SUMMARIES OF PRODUCT CHARACTERISTICS (SmPC)

1. Name of the finished pharmaceutical product

Zee 1

(Levonorgestrel Tablets BP)

2. Qualitative and quantitative composition

Each uncoated tablet contains

Levonorgestrel BP	1.5 mg
Excipients	Q.S.

3. Pharmaceutical form

Oral Tablet

4. Clinical particulars

1. Therapeutic indications

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

2. Posology and method of administration

Method of administration

For oral administration.

Posology

One tablet should be taken as soon as possible, preferably within 12 hours, and no later than 72 hours after unprotected intercourse.

If vomiting occurs within three hours of taking the tablet, another tablet should be taken immediately.

Women who have used enzyme-inducing drugs during the last 4 weeks and need emergency contraception are recommended to use a non-hormonal EC (emergency contraception), i.e. Cu-IUD or take a double dose of levonorgestrel (i.e. 2 tablets taken together) for those women unable or unwilling to use Cu-IUD.

Levonorgestrel 1.5mg tablets 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 (e.g. condom, diaphragm, spermicide, cervical cap) until the next menstrual period starts. The use of levonorgestrel does not contraindicate the continuation of regular hormonal contraception.

Paediatric population

There is no relevant use of levonorgestrel for children of prepubertal age in the indication emergency contraception.

4. Special warnings and special 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 Levonorgestrel Tablets BP 1.5 mg. A follow up physical or pelvic examination is recommended f there is any doubt concerning the general health or pregnancy status of any woman after taking Levonorgestrel Tablets BP 1.5 mg.

Existing Pregnancy: Levonorgestrel Tablets BP 1.5 mg are not effective in terminating an existing pregnancy

Effects on Menses: Some women may experience spotting a few days after taking Levonorgestrel Tablets BP 1.5 mg.

Menstrual bleeding patterns are often irregular among women using progestin only oral contraceptives and women using Levonorgestrel for postcoital and emergency contraception. If there is a delay in the onset of expected menses beyond 1 week, consider the possibility of pregnancy.

STI/HIV: Levonorgestrel Tablets BP 1.5 mg do not protect against HIV infect on (AIDS) or other sexually transmitted infections (STIs).

Physical Examination and Follow up: A physical examination is not required prior to prescribing Levonorgestrel Tablets BP 1.5 mg.

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 Levonorgestrel Tablets BP 1.5 mg.

Fertility Following Discontinuation: A rapid return of fertility is likely following treatment with Levonorgestrel Tablets BP 1.5 mg for emergency contraception; therefore, routine contraception should be continued or initiated as soon as possible following use of Levonorgestrel Tablets BP 1.5 mg to ensure ongoing prevention of pregnancy.

5. Interaction with other FPPS and other forms of interaction

Drugs or herbal products that induce enzymes, including CYP3A4, that metabolize progestin's may decrease the plasma concentrations of progestin's, and may decrease the effectiveness of progestin only pills. Some drugs or herbal products that may decrease the effectiveness of progesin only pills 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.

6. Use in Pregnancy and lactation

Pregnancy: Many studies have found no harmful effects on fetal development associated with long term use of contraceptive doses of oral progestin's.

The few studies of infant growth and development that have been conducted with progestin only pills have not demonstrated significant adverse effects.

Nursing Mothers: In general, no adverse effects of progestin only pills have been found on breastfeed ng performance or on the health, growth, or development of the infant However, isolated post marketing cases of decreased milk production have been reported Small amounts of progestin's pass into the breast milk of nursing mothers taking progestin only pills for long term contraception, resulting in detectable steroid levels in infant plasma.

Pediatric Use: Safety and efficacy of progestin only pills for long term contraception have been established in women of reproductive age Safety and efficacy are expected to be the same for post pubertal adolescents less than 17 years and for users 17 years and older Use of Levonorgestrel Tablets BP 1.5 mg emergency contraception before menarche is not indicated

Geriatric Use: This product is not intended for use in postmenopausal women.

Race: No formal studies have evaluated the effect of race However, clinical trials demonstrated a higher pregnancy rate in Chinese women with both Levonorgestrel Tablets BP 1.5 mg and the Yuzpe regimen (another form of emergency contraception) The reason for this apparent increase in the pregnancy rate with emergency contraceptives in Chinese women is unknown.

Hepatic Impairment: No formal studies were conducted to evaluate the effect of hepatic disease on the disposition of Levonorgestrel Tablets BP 1.5 mg.

Renal Impairment: No formal studies were conducted to evaluate the effect of renal disease on the disposition of Levonorgestrel Tablets BP 1.5 mg.

