Summary of Product Characteristics

1. Name of the medicinal product

Phloro-G® 80 mg Orally Disintegrating Tablets

2. Qualitative and quantitative composition

Phloroglucinol Dihydrate .....80.00 mg

Excipient with known effect: Mannitol.

For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Orally Disintegrating Tablets White or off-white tablets.

4. Clinical particulars

4.1 Therapeutic indications

Phloro-G is a smooth muscle antispasmodic drug. It is used for the

- symptomatic treatment of pain related to functional disorders of the digestive tract and biliary trac;
- treatment of acute spasmodic and painful manifestations of the urinary tract: colic nephritic;
- symptomatic treatment of painful spasmodic manifestations in gynaecology;
- adjuvant treatment of contractions during pregnancy in combination with rest.

4.2 Posology and method of administration

Phloro-G should always be taken exactly as described by the doctor or health care provider. You should check with your doctor, health care provider or pharmacist if you are not sure.

Phloro-G is a symptomatic treatment. If symptoms persist, the patient's condition should be reassessed.

Posology

Adult

The dosage of Phloro-G is 2 tablets, to be taken at the time of the crisis, to be renewed in case of significant spasms. A minimum interval of 2 hours must be observed between each dose and not more than 6 tablets should be taken in 24 hours.

Children

In children over 2 years of age, the dosage is 1 tablet to be taken at the time of the

crisis. to be renewed in case of important spasms. A minimum interval of 2 hours must be observed between each dose and not more than 2 tablets should be taken in 24 hours.

The efficacy of Phloro-G 80 mg in children under 2 years old has not been determined.

Method of administration

For oral use.

Adults: tablets should be dissolved in a glass of water or allowed to melt under the tongue for a rapid effect.
Children: tablets should be dissolved in a glass of water.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and special precautions for use:

Phloroglucinol should not be administered concomitantly with major analgesics such as morphine or morphine derivatives due to their spasmogenic effects.

4.5 Interactions with other medicinal products and other forms of interaction

Not applicable.

4.6 Pregnancy and lactation

Pregnancy

Animal studies have not demonstrated any teratogenic effect of phloroglucinol. A malformative effect in the human species is not expected in the absence of a teratogenic effect in animals, as, to date, substances responsible for malformations in the human species have always been found to be teratogenic in animals during well conducted studies on two species.
The relatively widespread use of phloroglucinol in clinical practice has not revealed any risk of malformative effects to date. However, epidemiological studies would be necessary to confirm the absence of risk.
Consequently, the use of phloroglucinol during pregnancy must be considered only when strictly necessary.

Lactation

In the absence of data, use of this medicinal product is not recommended while breastfeeding.

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

Class of organ systems	Adverse effect-preferred term	Frequency
Skin and subcutaneous tissue disorders	Eruption, rarely urticaria, pruritus, exceptionally angioedema anaphylactic shock (arterial hypotension), acute generalised exanthematous pustulosis	Frequency not determined

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system and the email: https://pv.pharmacyboardkenya.org/

4.9 Overdose

No case of overdose has been reported.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: MUSCULOTROPIC ANTISPASMODIC

ATC code: A03AX12 (A: Alimentary tract and metabolism) (G: Genito-urinary system).

Mechanism of action

Phloroglucinol has spasmolytic activity on smooth muscles and a visceral eff and anti-nociceptive, especially during episodes of acute pain.

Phloroglucinol compared with other smooth muscle spasmolysis medicine, the biggest characteristic is no fight choline action. While relieving the smooth muscle spasm, it does not produce a series of cholinolytic adverse reactions, and not cause the symptoms such as low blood pressure, heart rate and arrhythmia.
There are small impacts on cardiovascular function. It is only used to spasm smooth muscle, with little impacts on normal smooth muscle.

Effects on smooth muscle spasm

People have known the phloroglucinol for more than a century. They have done a lot of pharmacological researches on animals in vivo and in vitro, by using a variety of muscular spasm agents to induce all kinds of smooth muscle spasm, and observed spasmolysis effects of phloroglucinol. In the 1960s, it was confirmed that the phloroglucinol was with the clinical treatment on smooth muscle spasm, other few adverse reactions, excellent tolerability, and without any atropine adverse reactions.

Effects on physiological contractions of smooth muscles

In enough dosage of releasing spasm, there were no effects of Phloroglucinol on physiological contractions of gastrointestinal, biliary, biliary sphincter, urethra and uterus.

Effects on the cardiovascular system

Phloroglucinol will not change animals blood pressure, heart rate and heart blood supply, etc.

Effect on bile secretion

Phloroglucinol with low dosage will not change the bile secretion and components. But it with low dosage could increase bile secretion, but not change its components.

5.2 Pharmacokinetic properties

Absorption

After oral administration, the plasma peak is reached between 15 and 20 minutes. Human trials showed that t max of phloroglucinol oral lyophilized tablets was about 20 min, C_{max} was 923 $ng.mL^{-1}$, AUC was (1285±570) $ng.h.mL^{-1}$.

