SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF MEDICINAL PRODUCT

- **Brand Name** : LYDIA POSTPIL
- **Generic Name** : Levonorgestrel Tablets 1.5 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Label Claim:

Each uncoated tablet contains:

Levonorgestrel Ph. Eur……1.5 mg

Excipients…….....q.s.

Qualitative-Quantitative formula:

Sr. No.	Ingredients	Function	Quality reference	Qty./ tablet (mg)	Overages
1.	Levonorgestrel* {Levonorgestrel, Micro 20(THF/methanol, SO)}	API	Ph. Eur	1.5	--
2.	Lactose monohydrate**	Diluent	Ph. Eur/USP NF	120.0	--
3.	Maize Starch (Maize Starch B Pharma Grade)	Diluent and Disintegrant	Ph. Eur/USP NF	67.0	--
4.	Potato starch {Potato Starch Supra NP (Pharma Grade)}	Binder	Ph. Eur/USP NF	1.5	--
5.	Purified water***	Granulating liquid	In House	q. s.	--
6.	Maize Starch (Maize Starch B Pharma Grade)	Disintegrant	Ph. Eur/USP NF	5.00	--
7.	Colloidal silicon Dioxide (Aerosil 200)	Anti-adherent	Ph. Eur/USP NF	1.0	--
8.	Talc (Talc Luzenac Pharma)	Glidant	Ph. Eur/USP NF	2.0	--
9	Magnesium Stearate (Synpro Magnesium Stearate VG EP)	Lubricant	Ph. Eur/USP NF	2.00	--
			Total weight	**200.0**	

*Quantity to be calculated based on the actual assay on dried/anhydrous basis as per respective COA.
**Quantity to be compensated for the actual quantity of respective API.
***Used as a solvent and will not be present in the final product, except traces.

3. PHARMACEUTICAL FORM

Tablets.

White to off white, round bevel edged, flat faced tablets debossed with "J06" on one side and plain on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication

Levonorgestrel tablet 1.5mg is a progestin-only emergency contraceptive indicated for prevention of pregnancy following unprotected intercourse or a known or suspected contraceptive failure. To obtain optimal efficacy, the tablet should be taken as soon as possible within 72 hours of intercourse.

Levonorgestrel tablet 1.5mg is available only by prescription for women younger than age 17 years, and available over the counter for women of age 17 years and older.

Levonorgestrel tablet 1.5mg is not indicated for routine use as a contraceptive.

4.2 Posology and method of Administration

For oral administration: One tablet should be taken as soon as possible, preferably within 12 hours and no later than 72 hours after unprotected intercourse or a known or suspected contraceptive failure. Efficacy is better if Levonorgestrel tablet is taken as directed as soon as possible after unprotected intercourse.

Levonorgestrel tablet 1.5mg 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 barrier method (e.g. condom, diaphragm or cap) until the next menstrual period starts. The use of Levonorgestrel tablet 1.5mg does not contraindicate the continuation of regular hormonal contraception.

If vomiting occurs within two hours of taking the tablet another tablet should be taken immediately. The patient should contact her doctor, family planning clinic or pharmacist for advice and another tablet.

4.3 Contraindication

Levonorgestrel tablet is contraindicated for use in the case of known or suspected pregnancy and hypersensitivity to the active substance levonorgestrel or any of the excipients.

4.4 Special Warnings and Precautions for Use

Ectopic Pregnancy:

Ectopic pregnancies account for approximately 2% of all reported pregnancies. Up to 10% of pregnancies reported in clinical studies of routine use of progestin-only contraceptives are ectopic. A history of ectopic pregnancy is not a contraindication to use of this emergency contraceptive method. Healthcare providers, however, should consider the possibility of an ectopic pregnancy in women who become pregnant or complain of lower abdominal pain after taking the tablet. A follow-up physical or pelvic examination is recommended if there is any doubt concerning the general health or pregnancy status of any woman after taking the Levonorgestrel tablet.

Existing Pregnancy:

Levonorgestrel tablet is not effective in terminating an existing pregnancy.

