Professional information for BENYLIN® PAEDIATRIC

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

BENYLIN® PAEDIATRIC syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 mL contains:

Diphenhydramine hydrochloride 7 mg

Excipients with known effect:

Preservative:

Sodium benzoate 0, 5 % *m/v*

Contains alcohol: Ethanol 95 %: 5 % *v/v*

Contains sugar (Each 5 mL contains 1,5 g sucrose and 3,5 g glucose).

Contains sweetener (Each 5 mL contains 15 mg saccharin sodium).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Syrup.

A clear, bright red syrup having a raspberry odour and taste.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

BENYLIN® PAEDIATRIC is indicated for the relief of cough and its congestive symptoms and for treatment of hay fever and other allergic conditions affecting the upper respiratory tract.

4.2 Posology and method of administration

A maximum of four doses per day should not be exceeded.

Shake the bottle before use.

Children 6 to 12 years:	Two 5 mL medicine measures (10 mL) every 3 hours.
Children below 6 years of age:	Not recommended

4.3 Contraindications

Known hypersensitivity to diphenhydramine hydrochloride or to any of the other ingredients in BENYLIN® PAEDIATRIC (see section 6.1).

Diphenhydramine hydrochloride should not be used with monoamine oxidase inhibitors or within 14 days of stopping monoamine oxidase inhibitor treatment.

Contraindicated during acute asthmatic attacks, and in patients with impaired hepatic or renal function.

BENYLIN® PAEDIATRIC should not be used in children below 6 years of age.

4.4 Special warnings and precautions for use

BENYLIN® PAEDIATRIC may lead to drowsiness and impaired concentration which may be aggravated by the simultaneous intake of alcohol or other central nervous system depressant medicines.

In infants and children, it may act as a cerebral stimulant. Symptoms of stimulation include insomnia, nervousness, tachycardia, tremors and convulsions.

Large doses may precipitate fits in epileptics. Deepening coma, extrapyramidal effects and photosensitization of the skin may occur.

Elderly patients are more susceptible to the central nervous system depressant and hypotensive effects.

Do not use with any other product containing diphenhydramine even ones used on skin.

The positive results of skin tests may be suppressed.

Diphenhydramine hydrochloride has anticholinergic properties and should be used with care in conditions such as a respiratory condition including emphysema (adult products), chronic bronchitis, or acute or chronic bronchial asthma, glaucoma, urinary retention and prostatic hypertrophy. Diphenhydramine hydrochloride should be used with caution in patients with liver impairment or cardiovascular disease.

Patients should not use BENYLIN® PAEDIATRIC for persistent or chronic cough, such as occurs with asthma, or where cough is accompanied by excessive secretions, unless directed by a physician.

BENYLIN® PAEDIATRIC contains sugar: sucrose and glucose.
Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take BENYLIN® PAEDIATRIC.

BENYLIN® PAEDIATRIC contains sodium benzoate. An increase in bilirubinaemia following its displacement from albumin may increase neonatal jaundice which may develop into kernicterus (non-conjugated bilirubin deposits in the brain tissue).

4.5 Interaction with other medicines and other forms of interaction

The anticholinergic effects of atropine and tricyclic antidepressants may be enhanced by diphenhydramine hydrochloride. Monoamine oxidase inhibitors (MAOIs) may enhance the anticholinergic effects.

Diphenhydramine hydrochloride may mask the warning symptoms of damage caused by ototoxic medicines, such as aminoglycoside antibiotics, and may affect the metabolism of other medicines in the liver. It may enhance the sedative effect of central nervous system depressants including alcohol, barbiturates, hypnotics, narcotic analgesics, sedatives and tranquillisers.

4.6 Fertility, pregnancy and lactation

Safety in pregnancy and lactation has not been established.

Diphenhydramine crosses the placenta and is excreted into breast milk.

4.7 Effects on ability to drive and use machines

BENYLIN® PAEDIATRIC may cause drowsiness, dizziness or blurred vision. Patients should be warned not to drive a motor vehicle, operate dangerous machinery or climb dangerous heights as impaired decision making could lead to accidents.

4.8 Undesirable effects

Blood and the lymphatic system disorders:

Less frequent: thrombocytopenia

Frequency unknown: agranulocytosis, leucopenia and haemolytic anaemia

Immune system disorders:

Frequency unknown: allergic reactions, anaphylaxis

Endocrine disorders:

Less frequent: epigastric pain

Metabolism and nutrition disorders:

Less frequent: anorexia, increased appetite

Psychiatric disorders:

Less frequent: euphoria, confusional state, irritability, hallucination, nervousness

Nervous system disorders:

Frequent: sedation

Less frequent: headache, agitation, abnormal coordination, convulsion, dizziness, insomnia, paraesthesia, somnolence, tremor

Eye disorders:

Less frequent: blurred vision

Ear and labyrinth disorders:

Less frequent: tinnitus

Cardiac disorders:

Less frequent: palpitations, tachycardia

Vascular disorders:

Less frequent: hypotension

Respiratory, thoracic and mediastinal disorders:

Less frequent: tightness of the chest, dry throat, nasal dryness

Gastrointestinal disorders:

Less frequent: nausea, vomiting, diarrhoea, constipation, dryness of the mouth

Skin and subcutaneous tissue disorders:

Less frequent: rash, pruritus, urticaria

Musculoskeletal, connective tissue and bone disorders:

Less frequent: muscular weakness

Renal and urinary disorders:

Less frequent: difficulty in micturition, dysuria, urinary retention

General disorders and administration site conditions:

Less frequent: asthenia

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of BENYLIN® PAEDIATRIC is important. It allows continued monitoring of the benefit/risk balance of BENYLIN® PAEDIATRIC. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

For further information, please contact the Johnson & Johnson call centre on 0860 410032 (landline).

