

Bisolvon® Kids

Composition

5 ml syrup contain

4 mg N-cyclohexyl-N-methyl-(2-amino-3,5-dibromobenzyl)amine hydrochloride
(= bromhexine hydrochloride)

Excipients

Maltitol Liquid, Sucralose, Benzoic acid, Hydroxyethylcellulose, Strawberry Flavour, Cherry Flavour, Purified Water

Product Description

Clear to almost clear and colourless to almost colourless solution.

Indications

BISOLVON® acts as mucolytic to facilitate productive cough

Dosage and Administration

Syrup 4mg/5ml

Adults and children > 10 years : 3 x 10 ml daily

Children 6 - 10 years : 3 x 5ml daily

Children 2 - 5 years : 2 x 5ml daily

Or according to doctor's prescription

General

The syrup is sugar-free and therefore suitable for diabetics and small children.

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 or worsen during course of therapy.

Contraindications

BISOLVON® is contraindicated in patients known to be hypersensitive to bromhexine or other excipients of the formulations.

Special Warnings and Precautions

There have been very few reports of severe skin reactions such as erythema multiforme, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) and acute generalised exanthematous pustulosis (AGEP) associated with the administration of expectorants such as bromhexine hydrochloride. Mostly these could be explained by the severity of the patient's underlying disease 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 discontinued as a precaution.

BISOLVON® syrup 4mg/5ml contains 15 g maltitol liquid per maximum recommended daily dose. This product may have a mild laxative effect.

Interactions

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

Fertility, pregnancy and lactation

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 (see section Toxicology).

As a precautionary measure, it is preferable to avoid the use of BISOLVON[®] during pregnancy.

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 in breast milk.

A risk to the breastfed infant cannot be excluded.

BISOLVON[®] should not be used during breast-feeding.

Fertility

No studies on the effect on human fertility have been conducted with BISOLVON[®].

Based on available pre-clinical experience there are no indications for possible effects of the use of bromhexine on fertility (see section Toxicology).

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[®].

Side Effects

The following CIOMS frequency rating is used, when applicable:

Very common $\geq 10\%$; Common ≥ 1 and $< 10\%$; Uncommon ≥ 0.1 and $< 1\%$;

Rare ≥ 0.01 and $< 0.1\%$; Very rare $< 0.01\%$; Not known (cannot be estimated from available data).

Immune system disorders

Rare: hypersensitivity

Not known: anaphylactic reactions including anaphylactic shock

Respiratory, thoracic and mediastinal disorders

Not known: Bronchospasm

Gastro-intestinal disorders

Uncommon: Nausea, vomiting, diarrhoea and abdominal pain upper.

Skin and subcutaneous tissue disorders

Rare: rash

Not known: Severe cutaneous adverse reactions (including erythema multiforme, stevens-johnson syndrome/toxic epidermal necrolysis and acute generalized exanthematous pustulosis), angioedema, urticaria, pruritus.

Reporting of suspected adverse reactions

Report immediately if you experience any adverse reaction or undesirable condition during and after using the medicinal product to farmakovigilans@kalventis.com.

Overdose

Signs and Symptoms

No specific overdose symptoms have been reported in human.

Management

Based on accidental overdose and/or medication error reports the observed symptoms are consistent with the known side effects of BISOLVON® at recommended doses and may need symptomatic treatment.

Pharmacological Properties

Pharmacotherapeutic group: Expectorants, excl. combinations with cough suppressants

ATC-Code: R05CB02

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

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).

Pharmacodynamics

Drug/ drug interactions in Pharmacodynamics and Pharmacokinetics

Following the administration of bromhexine antibiotic concentrations (amoxicillin, erythromycin, 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.

Pharmacokinetics

Absorption

Bromhexine is rapidly and completely absorbed from the gastrointestinal tract.

After oral administration solid and liquid formulations show similar bioavailability.

The absolute bioavailability of bromhexine hydrochloride was about $22.2 \pm 8.5 \%$ and $26.8 \pm 13.1 \%$ for BISOLVON® tablets and solution, respectively.

