Summary of Product Characteristic
This information is intended for use by health professionals

1. Name of the medicinal product
AMOR™ Capsule, 0.75 mg

2. Quality and Quantitative Composition
Each capsule contains 0.75 mg levonorgestrel

Excipients: For a full list of excipients, see section 6.1.

3. Pharmaceutical Form
Hard gelatin capsules
Size 4, having red cap and pink body filled with a homogeneous white powder.

4. Clinical Particulars
4.1 Therapeutic indications
Emergency contraception within 72 hours of unprotected sexual intercourse or failure of a contraceptive method.

4.2 Posology and method of administration
Posology
The treatment necessitates the intake of two tablets in a single administration. The efficacy of the method is higher the sooner after the unprotected intercourse the treatment is initiated. Therefore, the two capsules must be taken **as soon as possible, preferably within 12 hours after the unprotected intercourse,** and no longer than 72 hours (3 days) after the intercourse.

AMOR™ Capsule can be taken at any moment during the menstrual cycle.

If vomiting occurs within three hours of taking the tablets, another two tablets should be taken immediately.
After using an emergency contraception, it is recommended to use a local contraceptive mean (condom, spermicide, and cervical cap) until the next menstrual periods resume. The use of *AMOR™ Capsule* does not contraindicate the continuation of regular hormonal contraception.

Method of administration
AMOR™ Capsule should be taken orally.

4.3 Contraindications
Hypersensitivity to levonorgestrel or any of the excipients.

4.4 Special warning and precautions for use
Levonorgestrel is not recommended in patients with severe hepatic dysfunction.
Severe malabsorption syndromes, such as Crohn's disease, might impair the efficacy of
Emergency contraception is an occasional method. It should in no instance replace a regular contraceptive method.

Emergency contraception does not prevent a pregnancy in every instance. 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 levonorgestrel 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 excluded.

If pregnancy occurs after treatment with levonorgestrel, the possibility of an ectopic pregnancy should be considered. The absolute risk of ectopic pregnancy is likely to be low, as levonorgestrel prevents ovulation and fertilisation. Ectopic pregnancy may continue, despite the occurrence of uterine bleeding.

Therefore, levonorgestrel is not recommended for patients who are at risk of ectopic pregnancy (previous history of salpingitis or of ectopic pregnancy).

Levonorgestrel contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

After Levonorgestrel intake, 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 levonorgestrel after regular hormonal contraception, pregnancy should be ruled out.

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

Levonorgestrel 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.

Limited and inconclusive data suggest that there may be reduced efficacy of Levonorgestrel 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.

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, mainly CYP3A4 enzyme inducers. Concomitant administration of efavirenz has been found to reduce plasma levels of levonorgestrel (AUC) by around 50%.

Drugs suspected of having similar capacity to reduce plasma levels of levonorgestrel include barbiturates (including primidone), phenytoin, carbamazepine, herbal medicines containing Hypericum perforatum (St. John's wort), rifampicin, ritonavir, rifabutin and Griseofulvin.
For women who have used enzyme-inducing drugs in the past 4 weeks and need emergency contraception, the use of non-hormonal emergency contraception (i.e. a Cu-IUD) should be considered. Taking a double dose of levonorgestrel (i.e. 3000 mcg within 72 hours after the unprotected intercourse) is an option for women who are unable or unwilling to use a Cu-IUD, although this specific combination (a double dose of levonorgestrel during concomitant use of an enzyme inducer) has not been studied.

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

4.6 Fertility, pregnancy and lactation
Fertility
Levonorgestrel increases the possibility of cycle disturbances which can sometimes lead to earlier or later ovulation date. These changes can result in modified fertility; however, there are no fertility data in the long term.

Pregnancy
Levonorgestrel 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 (see section 5.3).

Breast-feeding
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 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 reported.

Nevertheless, if women experience fatigue and dizziness after taking *AMOR™ Capsule*, they should not drive or use machines.

4.8 Undesirable effects
The following table gives the frequency of undesirable effects after intake of 1.5 mg levonorgestrel reported in clinical trials*.

Body System	**Frequency of adverse reactions**	
	Very common (≥ 1/10)	**Common (≥1/100 to 1/10)**
Nervous system disorders	Dizziness Headache	
Gastrointestinal disorders	Nausea Abdominal pain	Diarrhoea[1] Vomiting
Reproductive system and Breast disorders	Uterine pain Breast tenderness Delay of menses[3] Heavy menses[2] Bleeding[1]	Dysmenorrhoea[3]
General disorders and administration site conditions	Fatigue[1]	

* Trial 1 (n=544): Contraception, 2002, 66, 269-273
* Trial 2 (n=1359): Lancet, 2002, 360:1803-10
* Trial 3 (n=1117): Lancet 2010; 375:555-62
* Trial 4 (n=840): Obstetrics and Gynecology 2006; 108:1089-1097
[1] Not recorded in Trial 1
[2] Not recorded in Trial 2
[3] Not reported in Trial 1 or 2
[4] Delay defined as more than 7 days.