Distribution

The tissue distribution of phloroglucinol is rapid and extensive. After fifteen minutes of the rats administrated by intravenous injection (50 mg.kg-1 weight) of 3H-Phloroglucinol, the most high concentration was in kidney(5.9 μg.g-1), liver (6.0 μg.g-1) , and gut (4.6 μg.g-1). The concentration in brain tissue was very low. After 48 hours, the concentrations in liver and muscle were 2.3 μg.g-1 and 1.1 μg.g-1 respectively.

Biotransformation

Phloroglucinol is metabolised in the liver by glucuroconjugation.After Phloroglucinol entered into the body, it was rapidly distributed to the kidney, liver and intestinal, and play a role. The half-life of plasma was about fifteen minutes. The drug concentration reduced quickly in 4 hours of administration, after that, the drug concentration reduced slowly. The drug's metabolism in the body is mainly through the glucuronic acid conjugation and methylation in liver, in the form of the prototype, sulfonated, glucuronic acid combination or its hydroxyl metabolites such as 1,3- dimethoxy-5-phenol or the trimethoxybenzene from the urine.

Elimination

Elimination takes place via the urinary route in the glucuroconjugated form and via the biliary route in the free and conjugated form. The elimination half-life is of the order of 1h40.

5.3 Preclinical safety data:

Non-clinical data from conventional repeated dose toxicology, genotoxicity and reproductive function studies did not reveal any particular risk to humans.

Mutagenicity

After the female and male rats were administrated, we took the study on their three generations. 20 rats were divided into 4 groups, and given the different dosages of phloroglucinol in their food for 221 days (first generation), 105 days (second generation) and 115 days (third generation). There were no any changes on the organs and endocrines. And there were no changes on the pathological examination of embryo. The microbial gene mutation assay (Ames assay) showed that the phloroglucinol was without mutagenic (using the strain TA97, TA98 and TA100). In the chromosome aberration test of Chinese hamster ovary cells, the phloroglucinol is negative.

Common reproductive toxicity testing

20 pregnant rats, 4 groups, were given the same quantity of phloroglucinol from d7 to d15 of pregnant, the dosage were 0, 200, 300 and 400mg.kg^{-1} body weight. The macroscopic and microscopic examinations showed than there were no harmful effects on rat generations, and no teratogenic effects.

20 pregnant rabbits, 4 groups, were given the same quantity of phloroglucinol from d6 to d14 of pregnant, the dosage were 0, 400, 600 and 800mg.kg^{-1} body weight. The results showed that there were no adverse effects on fetal rabbits.

Teratogenicity testing

Acute toxicity

LD50 of mouse and rats administrated by oral, subcutaneous and intraperitoneal injection was about 4000mg.kg^{-1} body weight. LD50 of dogs administrated by intravenous injection was beyond 250mg.kg^{-1} body weight. The acute toxicity tests of these three animals showed that the toxicity of phloroglucinol is very low.

Subacute toxicity

Wistar rats of 3 groups were administrated 3 dosages of phloroglucinol by oral, and observed for 86 days. The test results showed that phloroglucinol had no adverse effects on the animal growths, appearances and microscopic histological of vital organs (kidney, spleen, heart, liver, parathyroid, adrenal and reproductive glands) and hematology.

Chronic toxicity

The chronic toxicity experiments of phloroglucinol were respectively administrated on three generations of male and female rats, the first generation for 215 days, the second for 125 days and the third generation for 115 days. The experimental results showed that there were no adverse effects of phloroglucinol on animal growths, appearances of vital organs, histology, blood and biochemical indexes.

Long-term Toxicity
8 dogs, divided into four groups, were given the mixture of phloroglucinol and three methyl benzene Phenol (1:1) according to the dose of 0, 20, 80, 125 $mg.kg^{-1}$ weight, for six months. The dogs were executed in June and September respectively. There were no toxicity effects. And there were no changes on hematology, blood biochemistry or urine biochemical parameters. The dosage of non-toxic role was 125 $mg.kg^{-1}$ weight.

6. Pharmaceutical particulars

6.1 List of excipients
Crospovidone, Mannitol, Microcrystalline Cellulose, Magnesium Stearate

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years

6.4 Special precaution for storage
Do not store above 30°C and protect from light and moisture.

6.5 Nature and contents of container
Al-Al blister, box, and carton
Pack sizes of 10 tablets (10 tablets/ blister, 1 blister/ pack).

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

7. MARKETING AUTHORIZATION HOLDER AND MANUFACTURER

Marketing Authorization Holder:
B & O PHARM
Rm. A-522, No. 188 Yesheng Road, Shanghai 201306, China

Manufacturer:
GUILIN PHARMACEUTICAL CO., LTD.
No.43 Qilidian Road, Guilin 541004, Guangxi, China

8. MARKETING AUTHORISATION NUMBER(S)

H2016/CTD3457/131

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
2016.03.29

10. DATE OF REVISION OF THE TEXT

06/2026