SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Revoke-1.5*

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

The tablet contains 1.5 mg levonorgestrel.

Each tablet also contains 154 mg of lactose monohydrate.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

Round, white to off-white, uncoated flat tablets debossed '145' on one side and the other side plain.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Emergency contraception within 72 hours of unprotected sexual intercourse or failure of a contraceptive method.

4.2 Posology and method of administration

For oral administration, the treatment course comprises a single tablet.

The highest efficacy is achieved if the tablet is taken as soon as possible (and no later than 72 hours) after unprotected intercourse.

If vomiting occurs within two hours of taking the tablet, another tablet should be taken immediately. If repeated vomiting occurs, the tablet may be administered vaginally.

Revoke-1.5 can be used at any time during the menstrual cycle unless menstrual bleeding is overdue.

After using emergency contraception it is recommended to use a local barrier method (condom, cervical cap) until the next menstrual period starts. The use of Revoke-1.5 does not contraindicate the continuation of regular hormonal contraception.

Revoke-1.5 is not recommended for use by young women aged under 16 years without medical supervision.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Emergency contraception is not effective in terminating an existing pregnancy.

Emergency contraception is an occasional method. It should **not** replace a regular contraceptive method.

Emergency contraception does not prevent a pregnancy in every instance.

Efficacy appears to decline with time (see section 5.1).

If there is uncertainty about the timing of the unprotected intercourse or if the woman has had unprotected intercourse more than 72 hours earlier in the same menstrual cycle, conception may

* Trade names are not prequalified by WHO. This is the national medicines regulatory authority's (NMRA) responsibility. Throughout this WHOPAR the proprietary name is given as an example only.

have occurred. Treatment with Revoke-1.5 following the second act of intercourse may therefore be ineffective in preventing pregnancy. If menstrual periods are delayed by more than 5 days or abnormal bleeding occurs at the expected date of menstrual periods or pregnancy is suspected for any other reason, pregnancy should be ruled out.

If pregnancy occurs after treatment with Revoke-1.5, the possibility of an ectopic pregnancy should be considered, especially in women in whom severe abdominal pain or fainting occurs, or if there is a history of ectopic pregnancy, Fallopian tube surgery or pelvic inflammatory disease. The absolute risk of ectopic pregnancy is likely to be low, as levonorgestrel prevents ovulation and fertilisation. Ectopic pregnancy may continue despite uterine bleeding. Therefore, Revoke-1.5 is not recommended for women at risk of ectopic pregnancy (history of salpingitis or of ectopic pregnancy).

Revoke-1.5 is not recommended in patients with severe hepatic dysfunction.

Severe malabsorption syndromes, such as Crohn's disease, might impair the efficacy of Revoke-1.5.

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

After taking Revoke-1.5, menstrual periods are usually normal and occur at the expected date. They can sometimes occur earlier or later than expected by a few days. Women should be advised to see a health care provider to initiate or adopt a method of regular contraception. If no withdrawal bleed occurs in the next pill-free period following the use of Revoke-1.5 after regular hormonal contraception, pregnancy should be ruled out.

Repeated administration within a menstrual cycle is not advisable because of the possibility of disturbing the cycle.

Any regular contraceptive method can be started immediately after the use of Revoke-1.5 emergency contraceptive pills. If the woman starts a hormonal contraceptive:

- she needs to abstain from sexual intercourse or use barrier contraception for 7 days;
- she should be advised to have a pregnancy test if she does not have a withdrawal bleed within 3 weeks.

Revoke-1.5 is not as effective as a conventional regular method of contraception and is suitable only as an emergency measure. Women who present for repeated courses of emergency contraception should be advised to consider long-term methods of contraception.

Use of emergency contraception does not replace the necessary precautions against sexually transmitted diseases.

4.5 Interaction with other medicinal products and other forms of interaction

The metabolism of levonorgestrel is enhanced by concomitant use of liver enzyme inducers.

