SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

YOYO EXP (TERBUTALINE SULFATE, BROMHEXINE HYDROCHLORIDE, GUAIPHENESIN & MENTHOL SYRUP)

2. Qualitative and quantitative composition

Each 5 ml contains:
Terbutaline sulfate BP .....1.25 mg
Bromhexine hydrochloride BP.....4 mg
Guaifenesin BP .....50 mg
Menthol BP .....2.5 mg
Flavoured syrupy base.....Q.S.
(For the full list of excipients, see section 6.1.)

3. Pharmaceutical form

Oral Suspension

An orange-coloured suspension.

4. Posology

4.1 Therapeutic Indications

Terbutaline sulphate, Bromhexine Hydrochloride and Guaiphenesin expectorant is indicated for clinical relief of productive cough associated with bronchitis, bronchial asthma, emphysema and other bronchopulmonary disorders where bronchospasm, mucous plugging and problems of expectoration co-exist.

4.2 Posology and Method of Administration

Adults

10 ml thrice daily

Children (6-12 years)

5-7.5 ml thrice daily

4.3 Contraindications

Hypersensitivity to any of the components of the formulation. It should not be used in patients with pre-existing ischaemic heart disease or those patients with significant risk factors for ischaemic heart disease. It is also contraindicated in patients with gastric ulceration.

4.4 Special warnings and precautions for use

Terbutaline: As for all beta2-agonists caution should be observed in patients with thyrotoxicosis. Cardiovascular effects may be seen with sympathomimetic drugs, including terbutaline. There is some evidence from post-marketing data and published literature of myocardial ischaemia associated with beta agonists. Due to the positive inotropic effect of

beta2-agonists, these drugs should not be used in patients with hypertrophic cardiomyopathy.
Tocolysis: Terbutaline should be used with caution in tocolysis and supervision of cardiorespiratory function, including ECG monitoring, should be considered. Treatment should be discontinued if signs of myocardial ischaemia (such as chest pain or ECG changes) develop. Terbutaline should not be used as a tocolytic agent in patients with significant risk factors for or pre-existing heart disease. During infusion treatment in pregnant women with beta2-stimulants in combination with corticosteroids a rare complication with a pathological picture resembling pulmonary oedema, has been reported. Increased tendency to uterine bleeding has been reported in connection with Caesarean section. However, this can be effectively stopped by propranolol 1-2 mg injected intravenously.
Respiratory indications: Patients with underlying severe heart disease (e.g. ischaemic heart disease, arrhythmia or severe heart failure) who are receiving Terbutaline should be warned to seek medical advice if they experience chest pain or other symptoms of worsening heart disease. Attention should be paid to assessment of symptoms such as dyspnoea and chest pain, as they may be of either respiratory or cardiac origin. Due to the hyperglycaemic effects of beta2-agonists, additional blood glucose controls are recommended initially in diabetic patients. Potentially serious hypokalaemia may result from beta2-agonist therapy. Particular caution is recommended in acute severe asthma as the associated risk may be augmented by hypoxia. The hypokalaemic effect may be potentiated by concomitant treatments. It is recommended that serum potassium levels are monitored in such situations. If a previously effective dosage regimen no longer gives the same symptomatic relief, the patient should urgently seek further medical advice. Consideration should be given to the requirements for additional therapy (including increased dosages of anti-inflammatory medication). Severe exacerbations of asthma should be treated as an emergency in the usual manner.
Bromhexine: Patients being treated with bromhexine should be notified of an expected increase in the flow of secretions. The use of Bromhexine without medical supervision is not intended in patients who suffer from such condition chronically. Medical advice should be sought if the symptoms last longer than 14 days and/or if the symptoms increase in spite of treatment with bromhexine. Since mucolytics may disrupt the gastric mucosal barrier bromhexine should be used with care in patients with a history of peptic ulcer disease (gastric ulcer). Care is also advisable in asthmatic patients. Clearance of bromhexine or its metabolites may be reduced in patients with severe hepatic or renal impairment. Bromhexine may increase the amount of antibiotic penetration. Antibiotics are medicines used to treat infections.
Guaiphenesin: Guaiphenesin should be not used for persistent or chronic cough, such as occurs with asthma, or where cough is accompanied by excessive secretions, unless directed by a physician. A persistent cough may be a sign of a serious condition. If cough persists for more than 7 days, tends to recur, or is accompanied by a fever, rash, or persistent headache, a physician should be consulted. Caution should be exercised in the presence of severe renal or severe hepatic impairment. The concomitant use of cough suppressants is not recommended. Patients with rare hereditary problems of fructose intolerance should not take this medicine. Not more than 4 doses should be given in any 24 hours. Avoid with any other cough and cold medicine. Consult a pharmacist or other healthcare professional before use in children under 6 years.