4.9 Overdose

Diphenhydramine hydrochloride:

Overdosage may be fatal especially in infants and children.

In infants and children CNS stimulation predominates over CNS depression causing ataxia, excitement, tremors, psychoses, hallucinations and convulsions; hyperpyrexia may also occur. Deepening coma and cardiorespiratory collapse may follow. In adults: CNS depression with drowsiness, coma and convulsions, progressing to respiratory failure or possibly cardiovascular collapse.

Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 10.1 Antitussives and expectorants.

Pharmacotherapeutic group: Antihistamines for systemic use.

ATC code: R06AA02

Diphenhydramine hydrochloride is an antihistaminic and, by its atropine like action, relieves cough.

5.2 Pharmacokinetic properties

Absorption:

Diphenhydramine is well absorbed from the gastrointestinal tract.

After a single 25 mg dose a maximum concentration of 44,2 ng/mL was reached at 2,3 hours.

After multiple oral doses of 50 mg diphenhydramine four times during each day to four subjects, minimum diphenhydramine plasma concentrations at steady state on the third day ranged from 57 – 150 ng/mL.

Distribution:

Diphenhydramine is widely distributed throughout the body, including the central nervous system.

The pharmacokinetics of diphenhydramine follows a two-compartment model in which the distribution or alpha phase is apparent over the first eight to ten hours. In the paediatric age

groups, when scaled to body size, the volume of distribution varies. In children aged 2 to less than 6 years, with a weight range of 11,34 to 22,68 kg, it is 327,9 L (24,6 %) while in children aged 6 to less than 12 years with a weight range of 21,32 to 43,09 kg, it is 316,1 L (28,2 %), while in the age group of 12 to less than 18 years, with a weight range of 35,38 to 68,95 kg, the volume of distribution is 308,7 L (31,2 %).

Diphenhydramine is highly protein bound, with free medicine concentrations of 24,0 ± 1,9 % and 14,8 ± 1,5 % measured in Asian and Caucasian plasma. In adults with liver disease, protein binding is lower, although the volume of distribution is comparable to healthy adults.

Metabolism:

Diphenhydramine undergoes first-pass metabolism with an absolute bioavailability of 72 % ± 8 %. It is extensively metabolised in the liver by demethylation to *N*-demethyl diphenhydramine (DMDP), and the extent of DMDP measured in plasma is highly correlated with the clearance of diphenhydramine. DMDP is subsequently demethylated to *N,N*-didemethyl diphenhydramine. Because only the latter, minor metabolic pathway of *N,N*-didemethylation appears to be mediated by cytochrome P450 2D6, diphenhydramine disposition in humans is not determined by CYP2D6 activity. Rather, clinical pharmacokinetics data suggest that diphenhydramine may be an inhibitor of CYP2D6 without being extensively metabolised by this cytochrome P450 isozyme. *N,N*-didemethyl diphenhydramine is further metabolised by oxidative deamination to diphenylmethoxyacetic acid.

Elimination:

Mean beta elimination half-lives from 8,5 and 11,5 hours in adults have been reported in studies in which blood is sampled up to 24 to 72 hours. The half-life is increased to 13,5 ± 4,2 h in the elderly and to 15,2 ± 1,5 h in adults with liver cirrhosis. Little, if any, diphenhydramine unchanged medicine is excreted in the urine.

In patients of various ages, total body oral clearance rates differ significantly (P < ,05). In elderly adults, the mean clearance rate was 11,7 ± 3,1 mL/min/kg, on the other hand it is 23,3 ± 9,4 mL in young adults, while in children, it is 49,2 ± 22,8 mL/min/kg.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

L-menthol

Citric acid (E330)

D & C Red No.10 (CI 14720) (colourant)

Ethanol 95 %

Glucose

Glycerine (E422)

Purified water

Raspberry flavour (flavourant)

Saccharin sodium (E954)

Sodium benzoate (E211)

Sodium citrate (E331)

Sucrose.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store in a cool place.

Store at or below 25 °C.

Keep container tightly closed.

Keep the container in the outer carton.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

Amber glass bottles containing 100 mL with a plastic measuring cup.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Johnson & Johnson (Pty) Ltd.

241 Main Road

Retreat

7945

South Africa

8. REGISTRATION NUMBER

H/10.1/12

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

18 April 1987

10. DATE OF REVISION OF THE TEXT

1 February 2022.