Drugs suspected of having the capacity to reduce the efficacy of levonorgestrel include barbiturates (including primidone), phenytoin, carbamazepine, herbal medicines containing St. John's wort (*Hypericum perforatum*), rifampicin, ritonavir, rifabutin, bosentan, felbamate, oxcarbazepine and griseofulvin.

Significant changes (increase or decrease) in the plasma levels of the progestogen have been noted in some cases of co-administration with HIV protease inhibitors or with non-nucleoside reverse transcriptase inhibitors. The potential interaction may require close monitoring, alteration of drug dosage or timing of administration.

Medicines containing levonorgestrel may increase the risk of ciclosporin toxicity due to possible inhibition of ciclosporin metabolism.

4.6 Pregnancy and lactation

Pregnancy

REVOKE - 1.5 should not be given to pregnant women. It will not interrupt the pregnancy.

In case of failure of this emergency contraception and developing pregnancy, epidemiological studies indicate no adverse effects of progestogens on the fetus.There are no clinical data on the potential consequences if doses greater than 1.5 mg levonorgestrel are taken (see section 5.3.).

Lactation

Levonorgestrel is secreted into breast milk. Potential exposure of an infant to levonorgestrel can be reduced if the breast-feeding woman takes the tablets immediately after feeding and avoids nursing following each REVOKE - 1.5 administration.

Fertility

Clinical experience reveal no effect on fertility after use of levonorgestrel. Non-clinical studies show no evidence of adverse effects in animals (see section 5.3)

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

The most common adverse events (>10%) in the clinical trial for women receiving levonorgestrel 0.75 mg included nausea (23%), abdominal pain (18%), fatigue (17%), headache (17%), dizziness (11%), breast tenderness (11%) and menstrual changes (26%).

The table below shows those adverse events that occurred in ≥ 5% of levonorgestrel 0.75 mg users.

Table 3 Adverse events in ≥ 5% of women, by frequency

Adverse events	Levonorgestrel 0.75 mg (n = 977)
Nausea	23.1%
Abdominal pain	17.6%
Fatigue	16.9%
Headache	16.8%
Heavier menstrual bleeding	13.8%
Lighter menstrual bleeding	12.5%
Dizziness	11.2%
Breast tenderness	10.7%
Vomiting	5.6%
Diarrhea	5.0%

Bleeding patterns may be temporarily disturbed, but most women will have their next menstrual period within 7 days of the expected time.

If the next menstrual period is more than 5 days overdue pregnancy should be ruled out.

The following very rare (less than 1 in 10 000) additional side effects have been reported in post-marketing surveillance:

Gastrointestinal disorders	abdominal pain
Skin and subcutaneous tissue disorders	rash, urticarial, pruritus
Reproductive system and breast disorders	pelvic pain, dysmenorrhea

General disorders and administration-site conditions face oedema

4.9 Overdose

Serious undesirable effects have not been reported following acute ingestion of large doses of oral contraceptives. Overdose may cause nausea and vomiting; withdrawal bleeding may occur. There are no specific antidotes and treatment should be symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Progestogens, ATC code: G03AD01

The precise mode of action of REVOKE - 1.5 is not known.

At the recommended regimen, levonorgestrel is thought to work mainly by preventing ovulation and fertilisation if the intercourse has taken place in the preovulatory phase, when the likelihood of fertilisation is the highest. It may also cause endometrial changes that discourage implantation. It is not effective once implantation has begun.

Efficacy: Results from a randomised, double-blind clinical study conducted in 2001 (Lancet 2002; 360: 1803-1810) showed that a 1.5-mg single dose of levonorgestrel (taken within 72 hours of unprotected sex) prevented 84% of expected pregnancies (compared with 79% when two 750-microgram tablets were taken 12 hours apart).

It is therefore, recommended that REVOKE - 1.5 tablet is taken as soon as possible (and no later than 72 hours) after unprotected intercourse.

At the recommended regimen, levonorgestrel is not expected to significantly modify blood clotting factors, or lipid and carbohydrate metabolism.