These undesirable effects usually disappear within 48 hours after the intake of *AMOR™ Capsule*. Breast tenderness, spotting and irregular bleeding are reported in up to 30 percent of patients and can last until the next menstrual period which can be delayed.

Hypersensitivity reactions such as pharyngeal/face oedema and cutaneous reactions have been reported after the intake of *AMOR™ Capsule*.

4.9 Overdose
Serious 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: EMERGENCY CONTRACEPTIVES – G03AD01

Mechanism of action
The precise mode of action of levonorgestrel is not known.

Pharmacodynamic effects
At the recommended regimen, levonorgestrel is thought to work mainly by preventing ovulation and fertilisation if 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. Levonorgestrel is not effective once the process of implantation has begun.

Clinical efficacy and safety

Results from a randomized, double-blind clinical study conducted in 2001 (Lancet 2002; 360: 1803-1810) showed that a 1500 microgram 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). There was no difference between pregnancy rates in case of women who were treated on the third or the fourth day after the unprotected act of intercourse (p>0.2).

Another study conducted in 1997 (Lancet 1998; 352: 428–33) showed that two 750 microgram doses taken 12 hours apart prevents 85% of expected pregnancies.

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.

Table 1: Meta-analysis on three WHO studies (Von Hertzen et al., 1998 and 2002; Dada et al., 2010)

BMI (kg/m2)	**Underweight 0 - 18.5**	**Normal 18.5-25**	**Overweight 25-30**	**Obese ≥ 30**
N total	600	3952	1051	256
N pregnancies	11	39	6	3
Pregnancy rate	1.83%	0.99%	0.57%	1.17%
Confidence Interval	0.92 – 3.26	0.70 – 1.35	0.21 – 1.24	0.24 – 3.39

Table 2: Meta-analysis on studies of Creinin et al., 2006 and Glasier et al., 2010

BMI (kg/m2)	**Underweight 0 - 18.5**	**Normal 18.5-25**	**Overweight 25-30**	**Obese ≥ 30**
N total	64	933	339	212
N pregnancies	1	9	8	11
Pregnancy rate	1.56%	0.96%	2.36%	5.19%
Confidence Interval	0.04 – 8.40	0.44 – 1.82	1.02 – 4.60	2.62 – 9.09

At the recommended regimen, levonorgestrel is not expected to induce significant modification of blood clotting factors, and lipid and carbohydrate metabolism.

Paediatric population
A prospective observational study showed that out of 305 treatments with levonorgestrel emergency contraceptive tablets, seven women became pregnant resulting in an overall failure rate of 2.3%. The failure rate in women under 18 years (2.6% or 4/153) was comparable to the failure rate in women 18 years and over (2.0% or 3/152).

5.2 Pharmacokinetic Properties
Orally administered levonorgestrel is rapidly and almost completely absorbed.
The results of a pharmacokinetic study carried out with 16 healthy women showed that following ingestion of single dose of 1.5 mg levonorgestrel maximum drug serum levels of 18.5 ng/ml were found at 2 hours.

After reaching maximum serum levels, the concentration of levonorgestrel decreased with a mean elimination half-life of about 26 hours.

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.

5.3 Preclinical safety Data
Animal experiments with levonorgestrel have shown virilisation of female fetuses at high doses.
Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeat-dose toxicity, genotoxicity, carcinogenicity potential, beyond the information included in other sections of the SPC.

6. Pharmaceutical Particulars
6.1 List of excipients
Capsule filling:
Microcrystalline Cellulose (101)
Starch
Capsule shell:
Gelatin
Light Blue (E133)
Lemon Virginia (E102)
Amaranth (E123)
Erythrosine (E127)
Titanium Pigment (E171)

6.2 Incompatibilities
Not applicable

6.3 Shelf life
36 months.

6.4 Special precautions for storage
Store below 30ºC. Keep in tightly closed container and protect from light.

6.5 Nature and contents of container
Two capsules in PVC/aluminium blister and cardboard cartons.

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

7. Marketing Authorization Holder
Hubei Gedian Humanwell Pharmaceutical Co., Limited
No.77, Wuhan Seven Optical Valley Road,
East Lake New Technology Development Zone,
Hubei Province, **China.**

8. Marketing Authorization Numbers
TAN 22 HM 0084

9. Date of first authorization/ renewal of the authorization
11/04/2022

10. Date of revision of the text