1 NAME OF THE MEDICINAL PRODUCT

Pepti-Calm 525.6mg/30ml Oral Suspension.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient	mg/30ml
Bismuth subsalicylate	525.6

Excipient(s) with known effect:	/30ml
Maltitol	10.20 g
Glycerin	11.34 g
Sodium benzoate	30 mg
Carmoisine edicol	0.48 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral suspension

Thick pink suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Indicated in adults and adolescents aged 16 or over for the symptomatic relief of the relief of indigestion, dyspepsia, nausea, upset stomach (due to overindulgence in food and drink) and diarrhoea.

4.2 Posology and method of administration

Posology
Adults and children over 16 years: 30ml to be taken every 30-60 minutes as required up to a maximum of eight doses in 24 hours.
Do not give to children under 16 years.

Paediatric population
Contraindicated in children aged under 16 years (see section 4.3).

Method of administration
Pepti-Calm can be taken before or after meals, on either an empty or full stomach.
For oral administration.

4.3 Contraindications

Pepti-Calm is contraindicated in:

- patients hypersensitive to bismuth subsalicylate or to any of the excipients listed in section 6.1;
- patients hypersensitive to aspirin or other salicylates;
- patients in concomitant treatment with aspirin or other salicylates;
- patients with a peptic ulcer;
- patients with blood clotting disorders;
- patients with bloody or black stool;
- children under 16 years of age (see section 4.4).

4.4 Special warnings and precautions for use

- Pepti-Calm should be stopped if symptoms get worse, if they last more than 2 days, or if ringing in the ears appears (tinnitus).
- This medicine should not be used if symptoms are severe or persist for more than 2 days.
- Pepti-Calm should not be used by those aged under 16 years, due to a possible association between salicylates and Reye's syndrome, a rare but very serious disease (see section 4.3). This is particularly important in those who have or are recovering from a viral infection such as chicken pox or flu.
- In patients with diarrhoea, especially in frail and elderly patients, fluid and electrolyte depletion may occur. In such cases administration of appropriate fluid and electrolyte replacement therapy is the most important measure.
- Do not take with aspirin or other salicylates.
- Caution should be exercised by patients who have blood clotting disorders

or gout or who are taking medicines for anti-coagulation (thinning of blood), diabetes or gout.

- Do not exceed the recommended dose. Do not use for more than 2 days except on the advice of a doctor. Use at doses higher than recommended or for prolonged periods is associated with an increased risk of severe side effects (notably bismuth and salicylate intoxication).
- Keep all medicines out of reach and sight of children.

Important information about some of the ingredients in this medicine.
Patients with rare hereditary problems of fructose intolerance should not take this medicine. This medicine contains maltitol which may have a mild laxative effect. Calorific value 2.3 kcal/g maltitol.

This medicine contains glycerin which may cause headache, stomach upset and diarrhoea.

This medicine contains 30 mg of sodium benzoate in each 30ml, which is equivalent to 1mg/ml.

This medicine contains carmoisine edicol (E122) which may cause allergic reactions.

This medicinal product contains 63 mg sodium per 30 ml dose, equivalent to 3.15 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5 Interaction with other medicinal products and other forms of interaction

Pepti-Calm contains salicylates therefore care should be exercised in patients taking:

- anti-coagulant therapy (blood thinners) as concomitant use may increase the risk and severity of bleeding;
- medicines for gout (e.g., probenecid, sulfinpyrazone) as concomitant use may increase the risk of hyperuricemia and worsening gout;
- sulfonylurea medicines for diabetes (e.g., chlorpropamide, glibenclamide) as concomitant use may increase the risk of hypoglycaemia;
- medicines for arthritis (e.g., methotrexate) due to potential drug interactions.

