SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

POTEX ™

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains

POTEX 2 tablets: Levonorgestrel BP, 0.75mg

POTEX 1 tablet: Levonorgestrel BP, 1.5mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

White tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

It is an emergency contraceptive for women indicated for use after unprotected sexual intercourse or sexual intercourse with failed protection. It is only used as a remedial measure for unprotected intercourse or failed contraception.

4.2 Posology and method of administration

POTEX 2 tablets: Take orally 2 tablets at one time or take one tablet first, then followed by the second tablet 12 hours later within 72 hours of unprotected sexual intercourse.
POTEX 1 tablet: Take orally one tablet within 72 hours of unprotected sexual intercourse.

4.3 Contraindications

POTEX ™ is contraindicated to women with mammary cancer, cancer of reproductive organ, liver dysfunction, or having hepatopathy and jaundice history recently, venous thrombus, cerebrovascular accident, hypertension, angiocardiopathy, diabetes, hyperlipemia, deprementia and women over forty years old.

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 have occurred. Treatment with POTEX ™ 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 POTEX ™, 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. Ectopic pregnancy may continue despite uterine bleeding. Therefore, POTEX ™ is not recommended for women at risk of ectopic pregnancy (history of salpingitis or of ectopic pregnancy).

POTEX ™ is not recommended in patients with severe hepatic dysfunction.

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

After taking POTEX ™, 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 make a medical appointment to initiate or adopt a method of regular contraception. If no withdrawal bleed occurs in the next pill-free period following the use of POTEX ™ 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 POTEX ™ 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.

POTEX ™ 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
POTEX ™ should not be given to pregnant women. It will not interrupt the pregnancy.

In case of failure of this emergency contraception with a 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 POTEX ™ administration.

Fertility
Clinical experience reveals 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

It is reported that the most common adverse events in the clinical trial for women receiving levonorgestrel 750 micrograms 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 750 micrograms users.

Adverse events in ≥ 5% of women, by frequency	
Adverse events	**Levonorgestrel 750 micrograms (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%
Diarrhoea	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.

4.9 Overdose

Serious undesirable effects have not been reported following acute ingestion of large doses of oral contraceptives. Overdose may cause nausea, and 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 POTEX^{TM} 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 the process of implantation has begun.

Efficacy: It has been estimated that levonorgestrel emergency contraceptive pills prevent 85% of expected pregnancies. Efficacy appears to decline with time after intercourse (95% within 24 hours, 85% if used between 24 and 48 hours, 58% if used between 48 and 72 hours).

It is therefore, recommended that the complete course of two POTEX 2 tablets is started as soon as possible (and no later than 72 hours) after unprotected intercourse.

At the recommended regimen, levonorgestrel is not expected to induce significant modification of 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.

It is reported that 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 0.25 mg levonorgestrel and 0.05 mg ethinyl estradiol, taken within 72 hours of intercourse, and two tablets taken 12 hours later).

5.2 Pharmacokinetic properties

It is reported that the pharmacokinetic parameters of levonorgestrel tablets 0.75mg 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)	2.47 ± 1.68	2.42 ± 1.24	–	–
C_{max} (ng/ml)	14.20 ± 4.83 (13.46)	13.97 ± 4.25 (13.48)	99.9	91.2–109.3
AUC_{0-t} (ng·hour/ml)	239 ± 102 (222)	243 ± 108 (226)	98.1	91.1–105.7
AUC_{0-inf} (ng·hour/ml)	252 ± 107 (235)	257 ± 112 (240)	97.9	90.8–105.5

* geometric mean

Levonorgestrel is not excreted in unchanged form but as metabolites. Levonorgestrel metabolites are excreted in about equal proportions with 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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Corn starch
Sucrose
Dextrin
Sodium carboxymethyl starch
Magnesium Stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

60 months.

6.4 Special precautions for storage

Store in a dry place not exceeding 30°C

6.5 Nature and contents of container

PVC /Aluminium blister strip. The blister strip is packed in a box.

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

China Resources Zizhu Pharmaceutical Co., Ltd.

No.27, Chaoyang North Road, Chaoyang District, Beijing, China.

8. MANUFACTURER ADDRESS

China Resources Zizhu Pharmaceutical Co., Ltd.

No.27, Chaoyang North Road, Chaoyang District, Beijing, China.

9. MARKETING AUTHORISATION APPLICANT

China Resources Zizhu Pharmaceutical Co., Ltd.

No.27, Chaoyang North Road, Chaoyang District, Beijing, China.

10. DATE OF REVISION OF THE TEXT

30 May, 2020