NEW ZEALAND DATA SHEET

1. HAEMOROL™ OILY PHENOL INJECTION 5% w/v injection (depot)

Phenol 5% w/v injection (depot)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

HAEMOROL OILY PHENOL INJECTION is a solution containing 250 mg phenol in almond oil to 5 mL (phenol 5% w/v).

Excipients with known effect: tree nuts.

For the full list of excipients, see **Section 6.1 List of excipients**.

3. PHARMACEUTICAL FORM

Injection.

HAEMOROL OILY PHENOL INJECTION is a clear, yellowish solution free from visible particles.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

HAEMOROL OILY PHENOL INJECTION is indicated for the sclerotherapy of haemorrhoids.

4.2. Dose and method of administration

HAEMOROL OILY PHENOL INJECTION is for submucosal injection only (i.e. local administration) (see **Section 4.4 Special warnings and precautions for use**). Personnel administering this treatment should be trained in the correct placement of submucosal injections. HAEMOROL OILY PHENOL INJECTION is not to be administered intrathecally, or injected into a blood vessel or into deep tissues (see **Section 4.4 Special warnings and precautions for use**).

HAEMOROL OILY PHENOL INJECTION is administered by submucosal injection of 2 to 5 mL. It may be injected into the submucosal space above each of the three principle haemorrhoids.

A maximum of 10 mL should be injected in any one treatment.

It is preferable that only sterile glass syringes be used for injecting this product, to minimise the possibility of absorption or extraction from plastic syringe components. However, plastic syringes with needles with plastic hubs may be used if the injection is to be administered immediately.

Paediatric population

HAEMOROL OILY PHENOL INJECTION is contraindicated for use in neonates or children (see **Section 4.4 Special warnings and precautions for use**).

4.3. Contraindications

HAEMOROL OILY PHENOL INJECTION is contraindicated:

- in patients who are hypersensitive to phenol or almond oil
- in neonates and children (see **Section 4.4 Special warnings and precautions for use**)
- for use over large areas, since sufficient amounts may be absorbed to give rise to toxic symptoms.

4.4. Special warnings and precautions for use

For submucosal injection only. Not for intrathecal use. Care should also be taken to avoid accidental intravenous injection.

The injection may cause severe pain if it is too close to the anal verge. Complications of therapy can include local ulceration and sterile abscess formation. These complications may be serious following a misplaced injection (e.g. prostatic abscess). Care in choosing the correct site of injection is mandatory. Solutions containing phenol should not be applied to large areas of skin or large wounds since sufficient phenol may be absorbed to give rise to toxic symptoms. Toxic symptoms may also arise through absorption of phenol vapour by the skin and lungs.

Use in the elderly

No data available.

Paediatric population

Safety in neonates and children has not been established. Significant absorption of phenol can occur in neonates. Toxic effects have been observed from other phenol formulations, and therefore HAEMOROL OILY PHENOL INJECTION is contraindicated for use in neonates or children.

Effects on Laboratory Tests

Absorbed phenol can interfere with the following laboratory tests:

- Plasma adrenaline (epinephrine) and noradrenaline (norepinephrine) estimation (trihydroxy-indole method)
- Ferric chloride test for ketones or salicylates in urine (but not the Phenistix test)
- Test for ionised calcium in serum
- Measurement of sulfonamides in serum
- Benedict test for glycosuria.

4.5. Interaction with other medicines and other forms of interaction

No significant drug interactions involving phenol are known.

4.6. Fertility, pregnancy and lactation

Pregnancy – Category B3

Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals have shown evidence of an increased occurrence of fetal damage, the significance of which is considered uncertain in humans.

Oral administration of phenol during mid gestation to rats and mice or during late gestation in rats caused embryonic and fetal resorptions, fetal and neonatal deaths reduced offspring weight and malformations (cleft palate, skeletal abnormalities). Adverse effects on the fetus were observed at phenol doses that were not toxic to the mother as well as at maternotoxic doses. The clinical relevance of the findings from rodent studies using oral phenol to human submucosal administration of HAEMOROL OILY PHENOL INJECTION is unclear. However, phenol should not be administered to pregnant women.

Breast-feeding

It is not known whether HAEMOROL OILY PHENOL INJECTION is excreted into breast milk. Since safety in neonates and children have not been established, HAEMOROL OILY PHENOL INJECTION should not be used during breast-feeding.