Special precautions with tetracycline antibiotics, as co-administration may alter the pharmacokinetics of some antibiotics such as tetracycline and doxycycline (tetracycline antibiotics can lead to reduced bioavailability of bismuth subsalicylate due to interaction with aluminium magnesium silicate in the formulation). Additionally, the absorption of tetracycline antibiotics can be reduced when concurrently taken with products containing bismuth. This interaction can be minimised by separating the doses of the two drugs by a couple of hours.

Do not use in patients taking aspirin or other salicylates due to the risk of overdose and salicylate toxicity.

4.6 Fertility, pregnancy and lactation

Pregnancy:

The safety of Pepti-Calm during pregnancy and lactation has not been established and therefore use during these periods is not recommended.

Animal studies are insufficient with respect to effects on pregnancy, embryonal/foetal development, parturition and postnatal development. The potential risk for humans is unknown. Pepti-Calm should not be used during pregnancy.

Lactation:

There is limited information on the excretion of bismuth subsalicylate in human or animal breast milk. Physico-chemical and available pharmacodynamic data on bismuth subsalicylate point to excretion in breast milk and a risk to the suckling child cannot be excluded. Pepti-Calm should not be used during breast-feeding.

4.7. Effects on ability to drive and use machines

No adverse effects known.

4.8 Undesirable effects

Tabulated list of adverse reactions

Adverse reactions are listed in the below table by System Organ Class and in order of decreased seriousness within each frequency grouping. Frequencies are defined as: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data).

The most common AEs are benign and transient blackening of the faeces (~15%) and discoloration (blackening) of the surface of the tongue (~8%). This phenomenon is caused by the reaction of malodorous sulfide gases from fermentation of food residues with bismuth resulting in an odorless black insoluble bismuth sulfide salt.

System Organ Class	Frequency	Adverse reaction
Gastrointestinal disorders	Common	Black tongue
	Very common	Black stool

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 Yellow Card Scheme at www.mhra.gov.uk/yellowcard

4.9 Overdose

Bismuth

Bismuth intoxication may present as an acute encephalopathy with confusion, myoclonic movements, tremor, dysarthria and walking and standing disorders. Bismuth intoxication may also include gastrointestinal disturbances, skin reactions, stomatitis and discolouration of the mucous membranes, and renal dysfunction as a result of acute tubular acidosis

Treatment includes gastric lavage, purgation, and hydration. Chelating agents may be effective in the early stages following ingestion and haemodialysis may be necessary.

Salicylate poisoning is usually associated with plasma concentrations >350mg/L (2.5mmol/L). Most adult deaths occur in patients whose concentrations exceed 700 mg/L (5.1mmol/L). Single doses less than 100mg/kg are unlikely to cause serious poisoning.

Common features of salicylate poisoning include vomiting, dehydration, tinnitus, vertigo, deafness, sweating, warm extremities with bounding pulses, increased respiratory rate and hyperventilation. Some degree of acid-base disturbance is present in most cases.

A mixed respiratory alkalosis and metabolic acidosis with normal or high arterial pH (normal or reduced hydrogen ion concentration) is usual in adults and children over the age of 4 years. In children aged 4 years or less, a dominant metabolic acidosis with low arterial pH (raised hydrogen ion concentration) is common. Acidosis may increase salicylate transfer across the blood brain barrier.

Uncommon features of salicylate poisoning include haematemesis, hyperpyrexia, hypoglycaemia, hypokalaemia, thrombocytopaenia, increased INR/PTR, intravascular coagulation, renal failure and non-cardiac pulmonary oedema.

Central nervous system features including confusion, disorientation, coma and convulsions are less common in adults than in children.

Give activated charcoal if an adult presents within one hour of ingestion of more than 250mg/kg. The plasma salicylate concentration should be measured, although the severity of poisoning cannot be determined from this alone and the clinical and biochemical features must be taken into account. Elimination is increased by urinary alkalinisation, which is achieved by the administration of 1.26% sodium bicarbonate. The urine pH should be monitored. Correct metabolic acidosis with intravenous 8.4% sodium bicarbonate (first check serum potassium). Forced diuresis should not be used since it does not enhance salicylate excretion and may cause pulmonary oedema.