Safety: Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

A double-blind, controlled clinical trial in 1,955 evaluable women compared the efficacy and safety of Levonorgestrel (one 0.75 mg tablet of levonorgestrel taken within 72 hours of unprotected intercourse, and one tablet taken 12 hours later) to the Yuzpe regimen (two tablets each containing 250 micrograms levonorgestrel and 50 micrograms ethinylestradiol, taken within 72 hours of intercourse, and two tablets taken 12 hours later).

5.2 Pharmacokinetic properties

Pharmacokinetic parameters of REVOKE - 1.5 (levonorgestrel test formulation) and the reference product are shown in the table below.

Pharmacokinetic Parameter	Test formulation (T) arithmetic mean ± SD (*)	Reference (R) arithmetic mean ± SD (*)	log-transformed parameters	
			Ratio T/R (%)	Conventional 90% CI (ANOVAlog)
t_{max} (hour)	2.13 (1 - 4)	2.13 (1 - 4)	–	–
C_{max} (ng/ml)	20.1 ± 6.6 (19.3)	17.5 ± 7.1 (16.3)	118.0	111.6 – 124.9
AUC_{0-72}	318 ± 138	312 ± 153	105.2	98.5 – 112.3

(ng·hour/ml)	(289)	(275)		

* geometric mean

Levonorgestrel is not excreted as metabolites. Levonorgestrel metabolites are excreted in about equal proportions in urine and faeces. The biotransformation follows the known pathways of steroid metabolism, the levonorgestrel is hydroxylated in the liver and the metabolites are excreted as glucuronide conjugates.

No pharmacologically active metabolites are known.

Levonorgestrel is bound to serum albumin and sex hormone binding globulin (SHBG). Only about 1.5% of the total serum levels are present as free steroid, but 65% are specifically bound to SHBG. The absolute bioavailability of levonorgestrel was determined to be almost 100% of the dose administered.

About 0.1% of the maternal dose can be transferred via milk to the nursed infant.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans, beyond the information included in other sections of the SmPC. Animal experiments with levonorgestrel have shown virilisation of female fetuses at high doses

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Povidone
Lactose monohydrate
Maize starch
Colloidal silicon dioxide
Magnesium Stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 30°C. Protect from light. Store the tablet in the blister in provided carton.

6.5 Nature and contents of container

PVC/PVdC-Aluminium blister, containing 1 tablet per blister card. One blister card per carton.

6.6 Special precautions for disposal and other handling

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

7. SUPPLIER

Mylan Laboratories Limited
Plot No.564/A/22, Road No.92, Jubilee Hills
Hyderabad, Telangana – 500033, India

8. WHO REFERENCE NUMBER (PREQUALIFICATION PROGRAMME)

RH031

9. DATE OF FIRST PREQUALIFICATION/LAST RENEWAL

21 October 2013

10. DATE OF REVISION OF THE TEXT

September 2014. Section 7 updated in February 2017.

References

Selected Practice Recommendations for Contraceptive Use, Second Edition 2004
World Health Organization
http://whqlibdoc.who.int/publications/2004/9241562846.pdf?ua=1

2008 Update of the above guideline, WHO
http://whqlibdoc.who.int/hq/2008/WHO_RHR_08.17_eng.pdf?ua=1

Medical Eligibility Criteria for Contraceptive Use, Fourth Edition 2010
World Health Organization
http://www.who.int/reproductivehealth/publications/family_planning/9789241563888/en/

US Selected Practice Recommendations for Contraceptive Use, 2013
US Centers for Disease Control and Prevention
MMWR , Recommendations and Reports, vol 62, No. 5, June 21, 2013
http://www.cdc.gov/mmwr/pdf/rr/rr6205.p

1.3.2 Labelling (outer and inner labels)

Labels (inner label and outer carton) for Levonorgestrel Tablets 1.5 mg is enclosed overleaf.

