Summary of Product Characteristics (SmPC)

Product Name:	**ROGOTINOR® TABLETS** (Levonorgestrel Tablets BP 0.75 mg)

1. Name of the medicinal product:
ROGOTINOR® TABLETS (Levonorgestrel Tablets BP 0.75 mg)

2. Qualitative and quantitative Composition:
Each tablet contains: Levonorgestrel BP 0.75 mg

3. Pharmaceutical form
Tablets

4. Clinical particulars

4.1 Therapeutic indications

Oral Contraception
The preparation is an oral contraceptive indicated for females having sexual intercourses occasionally. No more than 4 Tablets can be taken monthly at 2-to 4 occasions. To females having sexual intercourses more frequently combined oral contraceptives / or other contraceptive methods are recommended.

4.2 Posology and method of administration
Levonorgestrel tablet is an emergency contraceptive that can be used to prevent pregnancy following unprotected intercourse or a known or suspected contraceptive failure. To obtain optimal efficacy, the first tablet should be taken as soon as possible within 72 hours of intercourse. The second tablet must be taken 12 hours later.

One tablet should be taken orally within 72 hours after unprotected intercourse. The second tablet should be taken 12 hours after the first dose. Efficacy is better if it is taken as directed as soon as possible after unprotected intercourse. Rogotinor can be used at any time during the menstrual cycle. The user should be instructed that if she vomits within one hour of taking either dose of medication she should contact her health care professional to discuss whether to repeat that dose.

Method of Administration:
For oral administration.

4.3 Contraindications
Progestin-only contraceptive pills (POPs) are used as a routine method of birth control over longer periods of time, and are contraindicated in some conditions. It is not known whether these same conditions apply to the Rogotinor regimen consisting of the emergency use of two progestin pills. POPs however, are not recommended for use in the following conditions: Known or suspected pregnancy. Hypersensitivity to any component of the product Undiagnosed abnormal genital bleeding.

4.4 Special warnings and precautions for use:
Emergency contraception is an **occasional** method. It should in no instance replace a regular contraceptive method.

Emergency contraception does not prevent a pregnancy to occur in every instance, especially if uncertainty about the timing of the unprotected intercourse. Limited and inconclusive data suggest that there may be reduced efficacy of **ROGOTINOR® TABLETS** (Levonorgestrel Tablets BP 0.75 mg) with increasing body weight or body mass index (BMI) (see section 5.1). In all women, emergency contraception should be taken as soon as possible after unprotected intercourse, regardless of the woman's body weight or BMI. In case of doubt (menstrual periods delayed by more than five days or abnormal bleeding at the expected date of menstrual periods, symptoms of pregnancy), it is mandatory to check the absence of pregnancy by performing a pregnancy test.

If the woman has had unprotected intercourse more than 72 hours earlier in the same menstrual cycle, conception may have occurred. Treatment with **ROGOTINOR® TABLETS** (Levonorgestrel Tablets BP 0.75 mg) following the second act of intercourse may therefore be ineffective in preventing pregnancy.

If pregnancy occurs after treatment with **ROGOTINOR® TABLETS** (Levonorgestrel Tablets BP 0.75 mg), the possibility of an ectopic pregnancy should be considered. The absolute risk of ectopic pregnancy is likely to be low as **ROGOTINOR® TABLETS** (Levonorgestrel Tablets BP 0.75 mg) prevents ovulation and fertilisation. Ectopic pregnancy may continue, despite the occurrence of uterine bleeding. Therefore, **ROGOTINOR® TABLETS** (Levonorgestrel Tablets BP 0.75 mg) is not recommended for patients who are at risk of ectopic pregnancy (previous history of salpingitis or of ectopic pregnancy).
ROGOTINOR® TABLETS (Levonorgestrel Tablets BP 0.75 mg) is not recommended in patients with severe hepatic dysfunction. Severe malabsorption syndromes, such as Crohn's disease, might impair the efficacy of **ROGOTINOR® TABLETS** (Levonorgestrel Tablets BP 0.75 mg).
Cases of thromboembolic events have been reported after **ROGOTINOR® TABLETS** (Levonorgestrel Tablets BP 0.75 mg) intake. The possibility of occurrence of a thromboembolic event should be considered in women with other pre-existing thromboembolic risk factor(s), especially personal or family history suggesting thrombophilia. After **ROGOTINOR® TABLETS** (Levonorgestrel Tablets BP 0.75 mg) intake, menstrual periods are usually of normal abundance and occur at the expected date.
They can sometimes occur earlier or later than expected by a few days. It is recommended to have a medical visit to initiate or adapt a method of regular contraception. In case no menstrual period occurs in the next pill-free period following the use of **ROGOTINOR® TABLETS** (Levonorgestrel Tablets BP 0.75 mg) after regular hormonal contraception, pregnancy should be ruled out.