Haemodialysis is the treatment of choice for severe poisoning and should be considered in patients with plasma salicylate concentrations >700mg/L (5.1mmol/L),

or lower concentrations associated with severe clinical or metabolic features. Patients under 10 years or over 70 have increased risk of salicylate toxicity and may require dialysis at an earlier stage.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic code: ATC code A07B B

The demulcent base provides a protective coating of the lower oesophagus and a partial coating in the stomach which holds the bismuth subsalicylate in suspension (BSS).

Limited in vitro studies have shown BSS to have some activity against enteropathogens, i.e., Clostridium Bacteroides, E. Coli, Salmonella Shigella, Campylobacter (Helicobacter) and Yersinia, but not against anaerobes. There are insufficient data to determine whether these findings have any relevance to treatment outcomes in the patient population who may receive BSS.

5.2 Pharmacokinetic properties

Bismuth subsalicylate is converted to bismuth carbonate and sodium salicylate in the small intestine.

The oral bioavailability of bismuth administered as Bismuth subsalicylate is extremely low. Very little is known about bismuth distribution in human tissue. Renal clearance is the primary route of elimination for absorbed bismuth, however biliary clearance may also have a role. The remainder is eliminated as insoluble bismuth salts in the faeces. Following the maximum recommended daily adult dose, the mean biological half life is approximately 33 hours and peak plasma bismuth levels remain below 35ppb.

Salicylate is absorbed from the intestine and rapidly distributed to all body tissues. Peak plasma levels after maximum recommended daily dosing are about 110 micrograms/ml. Salicylate is rapidly excreted from the body and has a mean biological half life of approximately 4 - 5.5 hours.

5.3. Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included.

6 PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Maltitol liquid
Glycerin.
Dispersible cellulose (containing microcrystalline cellulose and sodium carboxymethylcellulose)
Xanthan gum
Citric acid monohydrate
Sodium citrate
Sodium benzoate
Rootbeer flavour (containing polypropylene glycol)
Carmoisine Edicol E (E122)
Purified water

6.2. Incompatibilities

None

6.3. Shelf-life

18 Months

6.4. Special precautions for storage

Do not store above 25°C

SUMMARY OF PRODUCT CHARACTERISTICS

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- Do not take with aspirin or other salicylates.
- Caution should be exercised by patients who have blood clotting disorders or gout or who are taking medicines for anti-coagulation (thinning of blood), diabetes or gout.
- Do not exceed the recommended dose. Do not use for more than 2 days except on the advice of a doctor. Use at doses higher than recommended or for prolonged periods is associated with an increased risk of severe side effects (notably bismuth and salicylate intoxication).
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5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

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Glycerin
Microcrystalline cellulose
Sodium carboxymethylcellulose
Xanthan gum
Citric acid monohydrate
Sodium citrate
Sodium benzoate
Rootbeer flavour (containing polypropylene glycol)
Carmoisine Edicol E (E122)
Purified water

6.2 Incompatibilities

None

6.3 Shelf-life

18 months

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

A 150ml, 180ml or 300ml white flint glass bottle with a roll on aluminium closure and expanded polyethylene liner.

6.6 Instructions for use/handling

Not applicable

7 MARKETING AUTHORISATION HOLDER

The Boots Company PLC
1 Thane Road West
Nottingham NG2 3AA

Trading as: BCM

8 MARKETING AUTHORISATION NUMBER

PL 00014/0615

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 02 November 2000

10 DATE OF (PARTIAL) REVISION OF THE TEXT

tbc

6.6. Instruction for use/handling

Not applicable

7. MARKETING AUTHORISATION HOLDER

The Boots Company PLC
1 Thane Road West
Nottingham NG2 3AA
United Kingdom

8. MARKETING AUTHORISATION NUMBER

PL 00014/0615

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

28/03/2006

10 DATE OF REVISION OF THE TEXT

14/04/2026