SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

Broncholyte® Elixir

2. **Qualitative and quantitative composition**

Each 5 ml contains Bromhexine Hydrochloride 4 mg.

Excipients with known effect: Contains Sorbitol Liquid

For full list of excipients, see Section 6.1

3. Pharmaceutical form

Oral Solution

A clear to almost clear, colourless to almost colourless solution with a fruity aromatic odour.

4. Clinical particulars

4.1 Therapeutic indications

As a mucolytic in the management of viscid mucoid secretions associated with bronchitis, bronchiectasis, sinusitis.

4.2 Posology and method of administration

Oral

Adults and children over 12 years: 2 × 5 ml three times daily to 3 × 5 ml four times daily.

Children 5 - 12 years: 1 × 5 ml four times daily

Children 2 - 5 years: 1 × 5 ml twice daily.

Broncholyte Elixir is sugar free and therefore suitable for diabetics.

4.3 Contraindications

Broncholyte Elixir should not be used in patients known to be hypersensitive to bromhexine or other components of the formulation.

In case of rare hereditary conditions that may be incompatible with an excipient of the product (please refer to “Special warnings and precautions”) the use of this product is contraindicated.

4.4 Special warnings and precautions for use

Bromhexine should be used with caution in patients with a history of, or existing, peptic ulceration.

There have been reports of severe skin reactions such as erythema multiforme, Stevens-Johnson syndrome (SJS)/ toxic epidermal necrolysis (TEN) and acute generalised exanthematous pustulosis (AGEP) associated with the administration of bromhexine hydrochloride. If symptoms or signs of a progressive skin rash (sometimes associated with blisters or mucosal lesions) are present, bromhexine hydrochloride treatment should be discontinued immediately and medical advice should be sought.

As the product contains sorbitol liquid, patients with rare hereditary problems of fructose intolerance should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

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

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited data from the use of bromhexine in pregnant women.

Animal 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 Broncholyte Elixir during pregnancy.

Lactation

It is unknown whether bromhexine/metabolites are excreted in human milk.

Available pharmacodynamic/toxicological data in animals have shown excretion of bromhexine/metabolites in breast milk. A risk to the breastfed infant cannot be excluded.

Broncholyte Elixir should not be used during breast-feeding.

Fertility

No studies on the effect on human fertility have been conducted with Broncholyte Elixir.

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

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 Broncholyte Elixir.

4.8 Undesirable effects

The following side effects have been reported based on clinical trials involving

3,992 patients

Frequencies

Very common ≥1/10

Common ≥ 1/100 < 1/10

Uncommon ≥ 1/1,000 < 1/100

Rare ≥ 1/10,000 < 1/1,000

Very rare < 1/10,000

Not known cannot be estimated from the available data

Immune system disorders

Hypersensitivity reactions Rare

Anaphylactic reactions Not known

including anaphylactic shock*,

angioedema* and pruritus*

Respiratory, thoracic and mediastinal disorders

Bronchospasm* Not known

Gastro-intestinal disorders

Abdominal pain upper Uncommon

Nausea Uncommon

Vomiting Uncommon

Diarrhoea Uncommon

Skin and subcutaneous tissue disorders

Rash Rare

Urticaria* Rare

Severe cutaneous adverse reactions Not known

(including erythema multiforme,

Stevens-Johnson syndrome/toxic

epidermal necrolysis and

acute generalized exanthematous

pustulosis)

**This adverse reaction has been observed in post-marketing experience. With 95 % certainty, the frequency category is not greater than rare (3/3,992), but might be lower. A precise frequency estimation is not possible as the adverse drug reaction did not occur in a clinical trial database of 3,992 patients.*

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: ADR e-Reporting Form online

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 Broncholyte Elixir at recommended doses and may need symptomatic treatment.

5. Pharmacological properties

5.1 Pharmacodynamic properties

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).

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

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

5.2 Pharmacokinetic properties

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 ± 8.5 % for Broncholyte Elixir, The first pass metabolism amounts to about 75-80%. Concomitant food 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 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 or oxytetracyclin. There is insufficient pharmacokinetic data to evaluate a possible drug-drug interaction between bromhexine and erythromycin.

Elimination

Bromhexine is a high extraction ratio drug after i.v. administration in the range of the hepatic blood flow, 843-1073 mL/min resulting in high inter- and intraindividual 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).

In general Bromhexine shows dose proportional pharmacokinetics in the range of 8-32 mg following oral administration. There are no data for bromhexine pharmacokinetics in the elderly or in patients with renal or liver insufficiency.

Bromhexine pharmacokinetics are not relevantly affected by co-administration of ampicillin or oxytetracycline.

Interaction studies with oral anticoagulants or digoxin were not performed.

5.3 Preclinical safety data

No details on schedule.

6. Pharmaceutical particulars

6.1 List of excipients

Sorbitol liquid 70% (E965)

Glycerol 99.7%

Benzoic acid (E210)

Tartaric Acid

Raspberry Essence

Sodium Carboxymethylcellulose

Ethanol 96%

De-mineralised water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Unopened: 3 years.

6.4 Special precautions for storage

Store in the original container.

6.5 Nature and contents of container

Broncholyte Elixir is available in Amber Pet bottle with Plain White plastic cap. The registered pack sizes are 100 ml.

A polypropylene measuring dish is provided.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7. Marketing authorisation holder

SYGEN PHARMACEUTICAL LTD

KM38 LAGOS ABEOKUTA EXPRESSWAY

SANGO OTA

OGUN STATE

NIGERIA

8. Marketing authorisation number

NAFDAC NO: 04-2904

9. Date of first authorisation/renewal of the authorisation

27th November 2006

10. Date of revision of the text 6th June 2024