Repeated administration within a menstrual cycle is not advisable, because of an undesirable high load of hormones for the patient and the possibility of severe disturbances of the cycle.
Women who present for
repeated courses of emergency contraception should be advised to consider long-term methods of contraception.
The use of emergency contraception does not replace the necessary precautions against sexually transmitted diseases.
Concomitant use of **ROGOTINOR® TABLETS** (Levonorgestrel Tablets BP 0.75 mg) and drugs containing ulipristal acetate is not recommended (see section 4.5).
This medicinal product contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction
Associations to be taken into consideration:
The metabolism of Levonorgestrel is enhanced by the concomitant use of liver enzyme inducers: anticonvulsant (phenobarbital, phenytoin, primidone, carbamazepine); rifabutin; rifampicin; griseofulvin; ritonavir; Hypericum perforatum (St. John's wort)**.** The efficacy of **ROGOTINOR® TABLETS** (Levonorgestrel Tablets BP 0.75 mg) may be decreased in case of concomitant intake of these active substances.
Ulipristal acetate is a progesterone receptor modulator that may interact with the progestational activity of levonorgestrel. Therefore the concomitant use of Levonorgestrel and drugs containing ulipristal acetate is not recommended.

4.6 Pregnancy and lactation Pregnancy
This medicinal product cannot interrupt an ongoing pregnancy.
In case of failure of this contraceptive mean with persisting pregnancy, epidemiological studies indicate no malformative effects of progestins on foetus.

Nothing is known on the consequences for the child if doses higher than 1.5 mg Levonorgestrel are taken.

Breastfeeding
Levonorgestrel is excreted into breast milk. Therefore, it is suggested to breastfeed immediately before taking **ROGOTINOR® TABLETS** (Levonorgestrel Tablets BP 0.75 mg) 750 microgram tablets and to skip nursing at least 8 hours following **ROGOTINOR® TABLETS** (Levonorgestrel Tablets BP 0.75 mg) administration.

Fertility
A rapid return to fertility is likely following treatment with **ROGOTINOR® TABLETS** (Levonorgestrel Tablets BP 0.75 mg) for emergency contraception; therefore, regular contraception should be continued or initiated as soon as possible following the use of **ROGOTINOR® TABLETS** (Levonorgestrel Tablets BP 0.75 mg) to ensure ongoing prevention of pregnancy.

Clinical experience reveal no effect on fertility in humans after use of levonorgestrel. Similarly nonclinical 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 effect on the ability to drive and use machines have been reported**.** Nevertheless, if women experience fatigue and dizziness after taking **ROGOTINOR®** **TABLETS** (Levonorgestrel Tablets BP 0.75 mg), they should not drive or use machines.

4.8 Undesirable effects
The most common adverse events in the clinical trial for women receiving Levonorgestrel tablets included nausea (23%), abdominal pain (18%), fatigue (17%), headache (17%), and menstrual changes. The table below shows those adverse events that occurred in ³ 5% of Levonorgestrel tablets users.