4.5 Interaction with other medicinal products and other forms of interaction

Terbutaline: Beta-blocking agents (including eye drops); especially the non-selective ones such as propranolol, may partially or totally inhibit the effect of beta-stimulants. Therefore terbutaline preparations and non-selective beta-blockers should not normally be administered concurrently. Terbutaline should be used with caution in patients receiving other sympathomimetic. Hypokalaemia may result from beta2-agonist therapy and may be potentiated by concomitant treatment with xanthine derivatives, corticosteroids and diuretics.
Bromhexine: Bromhexine may increase the concentration of concurrently administered antibiotics in bronchial secretions. No clinically relevant interactions with other medications have been reported.
Guaiphenesin: If urine is collected within 24 hours of a dose of Guaiphenesin, its metabolite may cause a colour interference with laboratory determinations of urinary 5-hydroxyindoleacetic acid (5-HIAA) and vanillylmandelic acid (VMA).
Others: Terbutaline sulphate, Bromhexine Hydrochloride and Guaiphenesin Expectorant should be used with caution in patients with diabetes mellitus, serious cardiovascular disorders, hypertension, hyperthyroidism and peptic ulcers.

4.6 Fertility, pregnancy and lactation
Pregnancy However, there are no adequate and well-controlled studies of this combination in pregnant women. Hence this combination should be administered with caution in pregnancy.
Lactation It is not known whether this combination is secreted in breast milk. However terbutaline is secreted in breast milk, but effect on the infant is unlikely at therapeutic doses. Therefore, this combination should be used with caution nursing mothers.
4.7 Effects on ability to drive and use machines
Most common adverse reactions to terbutaline are tremor, headache, tachycardia, palpitations, muscle spasms and hypokalaemia, this may affects ability to drive and useof machines.
4.8 Undesirable effects

Terbutaline: Most of the adverse reactions are characteristic of sympathomimetic amines. The majority of these effects have reversed spontaneously within the first 1-2 weeks of treatment. The frequency of side-effects is low at the recommended doses. The most common adverse reactions to terbutaline are tremor, headache, tachycardia, palpitations, muscle spasms and hypokalaemia. Rare cases of arrhythmias e.g. atrial fibrillation, supraventricular tachycardia and extra systoles, myocardial ischaemia, peripheral vasodilation, hypersensitivity reactions including angioedema, bronchospasm, hypotension, collapse, nausea, mouth and throat irritation, sleep disorder, behavioural disturbances such as agitation and restlessness, paradoxical bronchospasm, urticaria and rash.

Bromhexine Dermatologic Effects: skin rash, urticaria, Gastrointestinal Effects: nausea, epigastric pain, vomiting, and diarrhoea Hepatic Effects: Transient elevations in serum aminotransferase levels Neurologic Effects (Central nervous system): dizziness and headache Renal Effects: Nocturnal enuresis
Others:
• anaphylaxis
• bronchospasm, difficulty in breathing

• angioedema; swelling of the face, lips, mouth, tongue or throat which may cause difficulty swallowing or breathing.

Guaiphenesin

Side effects resulting from guaifenesin administration are very rare. Guaiphenesin has occasionally been reported to cause gastro-intestinal discomfort, nausea and vomiting, particularly in very high doses. Also, hypersensitivity reactions may occur.

Reporting of suspected adverse reactions:

Healthcare professionals are requested to report any suspected adverse reactions to report any suspected adverse reactions to the National Regulatory Agents.

4.9 Overdose

Terbutaline

Possible Symptoms and Signs

Headache, anxiety, tremor, nausea, tonic cramp, palpitations, tachycardia, arrhythmia. A fall in blood pressure sometimes occurs.

Laboratory findings; hypokalaemia, hyperglycaemia and lactic acidosis sometimes occur.

Treatment

Mild and moderate cases: Reduce the dose.