Fertility

The effects of HAEMOROL OILY PHENOL INJECTION on fertility and reproduction are unknown.

4.7. Effects on ability to drive and use machines

HAEMOROL OILY PHENOL INJECTION is presumed to be safe or unlikely to produce an effect on the ability to drive or use machinery.

4.8. Undesirable effects

More common reactions

A high incidence of pain has been reported after submucosal administration of HAEMOROL OILY PHENOL INJECTION. Discomfort and giddiness have also been reported. Local ulceration and sterile abscess formation may also occur.

Less common reactions

The following reactions have been reported rarely after injection of HAEMOROL OILY PHENOL INJECTION, generally as a result of misplaced injection: dysuria, transient incontinence, pyrexia, impotence, prostatic abscess.

Life threatening reactions

A case of necrotising fasciitis has been reported after injection sclerotherapy of haemorrhoids with 5% phenol in almond oil.

A case of retroperitoneal sepsis has also been reported. This reaction has also been reported rarely with other forms of haemorrhoid treatment, such as rubber band ligation.

Phenol-containing preparations:

Less common reactions

These reactions have been observed with topical use of various phenol preparations, although not necessarily HAEMOROL OILY PHENOL INJECTION itself.

Infections and infestations:

abscess, prostatic abscess, necrotising fasciitis, retroperitoneal sepsis

Immune system disorders:

allergic reactions/hypersensitivity

Nervous system:

dizziness, collapse

Eye disorders:

darkening of cornea (after prolonged use)

Cardiac disorders:

cardiac arrhythmia

Hepatobiliary disorders:
hepatitis

Skin and subcutaneous tissue disorders:
contact urticaria, darkening of skin on hands and face (after prolonged use)

Renal and urinary disorders:
dysuria, urinary incontinence, possibility of urine being tinted green

Reproductive system and breast disorders:
impotence

General disorders and administration site conditions:
pyrexia, pain, discomfort, irritation, ulcer, tissue necrosis

Life threatening reactions
Significant absorption of phenol can occur through skin and mucous membranes, resulting in serious, sometimes fatal, toxicity (see **Section 4.9 Overdose**).

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

4.9. Overdose

Symptoms

The symptoms of overdosage after submucosal injection of HAEMOROL OILY PHENOL INJECTION are not known, but are likely to be similar to symptoms observed after excessive exposure to phenol in other preparations.

Absorption of phenol after application of dilute phenol solutions to extensive wounds has resulted in abdominal pains, dizziness, methaemoglobinaemia, haemoglobinuria, cyanosis, cardiac arrhythmias, ECG abnormalities, and may result in respiratory failure, circulatory failure, coma and death.

The symptoms of oral ingestion may include local pain, nausea and/or vomiting, followed by pulmonary oedema and shock. Respiratory and circulatory damage may follow, and in severe cases fatal respiratory and circulatory failure may occur rapidly.

Treatment

There is no specific antidote for acute phenol overdose. Treatment of overdose is symptomatic and supportive.

Treatment may involve the following measures:

- For oral administration, immediate advice should be sought from the National Poisons Centre; activated charcoal may be useful
- If spillage onto skin occurs, remove all contaminated clothing, and rub contaminated skin for at least 10 minutes with swabs soaked in glycerol, a liquid macrogol or a mixture of 70% macrogol and 30% methylated spirits; water can be used initially if these are not available
- Support of respiratory functions
- Correction of fluid and electrolyte balance.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: C05BB05, ATC code: Antivaricose therapy

Mechanism of action

Phenol is an antiseptic and disinfectant. It is also corrosive. When applied to mucous membranes, it causes the surface to become white and opaque due to precipitation of proteins, and a slough is formed. When HAEMOROL OILY PHENOL INJECTION is injected into haemorrhoids, submucosal fibrosis is produced, fixing the mucosa to the underlying muscle.

Clinical trials

The long-term efficacy of HAEMOROL OILY PHENOL INJECTION was examined in 3 randomised controlled trials. Ambrose *et al* [1] compared HAEMOROL OILY PHENOL INJECTION (n=62) with infra-red photocoagulation (n=73) in patients treated with symptomatic first- or second-degree haemorrhoids. At 12 months, 26% of patients treated with HAEMOROL OILY PHENOL INJECTION were asymptomatic, compared to 30% of those treated with photocoagulation. Repeat photocoagulation was required in 7 patients compared with repeat injection in 1 ($p < 0.02$).