1.3.3 Patient Information Leaflet (PIL)

Patient information leaflet for Levonorgestrel Tablets 1.5 mg is enclosed overleaf.

PATIENT INFORMATION LEAFLET: INFORMATION FOR THE USER

PATIENT INFORMATION LEAFLET: INFORMATION FOR THE USER

Revoke-1.5*

(Levonorgestrel 1.5 mg tablets)

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, health care provider or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their condition is the same as yours.
- If any of the side effects become serious, or if you notice any side effects not listed in this leaflet, tell your health care provider or pharmacist.

What is in this leaflet:

1. WHAT REVOKE-1.5 IS AND WHAT IT IS USED FOR

Revoke-1.5 contains a synthetic hormone-like substance, levonorgestrel.

Revoke-1.5 prevents about 85% of expected pregnancies when the tablet is taken within 72 hours (3 days) of unprotected sex. Revoke-1.5 will not prevent pregnancy in every instance. The tablet is more effective the sooner after unprotected sex it is taken.

Revoke-1.5 is thought to work by:
- stopping your ovaries from releasing an egg;
- preventing sperm from fertilising any egg that may have been released already; or
- stopping a fertilised egg from attaching itself to your womb lining.

So Revoke-1.5 stops pregnancy before it is established. It does not work if you are already pregnant.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE REVOKE - 1.5

Before you take this medicine, your health care provider may check that you are not already pregnant.

You can use Revoke-1.5 at any time during your menstrual cycle, except if your period is late. If your period is late, you should tell your health care provider.

Do not take REVOKE - 1.5
- if you are allergic (hypersensitive) to levonorgestrel or to any of the other ingredients of Revoke-1.5. (listed in section 6)

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Warnings and precautions
You may already be pregnant if:
- your period is more than 5 days late or if you have unusual bleeding when your next period is due
- you have had unprotected sex more than 72 hours ago, and since your last period

You should ask your health care provider for advice about emergency contraception if you
- have a disease of your small bowel (such as Crohn's disease) that interferes with the digestion of your food;
- have severe liver problems;
- have ever had an ectopic pregnancy (where the baby develops outside the womb);
- have ever had salpingits (inflammation of the Fallopian tubes)
- are taking any of the medicines listed below, as these medicines may prevent Revoke-1.5 from working properly:
    - barbiturates and other medicines used to treat epilepsy (for example, primidone, phenytoin, and carbamazepine);
    - medicines used to treat tuberculosis (for example, rifampicin, rifabutin);
    - a treatment for HIV infection (for example, ritonavir);
    - a medicine used to treat fungal infections (for example, griseofulvin);
    - herbal remedies containing St John's wort *(Hypericum perforatum)*;
    - ciclosporin, a medicine used to suppress the immune system

If any of these apply to you, Revoke-1.5 may not be suitable for you, or other types of emergency contraception may be better for you.

If you are worried about sexually transmitted diseases
This medicine will not protect against sexually transmitted diseases, only condoms can do this. Ask your health care provider or family planning clinic for advice if you are worried about this.

Children
Levonorgestrel 1.5 mg is not indicated to be used before menarche.

Taking other medicines
Tell your health care provider if you are taking, have recently taken, or might take, any other medicines including medicines obtained without a prescription. You should tell your health care provider if you are taking any of the medicines listed in the section 'Warnings and precautions" above.

Pregnancy and breast-feeding
Pregnancy
You should not take this medicine if you are already pregnant. If you have had unprotected sex which was more than 72 hours ago, and since your last period, you may already be pregnant and the treatment won't work. If your last period was more than 5 days late or was unusually light or unusually heavy or you suspect that you might be pregnant (feeling sick, vomiting, breast tenderness etc.), you should check with your healthcare provider that you are not already pregnant.

If you do become pregnant even after taking this medicine, it is important that you see your health care provider. There is no evidence that Revoke-1.5 will harm an unborn baby, but your health care provider may want to check that the pregnancy is not ectopic (where the baby develops somewhere outside the womb). This is especially important if you develop severe abdominal pain or fainting after taking Revoke-1.5, or if you have previously had an ectopic pregnancy, Fallopian tube surgery or pelvic inflammatory disease.