Severe cases: Gastric lavage, administration of activated charcoal. Determination of acid-base balance, blood sugar and electrolytes, particularly serum potassium levels.Monitoring of the heart rate and rhythm and blood pressure. Metabolic changes should be corrected.

A cardioselective beta-blocker (e.g. metoprolol) is recommended for the treatment of arrhythmias causing haemodynamic deterioration. The beta-blocker should be used with care because of the possibility of inducing bronchoconstriction: use with caution in patients with a history of bronchospasm. If the beta $_2$-mediated reduction in the peripheral vascular resistance significantly contributes to the fall in blood pressure, a volume expander should be given.

Preterm labour: Pulmonary oedema: discontinue administration. A normal dose of loop diuretic (e.g. frusemide) should be given intravenously.

Increased bleeding in connection with Caesarian section: propranolol, 1-2mg intravenously.

Bromhexine

No symptoms of overdosage have been reported in man to date. If they occur, supportive and symptomatic treatment should be provided.

Guaiphenesin

The effects of acute toxicity from guaifenesin may include gastrointestinal discomfort, nausea and drowsiness. The drug is, however, rapidly metabolised and excreted in the urine. Patients

should be kept under observation and treated symptomatically. Overdosage may also give rise to nausea and vomiting. Treatment need only be symptomatic and supportive.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Terbutaline

Basic parameters have been evaluated in man after oral administration of therapeutic doses, e.g.

Renal clearance (CLR): 1.925/ml/min (males)

Renal clearance (CLR): 2.32ml/min (females)

Terminal half-life T½ has been determined after single and multiple dosing (mean values varied between 16-20 h)

Bioavailability

Food reduces bioavailability following oral dosing (10% on average).

Fasting values of 14-15% have been obtained.

Metabolism

The main metabolite after oral dosing is the sulphate conjugate and also some glucoronide conjugate can be found in the urine.

Guaiphenesin

Absorption

Guaiphenesin is well absorbed from the gastro-intestinal tract following oral administration, although limited information regarding its pharmacokinetics is available. After the administration of 600 mg Guaiphenesin to healthy adult volunteers, the C_{max} was approximately 1.4ug/ml, with t_{max} occurring approximately 15 minutes after drug administration.

Distribution

No information is available on the distribution of Guaiphenesin in humans.

Metabolism and elimination

Guaiphenesin appears to undergo both oxidation and demethylation. Following an oral dose of 600 mg guaifenesin to 3 healthy male volunteers, the t½ was approximately 1 hour and the drug was not detectable in the blood after approximately 8 hours.

Pharmacokinetics in Renal/Hepatic Impairment

There have been no specific studies of Guaiphenesin in subjects with renal or hepatic impairment. Caution is therefore recommended when administering this product to subjects with severe renal or hepatic impairment.

5.2 Pharmacokinetic properties

Terbutaline

Terbutaline is a selective beta $_2$ - adrenergic causing bronchodilation; increase in mucociliary clearance; suppression of oedema and anti-allergic effects.

The pharmacologic effects of beta-adrenergic agonist drugs, including terbutaline, are at least in part, attributable to stimulation through beta-adrenergic receptors on intracellular adenylcyclase, the enzyme that catalyses the conversion of adenosine triphosphate (ATP) to cyclic-3′,5′-adenosine monophosphate (cyclic AMP). Increased cyclic AMP levels are associated with relaxation of bronchial smooth muscle and inhibition of release of mediators of immediate hypersensitivity from cells, especially from mast cells.

Bromhexine:

Bromhexine is an expectorant/mucolytic agent. The drug is a benzylamine derivative (2-amino-3,5-dibromo-N-cyclohexyl N-methylbenzylamine hydrochloride) and also a derivative of vasicine and adhatodic acid, alkaloids obtained from the plant Adhatoda vasica.

Following oral administration, bromhexine has increased sputum volume and reduced the viscosity of bronchial secretions in chronic bronchitis patients. The drug has been reported to induce hydrolytic depolymerization of mucoprotein fibers and stimulate activity of the ciliated epithelium. An increase in lysosomal activity facilitated by bromhexine has been postulated. Improvements in pulmonary function in bronchitis patients appear secondary to easier expectoration.

An effect of bromhexine on increasing sputum concentrations of various antibiotics (eg, oxytetracycline, erythromycin, ampicillin, amoxicillin) has also been reported. However, some of these effects (exocrine stimulation, increased sputum concentrations) have not been confirmed in some studies.