The first pass metabolism amounts to about 75-80%.

Concomitant food leads to an increase of bromhexine plasma concentrations.

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 ± 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 were 1.5 - 3.2 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 (i.v.) administration in the range of the hepatic blood flow, 843-1073 mL/min) resulting in high inter- and intra-individual variability (CV > 30 %). After administration of radiolabelled bromhexine about 97.4 ± 1.9 % of the dose were recovered as radioactivity in urine, with less than 1% as parent compound. Bromhexine plasma concentrations showed a multiexponential decline. After administration of single oral doses between 8 and 32 mg, the terminal elimination half-life ranged between 6.6 and 31.4 hours. The relevant half-life to predict the multiple dose pharmacokinetics is about 1 hour, thus no accumulation was seen 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.

Clinical Studies

In clinical studies, bromhexine showed a secretolytic and secretomotor effect in the bronchial tract area, which facilitates expectoration and eases cough.

Nonclinical Safety Data

Single Dose Toxicity

Bromhexine hydrochloride showed low acute toxicity: Oral Lethal Dose (LD₅₀) values were > 5 g/kg in rats, > 4 g/kg in rabbits, > 10 g/kg in dogs, and > 1 g/kg in newborn rats. The intra peritoneal . LD₅₀ in rats was 2 g/kg. The LD₅₀ values for the syrup formulation were > 10 ml/kg in mice and rats. No specific clinical signs of toxicity were observed at these doses.

A single intraarticular injection of 4 mg bromhexine was well tolerated in rats and dogs. The lesions after intramuscular injection in rabbits compared well with those after physiological saline solution. Bromhexine hydrochloride was hemolytic *in vitro*.

Repeat Dose Toxicity

In repeat oral dose toxicity studies over 5 weeks, mice tolerated 200 mg/kg bromhexine hydrochloride representing the "no observed adverse effect level" (NOAEL). At 2000 mg/kg, mortality was high. The few surviving animals showed a reversible increase in liver weight and serum cholesterol. Rats tolerated 25 mg/kg over 26 or 100 weeks, while at 500 mg/kg, convulsions and deaths occurred. The centrilobular hepatocytes were enlarged due to vacuolic change. Another 2 year study confirmed that doses up to 100 mg/kg are well tolerated, while at 400 mg/kg, convulsions occurred sporadically in a few animals. Dogs tolerated 100 mg/kg (NOAEL) orally over 2 years.

BISOLVON[®] Syrup (0.8 mg/ml) was well tolerated up to 20 ml/kg in rats with a reversible centrilobular simple fatty change of liver. After intramuscular administration of 8 mg injectable solution in dogs for 6 weeks there was no local irritation or systemic toxicity.

Reproductive and Developmental Toxicity

Bromhexine hydrochloride was neither embryotoxic nor teratogenic (segment II) at oral doses up to 300 mg/kg in rats and 200 mg/kg in rabbits. Fertility (segment I) was not impaired at doses up to 300 mg/kg. The "NOAEL" during peri- and postnatal development (segment III) was 25 mg/kg.

Genotoxicity

Bromhexine hydrochloride had no mutagenic potential in the bacterial mutation assay and the mouse bone marrow micronucleus test.

Carcinogenicity

Bromhexine hydrochloride did not show a tumorigenic potential in the 2-year studies on rats given up to 400 mg/kg, and on dogs given up to 100 mg/kg.

Availability

Syrup 4 mg/5 ml Bottle of 60 ml Reg. No. DTL1821207237A1

**Store below 30°C, in a well-closed container.
Store in a safe place, out of the reach of children.**

**P No. 1
Awat! Obat Keras
Bacalah aturan memakainya**

Manufactured by:

PT. Menarini Indria Laboratories
Bekasi, Indonesia

For:

PT. Kalventis Sinergi Farma
Jakarta, Indonesia

Under license from:

Opella Healthcare International SAS, France

Revision date: 24 February 2026 (based CCDS V1)


Opella.