Breast-feeding
Very small amounts of the active ingredient of Revoke-1.5 may appear in your breast milk. This is not thought to be harmful to the baby, but if you are worried you can take your tablet immediately after

breastfeeding. In this way you are taking the tablet well before the next feed and reducing the amount of active ingredient your baby may take in with the breast milk.

Important information about some of the ingredients of Revoke-1.5
Revoke-1.5 contains lactose. If you know that you cannot tolerate some sugars, contact your health care provider before taking this medicine.

3. HOW TO TAKE REVOKE - 1.5

- Take the tablet **as soon as possible** (but no later than 72 hours) after you have had unprotected sex. Swallow the tablet whole, with water if necessary. Do not delay taking the tablet. The tablet works better the sooner you take it after having unprotected sex.

How often can you use REVOKE - 1.5?
You should only use Revoke-1.5 in an emergency and not as a regular method of contraception. If REVOKE - 1.5 is used more than once in a menstrual cycle, it is more likely to upset your menstrual cycle (period).

Revoke-1.5 does not work as well as regular methods of contraception. If you need repeated courses of emergency contraception, you should consider long-term methods of contraception.

If you take more Revoke-1.5 than you should (overdose)
Although there have been no reports of serious harm from taking too many tablets at once, you may feel sick, vomit, or have vaginal bleeding.

What to do if you are sick (vomit)

- If you are sick within 2 hours of taking the tablet, you will need to take another tablet. Talk to your pharmacist, doctor, nurse, health care provider or family planning clinic immediately for advice and to obtain another tablet.
- If you continue to vomit, you may insert the tablet in your vagina. You will need to obtain any extra dose. You should also contact your health care provider, as the tablets may not have worked properly.

After you have taken Revoke-1.5
After you have taken **Revoke-**1.5, if you want to have sex, and are not using the contraceptive pill, you should use condoms or a cap plus spermicide. This is because **Revoke-**1.5 won't work if you have unprotected sex again, before your next period is due.

After you have taken Revoke-1.5, if your next period is more than 5 days late or is unusually light or unusually heavy, you should contact your health care provider as soon as possible. If you do become pregnant even after taking this medicine, it is important that you see your health care provider.

Your health care provider can also tell you about longer-term methods of contraception which are more effective in preventing you from getting pregnant.

If you continue to use regular hormonal contraception such as the contraceptive pill and you do not have a bleed in your pill-free period, see your health care provider to make sure you are not pregnant.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Revoke-1.5 can cause side effects, but not everybody gets them.

The most common side effects are nausea, abdominal pain, fatigue, headache, menstrual changes and irregular bleeding until your next period. Dizziness, breast tenderness, vomiting and diarrhoea may also occur. Very rare side effects (which occur in fewer than 1 in every 10 000 women who use the product) include abdominal pain, rash, itching, dysmenorrhea (painful period) and puffiness of the face.

If you think that this medicine affects you in a way that is not mentioned above, tell your healthcare provider.

5. HOW TO STORE REVOKE - 1.5

Do not store above 30°C. Protect from light. Store the tablet in the blister in provided carton.
Keep this medicine out of the sight and reach of children.

Do not use Revoke-1.5 after the expiry date stated on the label. The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Revoke-1.5 contains

The active substance is 1.5 mg levonorgestrel in each tablet.
The other ingredients are lactose monohydrate, maize starch, povidone, colloidal silicon dioxide, magnesium stearate.

What Revoke-1.5 look like and contents of the pack

Round, white to off-white, uncoated flat tablets debossed ‘145’ on one side and the other side plain.

Packaging:
PVC/PVdC-Aluminium blister, containing 1 tablet per blister card. One blister card per carton.

If you are not sure about anything or you have any questions, please ask your pharmacist, your health care provider or visit a family planning clinic.

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