It has been suggested that a metabolite of bromhexine, ambroxol, may contribute to enhanced secretion from exocrine glands during bromhexine administration.

Guaiphenesin

Guaiphenesin is thought to exert its tgical action by stimulating receptors in the gastric mucosa. This increases the output from secretory glands of the gastrointestinal system and reflexly increases the flow of fluids from glands lining the respiratory tract. The result is an increase in volume and decrease in viscosity of bronchial secretions. Other actions may include stimulating vagal nerve endings in bronchial secretory glands and stimulating certain centres in the brain, which in turn enhance respiratory fluid flow. Guaiphenesin produces its expectorant action within 24 hours.

5.3 Preclinical safety data

Basic parameters have been evaluated in man after oral administration of therapeutic doses, e.g.

Renal clearance (CLR): 1.925/ml/min (males) Renal clearance (CLR): 2.32ml/min (females) Terminal half-life T½ has been determined after single and multiple dosing (mean values varied between 16-20 h)

Bioavailability: Food reduces bioavailability following oral dosing (10% on average). Fasting values of 14-15% have been obtained.

Metabolism: The main metabolite after oral dosing is the sulphate conjugate and also some glucoronide conjugate can be found in the urine.

Bromhexine:

Absorption Oral, well absorbed. Rapidly absorbed from the gastrointestinal tract. Peak plasma concentrations occur after about 1 hour following oral administration.

Distribution

It is widely distributed to body tissues. Bromhexine is highly bound to plasma proteins. Bromhexine crosses the blood-brain barrier and small amounts cross the placenta.
Metabolism

Bromhexine undergoes extensive first-pass metabolism in the liver: Ambroxol is a metabolite of bromhexine.

Excretion

Bromhexine is excreted primarily in the urine as metabolites. Only small amounts appear as unchanged drug. About 85 to 90% of a dose is excreted in the urine mainly as metabolites. Approximately 70% of an oral dose of bromhexine has been recovered in the urine within 24 hours. Other excretion: faeces, 4% Elimination Half-life: It has a terminal elimination half-life of 13 to 40 hours

Guaiphenesin:

Absorption: Guaiphenesin is well absorbed from the gastro-intestinal tract following oral administration, although limited information regarding its pharmacokinetics is available. After the administration of 600 mg Guaiphenesin to healthy adult volunteers, the Cmax was approximately 1.4ug/ml, with tmax occurring approximately 15 minutes after drug administration.

Distribution: No information is available on the distribution of Guaiphenesin in humans.
Metabolism and elimination: Guaiphenesin appears to undergo both oxidation and demethylation. Following an oral dose of 600 mg guaifenesin to 3 healthy male volunteers, the t½ was approximately 1 hour and the drug was not detectable in the blood after approximately 8 hours.

Pharmacokinetics in Renal/Hepatic Impairment: There have been no specific studies of Guaiphenesin in subjects with renal or hepatic impairment. Caution is therefore recommended when administering this product to subjects with severe renal or hepatic impairment.

6. Pharmaceutical particulars

6.1 List of excipients

SR. NO	INGREDIENTS	STANDARD

1.	Bronopol	BP
2.	Sodium Benzoate	USP
3.	Sucrose	BP
4.	Propylene Glycol	USP
5.	Aspartame	USP
6.	Citric Acid Mono	BP
7.	Sorbitol Solution 70%	IP
8.	Sunset Yellow FCF	IH
9.	Carmoisine	IH
10.	D.M.Water	BP

6.2 Incompatibilities
None known

6.3 Shelf life
36 Months

6.4 Special precautions for storage
Store below 30°C.

6.5 Nature and contents of container
100 ml Bottle.

6.6 Special precautions for disposal and other handling
None.

7 Marketing Authorization Holder and Manufacturing Site Address

Marketing Authorization Holder:
Krishna Chemists Limited
Industrial area, Lusaka road, 3rd floor, Metrix hardware,
PO Box:3328-00506,
Nairobi-Kenya

Manufactured in India by:
RELAX BIOTECH PVT LTD.
862/1, GIDC Makarpura,
Vadodara-390010., Gujarat, India.

8 Marketing Authorization Number

CTD10908

9. Date of first Registration/ Renewal of the Registration
29/07/2026

10. Date of Revision of the Text

29/07/2026