AUSTRALIAN PRODUCT INFORMATION – BISOLVON® CHESTY (BROMHEXINE HYDROCHLORIDE)

1 NAME OF THE MEDICINE

Bromhexine hydrochloride

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Bisolvon Chesty Oral Liquid contains 4 mg/5mL of bromhexine hydrochloride

Bisolvon Chesty Kids Oral Liquid contains 4 mg/5mL of bromhexine hydrochloride

Bisolvon Chesty Forte Oral Liquid contains 8 mg/5mL of bromhexine hydrochloride

Bisolvon Chesty Forte Tablets contains 8 mg per tablet of bromhexine hydrochloride

Excipients with known effect: sugars, sucralose, maltitol and benzoates.

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

3 PHARMACEUTICAL FORM

Bisolvon Chesty Oral Liquid is a clear to almost clear and colourless to almost colourless solution with an aroma of chocolate and cherry.

Bisolvon Chesty Kids Oral Liquid is a clear to almost clear and colourless to almost colourless solution with a fruity aromatic odour of strawberry.

Bisolvon Chesty Forte Oral Liquid is a clear to almost clear and colourless to almost colourless solution with an aroma of chocolate and cherry.

Bisolvon Chesty Forte Tablets are round, white and bevel-edged tablets. One side is scored and impressed with ‘51B’ on both sides of the score.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

For use as a mucolytic to break down mucus and help clear the chest in conditions accompanied by excessive mucus secretions, such as in the common cold, influenza, infections of the respiratory tract or in other conditions where excess mucus is produced.

4.2 DOSE AND METHOD OF ADMINISTRATION

Bisolvon Chesty Oral Liquid and Bisolvon Chesty Kids Oral Liquid

Adults & Children 12 years and over: 10 mL (8 mg) three times a day when necessary. May be increased to 20 mL (16 mg) three times a day for the first seven days.

Children 6 - 11 years: 10 mL (8 mg) three times a day when necessary.

Bisolvon Chesty Forte Oral Liquid

Adults & Children 12 years and over: 5 mL (8 mg) three times a day when necessary. May be increased to 10 mL (16 mg) three times a day for the first seven days.

Children 6 - 11 years: 5 mL (8 mg) three times a day when necessary.

Bisolvon Chesty Forte Tablets

Adults & Children 12 years and over: One tablet (8 mg) three times a day when necessary. May be increased to two tablets (16 mg) three times a day for the first seven days.

Children 6 - 11 years: One tablet (8 mg) three times a day when necessary.

For children between 6 to 11 years of age, use Bisolvon Chesty Oral Liquid, Bisolvon Chesty Forte Oral Liquid or Bisolvon Chesty Forte Tablets.

When infection is present, specific treatment with antibiotics could be indicated in addition to

Bisolvon Chesty therapy.

Medical advice should be sought if symptoms do not improve rapidly.

Method of administration

For oral use

4.3 CONTRAINDICATIONS

Bisolvon Chesty should not be used in patients known to be hypersensitive to bromhexine or any other excipients of the formulation.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Bisolvon Chesty should be used with caution in patients with severe liver disease and severe renal failure (refer to Section 5.2 Pharmacokinetic properties).

Use with caution in patients with gastric ulceration.

Patients should be advised to expect an increase in the flow of mucus secretions.

There have been very rare reports of severe skin lesions such as Stevens Johnson Syndrome and toxic epidermal necrolysis (TEN) in temporal association with the administration of mucolytic substances such as bromhexine. Mostly, these could be explained by the patient's underlying disease and/ or concomitant medication. In addition during the early phase of a Stevens-Johnson syndrome or TEN a patient can first experience non-specific influenza-like prodromes like e.g fever, aching body, rhinitis, cough and sore throat. Misled by these non-specific influenza-like prodromes it is possible that a symptomatic treatment is started with a cough and cold medication. Therefore, if new skin or mucosal lesions occur, medical advice should be sought immediately and treatment with bromhexine should be discontinued as a precaution.

Bisolvon Chesty Oral Liquid and **Bisolvon Chesty Kids Oral Liquid** contains at least 2.5 g of maltitol in each 5 mL and up to 2.4 g of sorbitol per maximum recommended daily dose of 60 mL. Products containing maltitol and sorbitol may have a laxative effect or cause diarrhoea in some people. This is more likely if several products containing maltitol, sorbitol or related substances are consumed simultaneously. Patients with rare hereditary fructose intolerance should not take these products.

Calorific value 2.3 kcal/g maltitol.

