National Agency for Food & Drug Administration & Control (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

SUMMARY OF PRODUCT CHARACTERISTICS

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ALBELIN BABY COUGH SYRUP

1. Name of the medicinal product
ALBELIN BABY COUGH SYRUP

2. Qualitative and quantitative composition

Each 5 ml contains:	
Diphenhydramine hydrochloride B.P	7mg
Menthol B.P	0.75mg
Ammonium chloride B.P	70mg
Sodium citrate B.P	30mg

For a full list of excipients, see section 6.1.

3. Pharmaceutical form
A Pink colored slightly viscous syrup.

4. Clinical particulars

4.1 Therapeutic indications
ALBELIN BABY COUGH SYRUP is indicated for the relief of cough and associated congestive symptoms.

4.2 Posology and method of administration
- **Children aged 6 to 12 years:** 10

mls four times a day (6 hourly)

Maximum daily dose: 40 mls syrup.

- Not to be used in children less than 2 years of age.
- To be used with caution and doctor's / pharmacist's advice in children 2 to 6 years of age.

The Elderly:

As for adults above (see Pharmacokinetics - The elderly).

Hepatic dysfunction

- Caution should be exercised if moderate to severe hepatic dysfunction is present (see Pharmacokinetics - Hepatic dysfunction).

Renal dysfunction

- It may be prudent to increase the dosage interval in subjects with moderate to severe renal failure (see Pharmacokinetics - Renal dysfunction).

Do not exceed the stated dose.

Keep out of the sight and reach of children.

Method of Administration Oral.

4.3 Contraindications

BABY COUGH is contraindicated in individuals with known hypersensitivity to Diphenhydramine, menthol, ammonium chloride, sodium citrate or to any of the excipients listed in section 6.1.

BABY COUGH should not be administered to patients currently receiving monoamine oxidase inhibitors (MAOIs) or within 14 days of stopping treatment (see section 4.5).

4.4 Special warnings and precautions for use

- Not to be used in children less than 2 years of age.

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ALBELIN BABY COUGH SYRUP

- To be used with caution and doctor's / pharmacist's advice in children 2 to 6 years of age.
- This product may cause drowsiness, If affected individuals should not drive or operate machinery.
- This product should not be used to sedate a child.
- BABY COUGH may enhance the sedative effects of central nervous system depressants including alcohol, sedatives, opioid analgesics, antipsychotics and tranquilizers. Alcoholic beverages should be avoided while taking this medicine (see section 4.5).
- Do not use with any other product containing diphenhydramine, including topical formulations used on large areas of skin.
- Subjects with hepatic disease or moderate to severe renal dysfunction should exercise caution when using this product (see Pharmacokinetics - Renal/Hepatic Dysfunction).
- Patients with the following conditions should be advised to consult a physician before using this medicine:
    - A chronic or persistent cough such as occurs with chronic bronchitis or emphysema, acute or chronic asthma, or where cough is accompanied by excessive secretions.
    - Susceptibility to angle-closure glaucoma.
    - Prostatic hypertrophy and/or urinary retention.
- Contains 3.5 g of glucose and 1 g of sucrose per 5 ml. This should be taken into account in patients with diabetes mellitus.
- Patients with rare hereditary problems of fructose intolerance, glucose- galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

ALBELIN BABY COUGH SYRUP

4.5 Interaction with other medicinal products and other forms of interaction

Diphenhydramine

CNS depressants: may enhance the sedative effects of CNS depressants including barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives, antipsychotics and alcohol.

Antimuscarinic drugs: may have an additive muscarinic action with other drugs, such as atropine and some antidepressants.

MAOIs: Not be used in patients taking MAOIs or within 14 days of stopping treatment as there is a risk of serotonin syndrome. **Menthol**

There are no known drug interactions associated with menthol.

4.6 Fertility, pregnancy and lactation

This product should not be used during pregnancy or breastfeeding unless the potential benefit of treatment to the mother outweighs the possible risks to the developing fetus or breastfeeding infant.

Diphenhydramine Pregnancy

Diphenhydramine has been in widespread use for many years without any apparent ill consequence. Diphenhydramine is known to cross the placenta and, therefore, should only be used during pregnancy if considered essential by a doctor.

Breastfeeding

Diphenhydramine is excreted into human breast milk, but levels have not been reported. Although the levels are not thought to be sufficiently high enough after therapeutic doses to affect the infant, the use of diphenhydramine during breast-feeding is not recommended.

