SUMMARY OF PRODUCT CHARACTERISTICS

NAME OF THE MEDICINAL PRODUCT : Pronta 1

1. 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.

2. PHARMACEUTICAL FORM

Tablet:

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

3. CLINICAL PARTICULARS

3.1. Therapeutic indications

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

3.2. 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 72hours) 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.

Pronta 1 can be used at any time during the menstrual cycle unless menstrual bleeding isoverdue.

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 Pronta 1 does not contraindicate the continuation of regular hormonal contraception.

Pronta 1 is not recommended for use by young women aged under 16 years without medicalsupervision.

3.3. Contraindications

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

3.4. 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 contraceptivemethod.

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

have occurred. Treatment with Pronta 1 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 forany other reason, pregnancy should be ruled out.

If pregnancy occurs after treatment with Pronta 1, the possibility of an ectopic pregnancy shouldbe 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, Pronta 1 is not recommended for women at risk of ectopic pregnancy (history of salpingitis or of ectopicpregnancy).

Pronta 1 is not recommended in patients with severe hepatic dysfunction.

Severe malabsorption syndromes, such as Crohn's disease, might impair the efficacy of Pronta1.

After taking Pronta 1, menstrual periods are usually normal and occur at the expected date. Theycan 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 withdrawalbleed occurs in the next pill-free period following the use of Pronta 1 after regular hormonal contraception, pregnancy should be ruled out.

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

Any regular contraceptive method can be started immediately after the use of Pronta 1 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 within3 weeks.

Pronta 1 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 sexuallytransmitted diseases.

3.5. 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, alterationof drug dosage or timing of administration.

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

3.6. Pregnancy and lactation

Pregnancy

Pronta 1 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 Pronta 1 administration.

Fertility

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

3.7. Effects on ability to drive and use machines

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

3.8. 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 mgusers.

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 menstrualperiod 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.

4. PHARMACOLOGICAL PROPERTIES

4.1. Pharmacodynamic properties

Pharmacotherapeutic group: Progestogens, ATC code: G03AD01

The precise mode of action of Pronta 1 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 Pronta 1 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).

4.2. Pharmacokinetic properties

Pharmacokinetic parameters of Pronta 1 (levonorgestrel test formulation) and the reference product are shown in the table below.

Pharmacokinetic Parameter	Test formulation	Reference	log-transformed parameters

	n(T) arithmetic mean ± SD(*)	(R) arithmetic mean ± SD(*)	Ratio T/R (%)	Conventional 90% CI (ANOVA log)
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} (ng·hour/ml)	318 ± 138 (289)	312 ± 153 (275)	105.2	98.5 – 112.3
* 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.

4.3.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 femalefetuses at high doses

5. PHARMACEUTICAL PARTICULARS

5.1. List of excipients

Povidone
Lactose monohydrate Maize starch
Colloidal silicon dioxide Magnesium Stearate

5.2. Incompatibilities

Not applicable.

5.3. Shelf life

36 months

5.4. Special precautions for storage

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

5.5. Nature and contents of container

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

5.6. Special precautions for disposal and other handling

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

6. SUPPLIER

Mylan Laboratories Limited
Plot No.564/A/22, Road No.92, Jubilee Hills
Hyderabad, Telangana – 500096, **India.**

7. MARKETING AUTHORIZATION REFERENCE NUMBER:

TAN 21 HM 0260

8. DATE OF FIRST PREQUALIFICATION/LAST RENEWAL

03rd June, 2021

9. DATE OF REVISION OF THE TEXT

September 2014. Section 7 updated in February 2017.