

# NEW ZEALAND DATA SHEET

## 1 PRODUCT NAME

BISOLVON CHESTY FORTE

Bromhexine hydrochloride tablets

Bromhexine hydrochloride Oral Solution

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet of Bisolvon Chesty Forte contains bromhexine hydrochloride 8 mg.

Each 5mL of Bisolvon Chesty Forte Oral contains bromhexine hydrochloride 8 mg.

## 3 PHARMACEUTICAL FORM

Oral tablet

Oral solution

## 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

Do not use 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.

Bisolvon Chesty Forte Tablets:

Adults and 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:

1 tablet three times a day when necessary.

Bisolvon Chesty Forte Oral Solution:

Adults and 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:

5mL (8 mg) three times a day when necessary.

The measuring cup provided should be used for dosing.

The oral liquid is alcohol-free and sugar-free and therefore suitable for diabetics.

When infection is present, specific treatment with antibiotics could be indicated in addition to BISOLVON CHESTY FORTE therapy.

BISOLVON can be taken with or without food (see Pharmacokinetics).

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Patients being treated with BISOLVON should be notified of an expected increase in the flow of secretions.

In acute respiratory indications, medical advice should be sought if symptoms do not improve after 4-5 days or worsen during the course of therapy.

### 4.3 Contraindications

BISOLVON CHESTY FORTE is contraindicated in patients known to be hypersensitive to bromhexine or any other component of the formulation.

Do not use BISOLVON CHESTY FORTE tablets or oral solution in children under 6 years of age.

In case of rare hereditary conditions that may be incompatible with an excipient of the product (refer to Warnings and Precautions), the use of the product is contraindicated.

### 4.4 Special warnings and precautions for use

BISOLVON CHESTY FORTE should be used with caution in patients with severe liver disease and severe renal failure (refer Pharmacokinetics).

Use with caution in patients with gastric ulceration.

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

One BISOLVON CHESTY FORTE tablet contains 74 mg of lactose, corresponding to 222 mg of lactose per recommended total daily dose (resp. 444 mg of lactose in case of double dose in adults and children over 12 years at commencement of treatment). Patients with rare hereditary galactose intolerance e.g. galactosaemia should not take this product.

BISOLVON CHESTY FORTE oral solution contains at least 7.5 g of maltitol and up to 1.2 g of sorbitol per maximum recommended total 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.

There have been very few reports of severe skin lesions such as Stevens Johnson Syndrome and toxic epidermal necrolysis (TEN) in temporal association with the administration of expectorants such as bromhexine hydrochloride. Mostly, these could be explained by the severity of the patient's underlying disease and or concomitant medication. In addition during the early phase of a Stevens-Johnson syndrome or TEN a patient may 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 hydrochloride should be discontinued as a precaution.

### 4.5 Interaction with other medicines and other forms of interaction

No clinically relevant unfavourable interactions with other medicines, such as ampicillin, oxytetracycline or erythromycin, have been reported (refer to Actions). Interaction studies with oral anticoagulants or digoxin were not performed.

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### 4.6 Fertility, pregnancy and lactation

**Fertility:** No studies on the effect on human fertility have been conducted with BISOLVON CHESTY FORTE. Based on available pre-clinical experience there are no indications for possible effects of the use of bromhexine on fertility.

**Use in pregnancy:** There are limited data from the use of bromhexine in pregnant women. Pre-clinical studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.

As a precautionary measure, it is preferable to avoid the use of BISOLVON CHESTY FORTE during pregnancy.

**Use in lactation:** It is unknown whether bromhexine/metabolites are excreted in human milk. Available pharmacodynamic/toxicological data in pre-clinical studies have shown excretion of bromhexine/metabolites in breast milk. A risk to the breastfed infant cannot be excluded. BISOLVON CHESTY FORTE should not be used during breast-feeding.

### 4.7 Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed with BISOLVON CHESTY FORTE.

### 4.8 Undesirable effects

**Immune system disorder:** hypersensitivity, anaphylactic reaction, anaphylactic shock

**Skin and subcutaneous tissue disorders:** angioedema, rash, urticaria, pruritus

**Respiratory, mediastinal and thoracic disorders:** bronchospasm

**Gastro-intestinal disorders:** Nausea, vomiting, diarrhoea and abdominal pain upper.

### 4.9 Overdose

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

Advice can be obtained from the Poisons Information Centre (telephone 0800 764 766).

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

**Pharmacotherapeutic group:** Expectorants, excl. combinations with cough suppressants  
**ATC-Code:** R05CB02

Bromhexine is a synthetic derivative of the herbal active ingredient vasicine.

### 5.2 Pharmacokinetic properties

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

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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.