Menthol

There are no adequate and well-controlled studies in pregnant women for menthol. Menthol is excreted in breast milk; when 100 mg of menthol was ingested, there was up to 5.87 ug/L of menthol in breast milk.

4.7 Effects on ability to drive and use machines

This product may cause drowsiness. If affected, the patient should not drive or operate machinery.

4.8 Undesirable effects

Diphenhydramine

Adverse drug reactions (ADRs) identified during clinical trials and post-marketing experience with Diphenhydramine are included in the table below by System Organ Class (SOC). The frequencies are provided according to the following convention:

Very common	≥1/10
Common	≥1/100 and < 1/10
Uncommon	≥1/1,000 and <1/100
Rare	≥1/10,000 and <1/1,000
Very rare	<1/10,000
Not known	(cannot be estimated from the available data)

System Organ Class (SOC)	**Frequency***	**Adverse Drug Reaction**
Blood and Lymphatic System Disorders	Rare	Blood disorders

Immune System Disorders	Rare	Hypersensitivity reactions

Psychiatric Disorders	Uncommon	Irritability Hallucination Nervousness
	Rare	Confusional state
Nervous System Disorders	Very common	Somnolence (usually diminishes within a few days)
	Common	Dizziness Headache Paradoxical stimulation Psychomotor impairment
	Uncommon	Agitation Paraesthesia Sedation
	Rare	Convulsion Depression Extrapyramidal effects Insomnia Tremor
Eye Disorders	Common	Vision blurred
Ear and Labyrinth Disorders	Uncommon	Tinnitus
Cardiac Disorders	Uncommon	Tachycardia
	Rare	Arrhythmia Palpitations

Vascular Disorders	Rare	Hypotension

Respiratory, Thoracic and Mediastinal Disorders	Common	Thickened respiratory tract secretions
	Uncommon	Chest discomfort Nasal dryness
Gastrointestinal Disorders	Common	Dry mouth Nausea Vomiting
Hepatobiliary Disorders	Rare	Liver dysfunction
Skin and Subcutaneous Tissue Disorders	Uncommon	Pruritus Rash Urticaria
Renal and Urinary Disorders	Common	Urinary retention
General Disorders and Administration site conditions	Common	Asthenia

(*) Frequency category based on clinical trials with single-ingredient diphenhydramine

Menthol

Adverse reactions to menthol at the low concentration present in Baby cough are not anticipated.

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.

4.9 Overdose

Symptoms and signs Diphenhydramine

Mild to Moderate Symptoms:

Drowsiness, anticholinergic syndrome (mydriasis, flushing, fever, dry mouth, urinary retention, decreased bowel sounds), tachycardia, mild hypertension, nausea and vomiting are common after overdose. Agitation, confusion and hallucinations may develop after moderate poisoning.

Severe Symptoms:

Effects may include delirium, psychosis, seizures, coma, hypotension, QRS widening, and ventricular dysrhythmias (including torsades de pointes), but are generally only reported in adults after large ingestions. Rhabdomyolysis and renal failure may rarely develop in patients with prolonged agitation, coma or seizure. Death may occur as a result of respiratory failure or circulatory collapse.

In children, CNS excitation, including hallucinations and convulsions may appear; with larger doses, coma or cardiovascular collapse may follow.

Menthol

Excessive use of menthol may lead to abdominal pain, vomiting, flushed face, dizziness, weakness, tachycardia, stupor, and ataxia.

Treatment

Treatment of overdose should be symptomatic and supportive. The benefit of gastric decontamination is uncertain. Consider activated charcoal (charcoal dose: 50 g for adults; 1 g/kg for children) only if the patient presents within 1 hour of ingestion of a potentially toxic amount

Seizures may be controlled with Diazepam or Thiopental Sodium. The intravenous use of Physostigmine may be efficacious in antagonizing severe anticholinergic symptoms.

Ammonium Chloride

Overdosage of Ammonium Chloride has resulted in a serious degree of metabolic acidosis, disorientation, confusion and coma.

Treatment

Should metabolic acidosis occur following overdosage, the administration of an alkalinizing solution such as sodium bicarbonate or sodium lactate will serve to correct the acidosis.

Over dosage with sodium salts may cause diarrhea, nausea and vomiting, hypernoia, and convulsions.

Particulars of its Treatment

If overdose occurs the patient should be monitored for evidence of toxicity and standard symptomatic and supportive treatment applied as necessary.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Diphenhydramine possesses antitussive, antihistaminic and anticholinergic properties. Experiments have shown that the antitussive effect (resulting from an action on the brainstem) is discrete from its antihistaminic effect.

The duration of activity of diphenhydramine is between 4 and 8 hours.