Effects on Menses:

Some women may experience spotting a few days after taking Levonorgestrel tablet. Menstrual bleeding patterns are often irregular among women using progestin-only oral contraceptives and women using Levonorgestrel for postcoital & emergency contraception. If there is a delay in the onset of expected menses beyond one week, consider the possibility of pregnancy.

STI/HIV:

Levonorgestrel tablet does not protect against HIV infection (AIDS) or other sexually transmitted infections (STIs).

Physical Examination and Follow-up:

A physical examination is not required prior to prescribing Levonorgestrel tablet. A follow-up physical or pelvic examination is recommended if there is any doubt concerning the general health or pregnancy status of any woman after taking the tablet.

Fertility Following Discontinuation:

A rapid return of fertility is likely following treatment with Levonorgestrel tablet for emergency contraception; therefore, routine contraception should be continued or initiated as soon as possible following use of the tablet to ensure ongoing prevention of pregnancy.

4.5 Interactions with other medicaments and other forms of interaction

Drugs or herbal products that induce enzymes, including CYP3A4 that metabolize progestins may decrease the plasma concentrations of progestins, and may decrease the effectiveness of progestin-only tablets. Some drugs or herbal products that may decrease the effectiveness of progestin-only tablet include Barbiturates, Bosentan, Carbamazepine, Felbamate, Griseofulvin, Oxcarbazepine, Phenytoin, Rifampin, St. John's wort, Topiramate.

Significant changes (increase or decrease) in the plasma levels of the progestin have been noted in some cases of co-administration with HIV protease inhibitors or with non-nucleoside reverse transcriptase inhibitors.

Consult the labeling of all concurrently used drugs to obtain further information about interactions with progestin-only pills or the potential for enzyme alterations.

4.6 Pregnancy and Lactation

Pregnancy

Levonorgestrel tablet 1.5mg should not be given to pregnant women. It will not interrupt a pregnancy. In the case of continued pregnancy, limited epidemiological data indicate no

adverse effects on the foetus but there are no clinical data on the potential consequences if doses greater than 1.5 mg of levonorgestrel are taken.

Lactation

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

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable Effects

As per a randomized, double-blinded multicenter clinical trial performed to evaluate safety of Levonorgestrel tablet 1.5mg, all women who had received at least one dose of study medication were included in the safety analysis: 1379 women in the Levonorgestrel tablet 1.5 mg (once daily dosing). The mean age of women given Levonorgestrel tablet was 27 years. The racial demographic of those enrolled was 54% Chinese, 12% Other Asian or Black, and 34% were Caucasian in the treatment group. 1.6% of women in the Levonorgestrel 1.5 mg tablet group were lost to follow-up. The most common adverse events (>10%) in the clinical trial for women receiving Levonorgestrel 1.5 mg tablet included heavier menstrual bleeding (30.9%), nausea (13.7%), lower abdominal pain(13.3%), fatigue (13.3%) & headache (10.3%).

Adverse events that were reported in > 4% of Levonorgestrel tablet users are enlisted below.

Most common adverse events	Levonorgestrel tablet [N=1359 (%)]
Heavier menstrual bleeding	30.9
Nausea	13.7
Lower abdominal pain	13.3
Fatigue	13.3

Headache	10.3
Dizziness	9.6
Breast tenderness	8.2
Delay of menses (> 7 days)	4.5

4.9 Overdose

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacokinetic Properties

Absorption

Following a single dose administration of Levonorgestrel tablet in 30 women under fasting conditions, maximum plasma concentrations of Levonorgestrel of 19.1 ng/ml were reached at 1.7 hours.

Effect of Food: The effect of food on the rate and the extent of Levonorgestrel absorption following single oral administration of Levonorgestrel tablet has not been evaluated.

Distribution

The apparent volume of distribution of Levonorgestrel is reported to be approximately 1.8 L/kg. It is about 97.5 to 99% protein-bound, principally to sex hormone binding globulin (SHBG) and to a lesser extent, serum albumin.

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.