### 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 70-80%. The absolute bioavailability of bromhexine hydrochloride is about  $22.2 \pm 8.5\%$  up to  $26.8 \pm 13.1\%$  for BISOLVON CHESTY FORTE tablets and oral solution, respectively. Concomitant food intake tended to increase bromhexine plasma concentrations probably due to partial inhibition of the first pass-effect.

### Distribution

After intravenous administrations bromhexine was rapidly and widely distributed throughout the body with a mean volume of distribution ( $V_{ss}$ ) of up to  $1209 \pm 206$  L (19 L/kg). The distribution into lung tissue (bronchial and parenchymal) was investigated after oral administration of 32 mg and 64 mg bromhexine. Lung-tissue concentrations two hours post dose 1.5 - 4.5 times higher in bronchiolo-bronchial tissues and between 2.4 and 5.9 times higher in pulmonary parenchyma compared to plasma concentrations. Unchanged bromhexine is bound to plasma proteins by 95% (non-restrictive binding).

### Metabolism

Bromhexine is almost completely metabolised to a variety of hydroxylated metabolites and to dibromanthranilic acid. All metabolites and bromhexine itself are conjugated most probably in form of N-glucuronides and O-glucuronides. There are no substantial hints for a change of the metabolic pattern by a sulphonamide, oxytetracycline or erythromycin. Thus relevant interactions with CYP 450 2C9 or 3A4 substrates are unlikely.

### Elimination

Bromhexine is a high extraction ratio drug (CL after intravenous administration is  $\sim 843$ -1073 mL/min) resulting in high inter- and intra-individual variability. Bromhexine is almost completely metabolised to a variety of hydroxylated metabolites and to dibromanthranilic acid. Ambroxol is a metabolite of bromhexine. After administration of radiolabelled bromhexine, about  $97.4 \pm 1.9\%$  of the dose was recovered in the urine, with less than 1% as the parent compound. Unchanged bromhexine is 95% bound to plasma proteins. Bromhexine plasma concentrations showed a multi-exponential decline. After administration of single oral doses between 8 and 32 mg, the terminal elimination 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).

### Linearity/Non-linearity

Bromhexine shows dose proportional pharmacokinetics in the range of 8-32 mg following oral administration.

### Special populations

There are no data for bromhexine pharmacokinetics 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.

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## 5.3 Preclinical safety data

Preclinically, it has been shown to increase the proportion of serous bronchial secretion. Bromhexine enhances mucus transport by reducing mucus viscosity and by activating the ciliated epithelium (mucociliary clearance). Clinical studies show that bromhexine has a secretolytic and secretomotoric effect in the bronchial tract area, which facilitates expectoration and eases cough.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Bisolvon Chesty Forte Tablets contain: lactose, maize starch, magnesium stearate.

Bisolvon Chesty Forte Oral Solution contains: Maltitol solution, sucralose, benzoic acid, menthol, chocolate flavour 96534-33, cherry flavour 96323-33 and purified water.

### 6.2 Incompatibilities

No information available

### 6.3 Shelf life

BISOLVON CHESTY FORTE Tablets: 36 months

BISOLVON CHESTY FORTE Oral Solution: 36 months

### 6.4 Special precautions for storage

Bisolvon Chesty Forte Tablets: Store below 30°C, out of the reach of children.

Bisolvon Chesty Forte Oral Solution: Store below 25°C, out of the reach of children.

### 6.5 Nature and contents of container

BISOLVON CHESTY FORTE tablets are round, white bevel-edged tablets. One side is scored and impressed with '51B' on both sides of the score. Each tablet contains 8 mg bromhexine hydrochloride and is available in blister packs of 10, 30, 50 and 100 tablets. Not all pack sizes may be available.

BISOLVON CHESTY FORTE oral solution is a clear to almost colourless solution with an aroma of chocolate and cherry, available in bottles of 200 mL. Each 5 mL contains 8 mg bromhexine hydrochloride.

### 6.6 Special precautions for disposal

No special requirements

## 7 MEDICINE SCHEDULE

Pharmacy only medicine

## 8 SPONSOR

sanofi-aventis new zealand limited

Level 8

# NEW ZEALAND DATA SHEET

56 Cawley Street  
Ellerslie, Auckland  
New Zealand  
Toll Free Number (medical information 0800 283 684)  
Email [medinfo.australia@sanofi.com](mailto:medinfo.australia@sanofi.com)

## 9 DATE OF FIRST APPROVAL

BISOLVON CHESTY FORTE Tablets: 31 December 1969

BISOLVON CHESTY FORTE Oral Solution: 3 December 1998

## 10 DATE OF REVISION OF THE TEXT

29 March 2019

## SUMMARY TABLE OF CHANGES

SECTION	CHANGE
6.5 Nature and contents of container	Deletion of the company logo in the description of the tablet appearance.
8 Sponsor	Removal of the building name from the address. Addition of email address.