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BISOLVON® KIDS

BISOLVON® KIDS mengandung bromheksin hidroklorida yang bekerja sebagai mukolitik untuk meredakan batuk berdahak.

Sediaan BISOLVON® KIDS	Kekuatan	Deskripsi Produk
Sirup 	4 mg/5 ml	Larutan bening/hampir jernih, dan tidak berwarna/hampir tidak berwarna

Zat tambahan:

Maltitol liquid, sucralose, benzoic acid, hydroxyethylcellulose, strawberry flavour, cherry flavour, purified water.

Dosis dan Cara Pemberian BISOLVON® KIDS

Sediaan	Usia	Dosis per hari
Sirup 4 mg/5 ml*	Dewasa dan anak >10 tahun	3 x 10 ml
	Anak 6-10 tahun	3 x 5 ml
	Anak 2-5 tahun	2 x 5 ml

Sirup yang digunakan bebas gula sehingga cocok untuk penderita diabetes dan anak-anak

Cara Kerja BISOLVON® KIDS

Bromheksin hidroklorida yang terkandung dalam **BISOLVON® KIDS** dapat mengurangi kekentalan dahak, melancarkan dan memudahkan proses pengeluaran dahak.



Jangan Gunakan **BISOLVON® KIDS** jika alergi/hipersensitif terhadap bromheksin hidroklorida atau komponen lain dalam formula.

Perhatikan keadaan berikut pada penggunaan **BISOLVON® KIDS**

- Segera berkonsultasi ke dokter apabila gejala batuk tidak membaik atau semakin memburuk.
- Hindari penggunaan lebih dari dosis maksimal harian yang dianjurkan karena memiliki efek laksatif ringan dari maltitol.
- Tidak ada interaksi klinis dengan obat lain

Penggunaan BISOLVON® KIDS pada Ibu Hamil dan Menyusui

Penggunaan **BISOLVON® KIDS** dalam kehamilan dan menyusui sebaiknya dihindari, kecuali atas petunjuk dari dokter.



Tidak ada studi mengenai efek penggunaan **BISOLVON® KIDS** terhadap kemampuan mengemudi dan mengoperasikan mesin yang pernah dilakukan.

BISOLVON® KIDS dapat mempunyai efek samping yang jarang terjadi, berupa reaksi alergi, ruam, mual, muntah, diare, serta nyeri perut bagian atas. Selain itu terdapat kemungkinan efek samping (belum pernah dilaporkan/diketahui) berupa reaksi alergi berat (anafilaksis), kesulitan bernapas (bronkospasme) pembengkakan (angioedema), biduran, gatal-gatal (pruritus), dan reaksi alergi kulit berat (*erythema multiforme*, *Stevens-Johnson syndrome/toxic epidermal necrolysis* dan *acute generalized exanthematous pustulosis*). Jika mengalami gejala-gejala tersebut, segera berkonsultasi ke dokter.

Pelaporan efek samping

Segera laporkan apabila Anda mengalami keluhan efek samping atau kondisi tidak nyaman selama dan setelah penggunaan obat kepada farmakovigilans@kalventis.com. Anda dapat membantu memberikan informasi terkait keamanan obat ini.

Tidak terdapat gejala spesifik overdosis yang dilaporkan terjadi pada manusia. Gejala yang muncul sesuai dengan gejala efek samping BISOLVON® KIDS. Jika mengalami gejala-gejala tersebut, segera berkonsultasi ke dokter.

Kemasan & Cara Penyimpanan BISOLVON® KIDS

Sirup 4 mg/5ml

Botol 60 ml

Reg. No. xxx

Simpan di bawah suhu 30° C, pada tempat tertutup rapat.

Simpan di tempat yang aman, jauh dari jangkauan anak-anak.



Diproduksi oleh:

PT Menarini Indria Laboratories
Bekasi, Indonesia

Untuk:

PT Kalventis Sinergi Farma,
Jakarta, Indonesia

Di bawah lisensi dari:

Opella Healthcare International SAS, France

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