Bisolvon Chesty Forte Oral Liquid contains at least 2.5g of maltitol in each 5 mL up to 1.2 g of sorbitol per maximum recommended daily dose of 30 mL. Products containing maltitol and sorbitol may have a laxative effect or cause diarrhoea in some people. This is more likely if several products containing maltitol, sorbitol or related substances are consumed simultaneously. Patients with rare hereditary fructose intolerance should not take these products.

Calorific value 2.3 kcal/g maltitol.

Bisolvon Chesty Forte Tablets contains 444 mg of lactose per maximum recommended daily dose. Patients with rare hereditary galactose intolerance e.g. galactosaemia should not take this product.

Use in hepatic impairment

Bisolvon Chesty should be used with caution in patients with severe liver disease. (refer to Section 5.2 Pharmacokinetic properties).

Use in renal impairment

Bisolvon Chesty should be used with caution in patients with severe renal failure (refer to Section 5.2 Pharmacokinetic properties)

Use in the elderly

There is no pharmacokinetic data available in the elderly or in patients with renal or liver insufficiency. (refer to Section 5.2 Pharmacokinetic properties)

Paediatric use

Do not use Bisolvon Chesty in children under 6 years of age.

Use in children aged 6 to 11 years only on the advice of a doctor, pharmacist or nurse practitioner.

Effects on laboratory tests

No data available

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No clinically relevant unfavourable interactions with other medicines have been reported.

Following the administration of bromhexine, the antibiotic concentrations of amoxycillin, erythromycin and oxytetracycline in the sputum and bronchopulmonary secretions are increased.

Also, interaction studies with oral anticoagulants or digoxin were not performed. Bromhexine pharmacokinetics are not relevantly affected by co-administration of ampicillin or oxytetracycline. There was also no relevant interaction between bromhexine and erythromycin according to a historical comparison. The lack of any relevant interaction reports during the long term marketing of the drug suggests no substantial interaction potential with these drugs.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy

Category A: Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

Bromhexine crosses the placental barrier. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

Clinical experience to date has shown no evidence of harmful effects on the foetus during pregnancy. Nonetheless, the usual precautions regarding the use of drugs during pregnancy should be observed. Especially during the first trimester, the use of Bisolvon is not recommended.

Use in lactation

Bromhexine is excreted in breast milk. Although unfavourable effects on breastfed infants would not be expected, Bisolvon Chesty is not recommended for use in breastfeeding mothers.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

When used as recommended and when there are no side effects, Bisolvon is not known to have any effect on the ability to drive or operate machinery.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Immune system disorder

Skin and subcutaneous tissue disorders and Respiratory, mediastinal and thoracic disorders.

Anaphylactic reaction including anaphylactic shock

Angioedema, bronchospasm, rash, urticaria, pruritus and other hypersensitivity.

Gastro-intestinal disorders

Nausea, vomiting, diarrhoea, upper abdominal pain and other mild gastrointestinal side effects.

Nervous system disorders

Headache, dizziness, sweating.

Hepatic system disorders

A transient rise in serum aminotransferase values.

Reporting suspected adverse effects

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 (Australia) or https://nzphvc.otago.ac.nz/reporting/ (New Zealand).

4.9 OVERDOSE

No specific overdose symptoms have been reported in man to date. Based on accidental overdose and/or medication error reports the observed symptoms are consistent with the known side effects of BISOLVON CHESTY at recommended doses and may need symptomatic treatment.

In case of overdose, immediately call the Poisons Information Centre telephone 13 11 26 (Australia) or the National Poisons Centre, 0800 POISON or 0800 764 766 (New Zealand).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Bromhexine hydrochloride is a mucolytic. It has been shown to enhance the transport of mucus by reducing its viscosity and by activating the ciliated epithelium (mucociliary clearance).

Clinical trials

Preclinical studies have shown that bromhexine increases the amount of thin watery bronchial secretion. Clinical studies show that bromhexine has a secretolytic and secretomotor effect in the bronchial tract area, which facilitates expectoration and eases cough.

Following the administration of bromhexine, the antibiotic concentrations of amoxycillin, erythromycin and oxytetracycline in the sputum and bronchopulmonary secretions are increased.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Following oral administration, bromhexine shows dose linear pharmacokinetics in the dose range of 8-32 mg. It is rapidly and completely absorbed from the gastrointestinal tract. The bioavailability after oral administration is substantially reduced by an extensive first-pass effect in the range of 75-80%. The absolute bioavailability of bromhexine hydrochloride is about 22.2 ± 8.5 % and 26.8 ± 13.1 % for Bisolvon tablets and solution, respectively. Concomitant food intake leads to an increase of bromhexine plasma concentrations.

