets, 1 blister strip with 20 tablets or 3 blister strips each with 14 tablets of 10 mg.

Not all listed pack sizes are marketed.

6.6 Special precautions for disposal

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

7. MARKETING AUTHORISATION HOLDER

Abbott B.V.
Wegalaan 9
2132 JD Hoofddorp
The Netherlands

8. MARKETING AUTHORISATION NUMBER

Duphaston 10 is authorised as RVG 05619.

9. DATE OF FIRST GRANTING OF THE AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first granting of the authorisation: 31 May 1968
Date of the last renewal: 31 May 2013

10. DATE OF REVISION OF THE TEXT

Last partial revision regarding sections 4.8 and 5.1: 27 November 2019