Summary of Product Characteristics

1. Name of the medicinal product

1.1 (Invented) name of the medicinal product

Trade/Proprietary Name: Phloro-G ™

Approved/Inn/Generic Name: Phloroglucinol orally disintegrating tablets

1.2 Strength

80mg

1.3 Pharmaceutical form

Tablet

2. Qualitative and quantitative composition

Name of ingredient	Qty (SI units)
Phloroglucinol dehydrate	80.00mg
Crospovidone	10.80mg
Mannitol	151.40mg
Microcrystalline cellulose	27.0mg
Magnesium stearate	0.8mg

3. Description

White or almost white tablet.

4. Clinical particulars

4.1 Therapeutic indications

Phloro-G™ is a smooth muscle antispasmodic drug. It is used to symptomatic treatment of pain related to functional disorders of the digestive tract and bile ducts, treatment of acute spasmodic painful disorders of the urinary tract: renal colic, symptomatic treatment of acute pain in gynaecology, and adjuvant treatment of contractions during pregnancy in combination with rest.

4.2 Posology and method of administration

Tablets for oral 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.

The dose of Phloro-G ™ is 6 orally disintegrating tablets per 24 hours.

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

4.3 Contraindications

Hypersensitivity to one of the ingredients.

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

Phloroglucinol cannot be used with analgin in mixed(which Can cause thrombophlebitis); and to avoid used with morphine and its derivatives, because the drug can cause spasm. There's a case of a reported adverse reactions clinically, which used phloroglucinol with pethidine caused sudden arrest of heart beat, rescued the patients in a timely manner, healing was better. So we should be vigilant the possibility of cardiac arrest and ready for emergency drugs when in both shared. Reasonable application of oxytocin and phloroglucinol after childbirth in the process, not only can speed labor, reduce the rate of dystocia, but all safe for mother and child. Active in the stages of period, joint application of phloroglucinol and diazepam can have the effect of double the cervical solution spasm, the effect of sedation and ease pain, to relieve labor pain, shorten labor, improve natural births consequently, and had no significant effect on neonatal Apgar score.

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

Skin and subcutaneous and allergic reactions: rash, rarely urticaria, exceptional angioedema, hypotension, anaphylactic shock.

4.9 Overdose

No overdose reported.

5. Pharmacological properties

5.1 Pharmacodynamic properties

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 would not change the blood pressure, heart rate and heart blood supplement of animals.

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 of Drug

Human trials showed that t max of phloroglucinol oral lyophilized tablets was about 20 min, ρ max was 923 $ng.mL^{-1}$, AUC was (1285±570)$ng.h.mL^{-1}$.

The distribution, metabolism and excretion of drug in vivo

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$\mu g.g^{-1}$), liver (6.0 $\mu g.g^{-1}$) , and gut (4.6 $\mu g.g^{-1}$). The concentration in brain tissue was very low. After 48 hours, the concentrations in liver and muscle were 2.3$\mu g.g^{-1}$ and 1.1$\mu g.g^{-1}$ respectively.

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.

5.3 Preclinical safety data：

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 400$mg•kg^{-1}$ 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 LD_{50} of mouse and rats administrated by oral, subcutaneous and intraperitoneal injection was about 4000mg•kg^{-1} body weight. LD_{50} 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

3years

6.4 Special precaution for storage

Stored below 30℃, protected from light.

6.5 Nature and contents of container

Al-Al blister, box, and carton

6.6 Instructions for use and handling <and disposal>

No special requirement.

7. MARKETING AUTHORISATION HOLDER

B&O PHARM

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8. DATE OF REVISION OF THE TEXT

August, 2020