Distribution

After intravenous administration, bromhexine was rapidly and widely distributed throughout the body with a mean volume of distribution (Vss) of up to 1209 ± 206 L (19 L/kg). The distribution of bromhexine in lung tissue (bronchial and parenchymal) was investigated after oral administration of 32 mg and 64 mg bromhexine. Bromhexine lung tissue concentrations two hours post-dose were 1.5 to 3.2 times higher in bronchiolo-bronchial tissues and between 3.4 and 5.9 times higher in pulmonary parenchyma compared to plasma concentrations. Bromhexine crosses the blood-brain barrier and only a small amount crosses the placenta. Unchanged bromhexine is 95% bound to plasma proteins.

Metabolism and Excretion

Bromhexine has a high extraction ratio drug after intravenous administration (clearance is 843-1073 mL/min, within the range of the hepatic blood flow) resulting in high inter- and intra-individual variability (CV > 30%). After administration of radiolabelled bromhexine, about 97.4 ± 1.9% of the dose was recovered in the urine, with less than 1% as the parent compound. Bromhexine plasma concentrations showed a multi-exponential decline. After administration of single oral doses between 8 and 32 mg, the terminal half-life of bromhexine ranged between 6.6 and 31.4 hours. The relevant half-life to predict the multiple dose pharmacokinetics is about 1 hour. No accumulation was observed after multiple dosing (accumulation factor 1.1).

Bromhexine is almost completely metabolised to a variety of hydroxylated metabolites and to dibromanthranilic acid. Ambroxol is a metabolite of bromhexine.

There is no pharmacokinetic data available in the elderly or in patients with renal or liver insufficiency. Extensive clinical experience did not give rise to relevant safety concerns in these populations. However, reduced clearance of bromhexine parent substance may be expected in the case of severe liver disease; in the case of severe renal insufficiency, accumulation of metabolites cannot be ruled out.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Bisolvon Chesty and Bisolvon Chesty Forte Oral Liquid also contain Maltitol solution, sucralose, benzoic acid, menthol, chocolate flavour 96534-33, cherry flavour 96323-33 and purified water.

Bisolvon Chesty Kids Oral Liquid also contains maltitol solution, sucralose, benzoic acid, hydroxyethylcellulose, cherry flavour 96323-33, strawberry flavour 12006M and purified water.

Bisolvon Chesty Forte Tablets contain bromhexine hydrochloride 8 mg per tablet. Each tablet also contains lactose, maize starch and magnesium stearate.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

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). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Bisolvon Chesty Oral Liquid and Bisolvon Chesty Forte Oral Liquid (bottles) should be stored below 25°C.

Bisolvon Chesty Forte Tablets should be stored below 25°C.

6.5 NATURE AND CONTENTS OF CONTAINER

Bisolvon Chesty Oral Liquid:

Container type

Bottle

Pack sizes

Packs of 200mL and 250 mL

Bisolvon Chesty Kids Oral Liquid:

Container type

Bottle,

Pack sizes

60 mL, 100 mL, 125 mL, 200 mL, 250 mL

Note: Not all pack sizes may be available.

Bisolvon Chesty Forte Oral Liquid:

Container type

Bottle,

Pack sizes

200 mL, 250 mL

Note: Not all pack sizes may be available.

Bisolvon Chesty Forte Tablets:

Container type

Blister, Al/PVC/PVDC

Pack sizes

Packs of 10, 20, 30, 50 or 100 tablets.

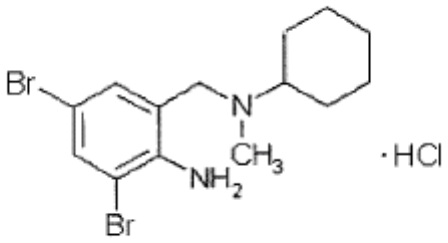
Note: Not all pack sizes may be available.

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

Chemical structure



CAS number

611-75-6

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 2 –Pharmacy Medicine

8 SPONSOR

Sanofi Consumer Healthcare,

87 Yarraman Place, Virginia,

Qld 4014 Australia.

Toll-free: 1800 818 806

Sanofi-Aventis New Zealand Limited,

Auckland, New Zealand.

Toll-free: 0800 283 684

www.bisolvon.com.au

9 DATE OF FIRST APPROVAL

BISOLVON CHESTY Oral Liquid	AUST R 133244	27/11/06
BISOLVON CHESTY KIDS Oral Liquid	AUST R 182576	28/04/11
BISOLVON CHESTY FORTE Oral Liquid	AUST R 133204	23/11/06
BISOLVON CHESTY FORTE Tablets	AUST R 125375	25/01/06

10 DATE OF REVISION

19 August 2024

Summary table of changes

Section Changed	Summary of new information
6.5	Inclusion of new pack size ‘200mL’