Metabolism

Following absorption, Levonorgestrel is conjugated at the 17β-OH position to form sulfate conjugates and, to a lesser extent, glucuronide conjugates in plasma. Significant amounts of

conjugated and unconjugated 3α, 5β-tetrahydrolevonorgestrel are also present in plasma, along with much smaller amounts of 3α, 5αtetrahydrolevonorgestrel and 16βhydroxylevonorgestrel. Levonorgestrel and its phase I metabolites are excreted primarily as glucuronide conjugates. Metabolic clearance rates may differ among individuals by several-fold, and this may account in part for the wide variation observed in Levonorgestrel concentrations among users. No pharmacologically active metabolites are known.

Excretion

Levonorgestrel is not excreted in unchanged form but as metabolites. About 45% of levonorgestrel and its metabolites are excreted in the urine and about 32% are excreted in feces, mostly as glucuronide conjugates.

Specific Populations

- **Pediatric**: This product is not intended for use in the premenarcheal population, and pharmacokinetic data are not available for this population.
- **Geriatric**: This product is not intended for use in postmenopausal women, and pharmacokinetic data are not available for this population.
- **Race**: No formal studies have evaluated the effect of race.
- **Hepatic Impairment:** No formal studies were conducted to evaluate the effect of hepatic disease on the disposition of Levonorgestrel tablet.
- **Renal Impairment:** No formal studies were conducted to evaluate the effect of renal disease on the disposition of Levonorgestrel tablet.

5.2 Pharmacodynamic Properties

Pharmacotherapeutic group: Sex hormones and modulators of the genital system, Emergency contraceptives; ATC code: G03AD01

The precise mode of action of Levonorgestrel tablets 1.5 mg is not known.

At the recommended regimen, levonorgestrel is thought to work mainly by preventing ovulation and fertilization (by altering tubal transport of sperm and/or ova), if intercourse has

taken place in the preovulatory phase, when the likelihood of fertilization is the highest. It may also cause endometrial changes that discourage implantation. Levonorgestrel tablets 1.5 mg is not effective once the process of implantation has begun.

5.3 Preclinical Safety Data

Levonorgestrel is a well-established progestogen with anti-estrogenic activity. The safety profile following systemic administration is well documented and reveals no special concerns for use beyond that already listed in this text.

Animal experiments with levonorgestrel have shown virilisation of female fetuses at high doses. In acute toxicity studies performed in mice and rats levonorgestrel induced a decrease of body weight and dermatitis-like (non-irritative or non-allergic) changes on the skin. In repeat dose toxicity studies performed in mice, rats and rabbits, there were no overt signs of toxicity and no target organs or functions were identified other than the reproductive system.

Carcinogenicity: There is no evidence of increased risk of cancer with short-term use of progestins. There was no increase in tumorgenicity following administration of levonorgestrel to rats for 2 years at approximately 5 µg/day, to dogs for 7 years at up to 0.125 mg/kg/day, or to rhesus monkeys for 10 years at up to 250 µg/kg/day. In another 7 year dog study, administration of levonorgestrel at 0.5 mg/kg/day did increase the number of mammary adenomas in treated dogs compared to controls. There were no malignancies.

Genotoxicity: Levonorgestrel was not found to be mutagenic or genotoxic in the Ames Assay, in vitro mammalian culture assays utilizing mouse lymphoma cells and Chinese hamster ovary cells, and in an in vivo micronucleus assay in mice.

Fertility: There are no irreversible effects on fertility following cessation of exposures to levonorgestrel or progestins in general.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Lactose Monohydrate

Maize Starch

Potato Starch

Purified Water

Talc

Colloidal Silicon Dioxide

Magnesium Stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 Months.

Do not use the drug after expiry of its shelf life.

6.4 Special Precaution for Storage

Store at temperature not exceeding 30^0 C.

Keep out of reach of children.

6.5 Nature and contents of container

Each carton contains single blister containing one tablet of Levonorgestrel 1.5 mg packed along with a package insert.

6.6 Special precautions for disposal and other handling

No Special Requirements.

7. MARKETING AUTHORISATION HOLDER

Naari Pte

Singapore.

8. MARKETING AUTHORISATION NUMBER(S)

Not Applicable.

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION

Not Applicable.

10. DATE OF REVISION OF THE TEXT

December,2016