7. Undesirable effects

Clinical Trial Experience

- Nausea
- Abdominal Pain
- Fatigue
- Headache
- Heavier Menstrual Bleeding
- Lighter Menstrual Bleeding
- Dizziness
- Breast Tenderness
- Vomiting
- Diarrhea

Post marketing Experience

The following adverse reactions have been identified during post approval use of Levonorgestrel Tablets BP 1.5 mg. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure

Gastrointestinal Disorders: Abdominal Pain, Nausea, Vomiting

General Disorders and Administration Site Conditions: Fatigue

Nervous System Disorders: Dizziness, Headache

Reproductive System and Breast Disorders: Dysmenorrhea, Irregular Menstruation, Oligomenorrhea, Pelvic Pain

8. Overdose

There are no data on over dosage of Levonorgestrel Tablets BP 1.5 mg, although the common adverse event of nausea and associated vomiting may be anticipated.

5. Pharmacological properties

5.1 Pharmacodynamic properties

1. Pharmacotherapeutic group: Sex hormones and modulators of the genital system, emergency contraceptives

SUMMARIES OF PRODUCT CHARACTERISTICS (SmPC)

2. **ATC code:** G03AD01

3. **Mechanism of action:** Emergency contraceptive pills are not effective if a woman s already pregnant Levonorgestrel tablets are believed to act as an emergency contraceptive principally by prevent ng ovulation or fertilization (by after ng tubal transport of sperm and/or ova) In addition, it may inhibit implantation (by altering the endometrium) It is not effective once the process of implantation has begun.

5.2. Pharmacokinetic properties

1. **Absorption:** No specific investigation of the absolute bioavailability of Levonorgestrel in humans has been conducted, however, literature indicates that Levonorgestrel is rapidly and completely absorbed after oral administration (bioavailability about 100%) and is not subject to first pass metabolism.

2. **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.

3. **Biotransformation:** Following absorption, Levonorgestrel is conjugated at the 17βOH 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, 5α tetrahydrolevonorgestrel and 16β hydroxylevonorgestrel 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.

4. **Elimination:** About 45 % of Levonorgestrel and its metabolites are excreted in the urine and about 32 % are excreted in feces, mostly as glucuronide conjugates.

5. Characteristics in patients

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 on pharmacokinetics of Levonorgestrel Tablets BP 1.5 mg However, clinical trials demonstrated a higher pregnancy rate in Chinese women with both Levonorgestrel Tablets BP 1.5 mg and the Yuzpe regimen (another form of emergency contraception). The reason for this apparent increase in the pregnancy rate with emergency contraceptives in Chinese women is unknown.

Hepatic Impairment: No formal studies were conducted to evaluate the effect of hepatic disease on the disposition of Levonorgestrel Tablets BP 1.5 mg.

Renal Impairment: No formal studies were conducted to evaluate the effect of renal disease on the disposition of Levonorgestrel Tablets BP 1.5 mg.

5.3. Preclinical safety data

Carcinogenicity: There is no evidence of increased risk of cancer with short term use of progestin's. There was no increase in tumorigenicity following administration of Levonorgestrel to rats for 2 years at approximately 5 mcg/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 mcg/kg/day In another 7 year dog study, administration of Levonorgestrel at 0.5 mg/kg/day and increase the number of mammary adenomas in treated dogs compared to controls. There were no malignancy.

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 follow ng cessation of exposures to Levonorgestrel or progestin's in general.

SUMMARIES OF PRODUCT CHARACTERISTICS (SmPC)

6. Pharmaceutical particulars

1. List of excipients

- Croscarmellose Sodium BP
- Lactose Monohydrate BP
- Lactose DC 21
- Maize Starch BP
- Povidone BP
- Purified Water BP
- Tween 80 (Polysorbate 80) BP
- Aerosil (Colloidal Silicon Dioxide) BP
- Polacrilin Potassium (Kyron T-314) USP
- Magnesium Stearate BP
- Microcrystalline Cellulose (Accel-102) USP
- Sodium Lauryl Sulphate BP

2. Incompatibilities: Not applicable

3. In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products: This medicinal product must not be mixed with other medicinal products.

4. Shelf life: 36 months

5. Special precautions for storage:

Store below 30^{o}C. Protect from light and moisture.

Keep the medicine out of reach of children.

6. Special precautions for usage / preparation before use: No special requirement.

SUMMARIES OF PRODUCT CHARACTERISTICS (SmPC)

7. **Packing Style:** 1 Tablet packed in Alu/PVC Blister pack, such 1 Blister packed in carton along with insert.

8. **Manufactured By**

Corona Remedies Pvt. Ltd.

Village Jatoli, Post Office- Ochghat,

Tehsil Solan, Dist. Solan (H.P.), Solan, India