

**HAEMOROL™ OILY PHENOL INJECTION
(PHENOL)****1 NAME OF THE MEDICINE**

Phenol

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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

Excipients of known effect: tree nuts.

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

3 PHARMACEUTICAL FORM

Haemorol is a clear, yellowish solution, free from visible particles.

4 CLINICAL PARTICULARS**4.1 THERAPEUTIC INDICATIONS**

Haemorol is indicated for the treatment of symptomatic haemorrhoids in patients with an inadequate response to conservative therapy such as dietary manipulation. It must only be injected submucosally and its use is usually confined to first degree or second degree haemorrhoids.

4.2 DOSE AND METHOD OF ADMINISTRATION

Haemorol is for submucosal injection only (i.e. local administration); personnel administering this treatment should be trained in the correct placement of submucosal injections. Haemorol 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 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. The total maximum volume that may be injected in any one treatment is 10 mL. 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.

4.3 CONTRAINDICATIONS

Haemorol is contraindicated in patients hypersensitive to phenol or almond oil, in neonates and children (see Section 4.4 Special Warnings and Precautions for Use), and 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

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Haemorol is for submucosal injection only. It is not for intrathecal use or for injection into a blood vessel or into deep tissues. Complications of therapy can include local ulceration and sterile abscess formation. These complications may be serious following a misplaced injection (e.g. prostatic abscess). Obviously, 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 use

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

Effect on laboratory tests

Absorbed phenol can interfere with the following laboratory tests:

- Plasma adrenaline and noradrenaline estimation (trihydroxyindole method)
- Ferric chloride test for ketones or salicylates in urine (but not the Phenistix test)
- Test for ionised calcium in serum
- Measurement of sulphonamides in serum
- Benedict test for glycosuria

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No significant drug interactions involving phenol are known.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

The effects of Haemorol on the reproductive cycle and fertility are unknown.

Use in 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 is unclear. However, phenol should not be administered to pregnant women.

Use in lactation

It is not known whether Haemorol is excreted into breast milk. Since safety in neonates and children has not been established, Haemorol should not be used during lactation.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

More common reactions

A high incidence of pain has been reported after submucosal administration of Haemorol. 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, generally as a result of misplaced injection: haematuria, haematospermia, epididymitis, urethral stricture, chronic cystitis, urolithiasis, seminal vesicle abscess, urinary perineal fistula, dysuria, transient incontinence, pyrexia, impotence (which may be permanent), 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 are attributable to topical exposure to various phenol preparations, although not necessarily Haemorol itself.

Body as a whole:

pyrexia, allergic reactions.

Cardiovascular system:

cardiac arrhythmia.

Central nervous system:

dizziness, collapse.

Dermatological:

contact urticaria, darkening of skin on hands and face (after prolonged exposure).

Ocular:

darkening of cornea (after prolonged exposure).

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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 registration 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 at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

The symptoms of overdosage after submucosal injection of Haemorol, are not known since there have been no reports of overdose for the treatment of sclerotherapy of haemorrhoids.

The following information relates to phenol containing products:

Symptoms of overdosage

Symptoms of overdose with Haemorol may be similar to those 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 arrhythmia's, 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 of overdosage

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

Treatment may involve the following measures:

- For oral administration, immediate advice should be sought from a Poisons Information 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 function.
- Correction of fluid and electrolyte balance.

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

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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 is injected into parahaemorrhoidal submucosa, fibrosis is produced, fixing the mucosa to the underlying muscle.

Clinical trials

The long term efficacy of Haemorol was examined in 3 randomised controlled trials. Ambrose *et al* [1] compared Haemorol (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 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 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 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 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 with RBL in 269 patients with symptomatic first to fourth degree haemorrhoids. Questionnaires were completed by 215 patients (109 Haemorol, 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 ($p < 0.01$). At the time of follow up, 17% of respondents in the Haemorol 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 following submucosal administration (when used in the treatment of haemorrhoids) is not known. Since Haemorol produces submucosal fibrosis, fixing the mucosa to the underlying muscle, the amount of phenol entering the systemic circulation would be minimal.

Distribution

No data available.

Metabolism

It is metabolised in the liver, mainly via conjugation 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.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

Phenol causes chromosomal damage in mammalian cells *in vitro* and *in vivo*; gene mutations in mammalian cells *in vitro*; and sister chromatid exchanges in mammalian cells *in vitro*. Phenol is also metabolised to substances (e.g. hydroquinone, 1,4-benzoquinone and catechol) that cause chromosomal damage and gene mutations.

Carcinogenicity

Administration of phenol via the drinking water for 103 weeks to male rats caused increases in monocytic leukaemias, thyroid C cell tumours and adrenal gland phaeochromocytomas. These changes were not dose related and there was no evidence of increased tumour development in female rats or in mice of either sex. Phenol also caused skin papillomas and carcinomas when applied topically to mice. 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 is unclear.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Haemorol, Oily Phenol Injection contains phenol 250 mg in almond oil to 5 mL (phenol 5% w/v).

6.2 INCOMPATIBILITIES

Haemorol is reported to be incompatible with alkaline salts and non-ionic surfactants.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG)¹. The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C. Protect from light.

6.5 NATURE AND CONTENTS OF CONTAINER

It is presented in a 5 mL vial in a pack of 5 vials.

Phebra product code - INJ155

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Phenol is a colourless or faintly pink or faintly yellow deliquescent crystalline solid. It is soluble in water, and very soluble in alcohol, chloroform, ether, glycerol and fixed and volatile oils.

The molecular formula of phenol is C₆H₅OH. Its molecular weight is 94.1.

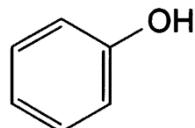
¹ AUST R 161711

PRODUCT INFORMATION

Haemorol Injection



Chemical structure



CAS number

108-95-2

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 - Prescription Only Medicine

8 SPONSOR

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9 DATE OF FIRST APPROVAL

4 Sep 2009

10 DATE OF REVISION

30 Jun 2020

11 REFERENCES

- [1] Ambrose NS, Morris D, Alexander-Williams J. A randomised trial of photocoagulation or injection sclerotherapy for the treatment of first- and second degree haemorrhoids. *Dis. Colon Rectum* 28: 238-240, 1985.
- [2] Cheng FCY, Shum DWP, Ong GB. The treatment of second degree haemorrhoids by injection, rubber band ligation, maximal anal dilatation and haemorrhoidectomy: A prospective clinical trial. *Aust.N.Z.J.Surg* :566-568, 1981.
- [3] Gartell PC, Sheridan RJ, McGinn H. Out-patient treatment of haemorrhoids: a randomised clinical trial to compare rubber band ligation with phenol injection. *Br.J.Surg.* 72: 478-479, 1985.

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SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	PI reformatted to align with new format
2	Included excipients of known effect
3	Editorial update on pharmaceutical form
4.8	Minor editorial change - typo
6.7	Relocate the physicochemical properties from section 2
8	Addition of overseas' distributor details