Menthol has mild local anaesthetic and decongestant properties.

Ammonium chloride has irritant effect on mucous membrane and is considered to have expectorant properties.

Sodium Citrate

The effect of sodium citrate is that it renders the urine to become less acidic. It is an antitussive and mucolytic agent that breaks down the mucus

so that coughing up phlegm becomes easier. It acts as an expectorant that thins the mucus.

5.2 Pharmacokinetic properties

Absorption

Diphenhydramine and menthol are well absorbed from the gut following oral administration. Peak serum levels of diphenhydramine following a 50 mg oral dose are reached at between 2 and 2.5 hours.

Distribution

Diphenhydramine is widely distributed throughout the body, including the CNS. Following a 50 mg oral dose of diphenhydramine, the volume of distribution is in the range 3.3 - 6.8 l/kg, and it is some 78% bound to plasma proteins.

Metabolism and Elimination

Diphenhydramine undergoes extensive first pass metabolism. Two successive N-demethylations occur, with the resultant amine being oxidized to a carboxylic acid. Values for plasma clearance of a 50 mg oral dose of diphenhydramine lie in the range 600-1300 ml/min and the terminal elimination half-life lies in the range 3.4 - 9.3 hours. Little unchanged drug is excreted in the urine. Menthol is hydroxylated in the liver by microsomal enzymes to p-methane-3,8 diol. This is then conjugated with glucuronide and excreted both in urine and bile as the Glucuronide.

Ammonium chloride is also absorbed by the gastrointestinal tract. Following oral administration, it is rapidly absorbed from the gastrointestinal tract whereby complete absorption occurs within 3 to 6 hours. ii. Metabolism

In a test carried out on healthy male and female volunteers, they were orally administered with ammonium chloride. They produced transient increase in blood pH. Those who suffered from cirrhosis showed a greater and more prolonged increase over a higher baseline. This means that their

livers metabolized ammonium chloride to from urea and hydrochloric acid. iii. Excretion

Ammonium chloride is excreted by the kidneys in form of urine. Sodium Citrate

i. Absorption and Excretion
ii. Sodium citrate is absorbed and renally eliminated causing metabolic alkalosis and urinary alkalization in sufficient doses.

Menthol

Metabolism and Elimination

Menthol is hydroxylated in the liver by microsomal enzymes to pmethane -3,8 diol. This is then conjugated with glucuronide and excreted both in urine and bile as the glucuronide.

The Elderly

Pharmacokinetic studies indicate no major differences in distribution or elimination of Diphenhydramine compared to younger adults.

Renal Dysfunction

The results of a review on the use of Diphenhydramine in renal failure suggest that in moderate to severe renal failure, the dose interval should be extended by a period dependent on Glomerular filtration rate (GFR).

Hepatic Dysfunction

After intravenous administration of 0.8 mg/kg Diphenhydramine, a prolonged half-life was noted in patients with chronic liver disease which correlated with the severity of the disease. However, the mean plasma

clearance and apparent volume of distribution were not significantly affected.

5.3 Preclinical safety data

Mutagenicity

The results of a range of tests suggest that neither diphenhydramine nor menthol have mutagenic potential.

Carcinogenicity
There is insufficient information to determine the carcinogenic potential of diphenhydramine or menthol, although such effects have not been associated with these drugs in animal studies.
Teratogenicity
The results of a number of studies suggest that the administration of either diphenhydramine or menthol does not produce any statistically significant teratogenic effects in rats, rabbits and mice.
Fertility
There is insufficient information to determine whether diphenhydramine has the potential to impair fertility, although a diminished fertility rate has been observed in mice in one study.

6. Pharmaceutical particulars

6.1 List of excipients

NA SACCHARINE
PROPYL PARABEN
METHYL PARABEN
NATROSOL
CITRIC ACID
SORBITOL
GLYCERINE
PROPYLENE GLYCOL

6.2 Incompatibilities

None known

6.3 Shelf life

36 months

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6.4 Special precautions for storage

Do not store above 30°C

6.5 Nature and contents of container

Bottle:	Amber PET , Plain PET
Closures:	28mm ROPP, tamper evident, child resistant.
Pack Sizes:	200ml. 2L

6.6 Special precautions for disposal and other handling No special requirements.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required (these should be disposed of in line with local requirements). These measures will help to protect the environment.

SUMMARY OF CHARACTERISTICS

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7. APPLICANT/MANUFACTURER

ALBEN HEALTH CARE INDUSTRIES LTD., ONITSHA AWKA ROAD, OGIDI ANAMBRA