Adverse Events in Less Than or Equal to 5% of Women, by % Frequency

Most Common Adverse Events	Levonorges 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
Other complaints	9.7
Vomiting	5.6
Diarrhea	5.0

It demonstrated a superior safety profile over the Yuzpe regimen for the following adverse events:

Nausea: Occurred in 23% of women Vomiting: Occurred in 6% of women

4.9 Overdose
There are no data on over dosage of Levonorgestrel tablet, although the common adverse event of nausea and its associated vomiting may be anticipated.

5. Pharmacological properties

5.1 Pharmacodynamic properties Pharmacotherapeutic group:

Oral Contraceptive **ATC code -** G03AD01

The primary mechanism of action is blockade and/or delay of ovulation via suppression of the luteinizing hormone (LH) peak. Levonorgestrel interferes with the ovulatory process only if it is administered before the onset of the LH surge. Levonorgestrel has no emergency contraceptive effect when administered later in the cycle.

In clinical trials, the proportion of pregnancies avoided after the use of Levonorgestrel varied from 52% (Glasier, 2010) to 85% (Von Hertzen, 2002) of expected pregnancies. Efficacy appears to decline with time after intercourse.

There is limited and inconclusive data on the effect of high body weight/high BMI on the contraceptive efficacy. In three WHO studies no trend for a reduced efficacy with increasing body weight/BMI was observed (Table 1), whereas in the two other studies (Creinin et al., 2006 and Glasier et al., 2010) a reduced contraceptive efficacy was observed with increasing body weight or BMI (Table 2). Both meta-analyses excluded intake later than 72 hours after unprotected intercourse (i.e. off-label use of Levonorgestrel) and women who had further acts of unprotected intercourse.

At the used regimen, Levonorgestrel is not expected to induce significant modifications of blood clotting factors, and lipid and carbohydrate metabolism

5.2 Pharmacokinetic properties
Bioavailability of oral Levonorgestrel is approximately 100 percent. In the plasma, it is strongly bound to SHBG. Levonorgestrel is eliminated via kidney (60-80%) and liver (40-50%).

After oral administration of 1.5 mg Levonorgestrel, the plasma terminal half-life of the product is estimated to 43 hours. The maximal plasma concentration of Levonorgestrel (approximately 40 nmol/l) is reached within 3 hours. Levonorgestrel is hydroxylated in the liver and the metabolites are excreted as glucuronide conjugates

5.3 Preclinical safety data
Nonclinical data reveal no special hazard for humans, beyond the information included in other sections of the SPC. Animal experiments with Levonorgestrel have shown virilization of female fetuses at high doses.
A preclinical study conducted in mice showed no effect on fertility in the progeny of treated dams. Two studies investigating the consequence of exposure to Levonorgestrel on the development of pre-embryos before implantation, showed that Levonorgestrel had no adverse effects on fertilisation and the in vitro growth of mouse pre-embryos.

6 Pharmaceutical particulars

6.1 List of excipients
Lactose BP Starch BP
Magnesium stearate BP Purified water BP

6.2 Incompatibilities
None known.

6.3 Shelf life
36 months

6.4 Special precautions for storage
Store below 30°C. Protect from light and humidity.
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6.5 Nature and contents of container
A single Blister containing 10 tablets packed in a Cardboard Box.

6.6 Special precautions for disposal and other handling
No special requirements.

7. Marketing authorization holder Marketing Authorization Holder:
Name : **ROYAL GROUP**
Address: ONB-E/2, Mehar sons Estate,
Talpur Road, Karachi-74000, Pakistan.
Phone: +92-21-32400270 Extension: 232
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Email: info@royalgroupweb.com

Manufactured by:
HUAZHONG PHARMACEUTICAL CO., LTD
No. 118, Xianshan Road, Xiangyang City, Hubei, China.

8. Marketing authorization number(s)
Not Applicable

9. Date of first authorization/renewal of the authorization
Not Applicable

10. Date of Revision of the Text:
Not Applicable

11. Dosimetry (If Applicable):
Not Applicable

12. Instructions for Preparation of Radiopharmaceuticals (If Applicable):
Not Applicable