Cheng *et al* [2] compared HAEMOROL OILY PHENOL INJECTION with rubber band ligation (RBL), maximal anal dilatation and haemorrhoidectomy (n=30 per group) in patients with symptomatic second-degree haemorrhoids. At 12 months, 60% of patients treated with HAEMOROL OILY PHENOL INJECTION were asymptomatic, compared to 83%, 80% and 97% of those treated with RBL, maximal anal dilatation and haemorrhoidectomy, respectively. Pain due to treatment was also assessed with 27/30 patients treated with HAEMOROL OILY PHENOL INJECTION experiencing no pain compared to 26/30 patients in the RBL group, 25/30 in the maximal anal dilatation group and 0/30 in the haemorrhoidectomy group.

Gartell *et al* [3] compared HAEMOROL OILY PHENOL INJECTION with RBL in 269 patients with symptomatic first to fourth degree haemorrhoids. Questionnaires were completed by 215 patients (109 HAEMOROL OILY PHENOL INJECTION, 106 RBL) over a 6-year period with a mean follow up of 2.75 years. A successful outcome was achieved in 89% of patients receiving RBL therapy compared to 70% of patients treated with HAEMOROL OILY PHENOL INJECTION ($p < 0.01$). At the time of follow up, 17% of respondents in the HAEMOROL OILY PHENOL INJECTION group were asymptomatic, compared to 36% of those who had undergone RBL ($p < 0.01$).

5.2. Pharmacokinetic properties

Absorption

Phenol is readily absorbed through intact skin, mucous membranes and the gastrointestinal tract.

The extent of systemic absorption of HAEMOROL OILY PHENOL INJECTION following submucosal administration (when used in the treatment of haemorrhoids) is not known. Since HAEMOROL OILY PHENOL INJECTION produces submucosal fibrosis, fixing the mucosa to the underlying muscle, the amount of phenol entering the systemic circulation would be minimal.

Metabolism

It is metabolised in the liver, mainly via conjunction to phenyl glucuronide and phenyl sulfate, although small amounts are oxidised to catechol and quinol prior to further conjugation.

Excretion

The metabolites are excreted in the urine. Ninety-nine percent of an absorbed dose is excreted in the urine in 24 hours. On oxidation to quinones they may tint the urine green.

5.3. Preclinical safety data

Genotoxicity

The mutagenic potential of phenol has been assessed in numerous mutation assay systems including *in vitro* tests (e.g. Ames test) and *in vivo* tests (e.g. the mouse micronucleus test). The results of these tests indicate that phenol is considered to have mutagenic potential.

Carcinogenicity

Phenol is not carcinogenic in mice or rats of either sex at doses up to 5,000 ppm in drinking water. Other studies have not shown a carcinogenic effect of phenol, but a clear no-effect dose has not been established. The clinical relevance of these findings to the submucosal administration of HAEMOROL OILY PHENOL INJECTION is unclear.

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Almond oil

6.2. Incompatibilities

Phenol is reported to be incompatible with alkaline salts, non-ionic surfactants, acetanilide, phenazone, piperazine, quinine salts, phenacetin and iron salts. Phenol coagulates albumin and gelatinises collodion. It is also corrosive. It is preferable that only sterile glass syringes be used for injecting this product, to minimise the possibility of absorption or extraction from plastic syringe components. However, plastic syringes with needles with plastic hubs may be used if the injection is to be administered immediately.

6.3. Shelf life

HAEMOROL OILY PHENOL INJECTION has a shelf life of three years from the date of manufacture.

6.4. Special precautions for storage

Store below 25 °C. Protect from light.

6.5. Nature and contents of container

HAEMOROL OILY PHENOL INJECTION is presented in a 5 mL glass vial; 5 vials are packed in a carton.

6.6. Special precautions for disposal

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription medicine.

8. SPONSOR

AFT Pharmaceuticals Ltd
PO Box 33-203
Takapuna
Auckland 0740
Phone: 0800 423 823
Email: customer.service@aftpharm.com

9. DATE OF FIRST APPROVAL

20/02/1986

10. DATE OF REVISION OF TEXT

11/09/2020