

IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0823/001/002

Case No: 2055920

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

McNeil Healthcare (Ireland) Ltd

Airton Road, Tallaght, Dublin 24, Ireland

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Benylin Dual Action Dry Syrup

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **02/10/2008** until **14/03/2009**.

Signed on behalf of the Irish Medicines Board this

A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Benylin Dual Action Dry Syrup

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of Benylin Dual Action Dry Syrup contains

Pseudoephedrine Hydrochloride 30 mg
Dextromethorphan Hydrobromide 10 mg
Triprolidine Hydrochloride 1.25 mg

For excipients, see 6.1

3 PHARMACEUTICAL FORM

Syrup

A clear, bright red, blackberry-flavoured syrup.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

BENYLIN Dual Action Dry Syrup is indicated for the relief of dry cough and upper respiratory tract congestion such as is associated with the common cold and influenza.

4.2 Posology and method of administration

For oral use.

Adults and Children over 12 years:

10 ml every 4-6 hours, up to four times a day

Children 6 to 12 years:

5 ml every 4-6 hours, up to four times a day

Children 2 years to 5 years:

2.5 ml every 4-6 hours, up to four times a day

Children under 2 years:

Not recommended.

4.3 Contraindications

BENYLIN Dual Action Dry Syrup is contraindicated in patients hypersensitive to the product or any of its ingredients.

BENYLIN Dual Action Dry Syrup is contraindicated in patients who are receiving monoamine oxidase inhibitors or who have received these within the previous 14 days.

BENYLIN Dual Action Dry Syrup is contraindicated in patients with severe hypertension or severe coronary artery disease.

The antibacterial agent, furazolidone, is known to cause a dose-related inhibition of monoamine oxidase. Therefore BENYLIN Dual Action Dry Syrup should not be administered concurrently with furazolidone.

BENYLIN Dual Action Dry Syrup is contraindicated in patients at risk of developing respiratory failure.

BENYLIN Dual Action Dry Syrup is contraindicated in patients where cough is associated with asthma or where cough is accompanied by excessive secretions.

Benylin Dual Action Dry Syrup is contraindicated for use in children under 2 years of age.

4.4 Special warnings and precautions for use

As with other sympathomimetic agents, Benylin Dual Action Dry Syrup should be used with caution in patients with hypertension, heart disease, hyperthyroidism, elevated intraocular pressure and prostatic enlargement.

Benylin Dual Action Dry Syrup should only be used under medical supervisions for persistent or chronic cough such as occurs with smoking, asthma or emphysema, or where cough is accompanied by excessive secretions.

If symptoms persist, please consult your doctor.

Patients who are taking other medication and/or under the care of a physician, should consult their doctor/pharmacist before taking this product.

Use with caution in severe renal or hepatic impairment.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase - isomaltase insufficiency should not take this medicine.

Not more than 4 doses should be given in any 24 hours. Do not exceed the stated dose.

Do not take 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

This product may potentiate the effects of alcohol and other central nervous system depressants. Concomitant use with sympathomimetic agents such as decongestants, tricyclic antidepressants, appetite suppressants and amphetamine-like psychostimulants, or with monoamine oxidase inhibitors which interfere with the catabolism of sympathomimetic amines, may cause a rise in blood pressure.

Because of its pseudoephedrine content, the product may partially reverse the hypotensive action of drugs which interfere with sympathetic activity including bretylium, betanidine, guanethidine, debrisoquine, methyldopa, alpha- and beta-adrenergic blocking agents.

Furazolidone causes a dose-related inhibition of monoamine oxidase. Although there are no reports to date of hypertensive crisis caused by concurrent use with this product, the combination should be avoided.

4.6 Pregnancy and lactation

Although pseudoephedrine, dextromethorphan and triprolidine have been in widespread use for many years without apparent ill consequence, there are no specific data on their use during pregnancy. Caution should therefore be exercised by balancing the potential benefit of treatment to the mother against any possible hazards to the developing foetus. The product should not be used in pregnancy unless considered essential by the physician.

It is not known whether dextromethorphan or its metabolites are excreted in breast milk.

Pseudoephedrine and triprolidine are excreted in breast milk in small amounts, but the effect of this on breast-fed infants is not known.

There is no experience of the effect of BENYLIN Dual Action Dry Syrup on human fertility.

4.7 Effects on ability to drive and use machines

The product may act as a cerebral stimulant in children, and occasionally in adults. Central nervous system depression or excitation may occur, with symptoms such as drowsiness, sleep disturbance and more rarely, hallucinations. Patients receiving it should not drive or operate machinery unless it has been shown that their physical and mental ability remains unaffected.

4.8 Undesirable effects

The product may act as a cerebral stimulant in children and occasionally in adults. Central nervous system depression or excitation may occur, with symptoms such as drowsiness, sleep disturbance and more rarely, hallucinations.

This product may potentiate the effects of alcohol and other central nervous system depressants. Anti-cholinergic side effects include tachycardia, dryness of mouth, nose and throat, gastrointestinal disturbances, e.g. colic, urinary retention and headache. Skin rash has also been reported.

The product can occasionally cause drowsiness, dizziness, confusion, excitation, gastrointestinal disorders, bronchoconstriction and dyspnoea.

4.9 Overdose

Symptoms and Signs: The effects of acute toxicity from BENYLIN Dual Action Dry Syrup may include drowsiness, lethargy, dizziness, ataxia, nystagmus, weakness, hypotonicity, respiratory depression, dryness of the skin and mucous membranes, tachycardia, hypertension, hyperpyrexia, hyperactivity, irritability, convulsions, difficulty with micturition, nausea and vomiting.

Treatment: Necessary measures should be taken to maintain and support respiration and control convulsions. Gastric lavage should be performed up to 3 hours after ingestion, if indicated. Catheterisation of the bladder may be necessary. If desired, the elimination of pseudoephedrine can be accelerated by acid diuresis or by dialysis.

Naloxone has been used successfully as a specific antagonist to dextromethorphan toxicity in a child.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pseudoephedrine has a direct and indirect sympathomimetic activity and is an orally effective upper respiratory decongestant. Pseudoephedrine is substantially less potent than ephedrine in producing both tachycardia and elevation of systolic blood pressure and considerably less potent in causing stimulation of the central nervous system. Pseudoephedrine produces its decongestant effect within 30 minutes, persisting for at least 4 hours.

Dextromethorphan has an antitussive action. It controls coughs by depressing the medullary cough centre. A single oral dose of 10 - 20 mg dextromethorphan produces its antitussive action within 1 hour and lasts for at least 4 hours.

Tripolidine provides antihistamine activity by antagonising H₁-receptors. After oral administration of a single dose of 2.5 mg tripolidine to adults the onset of action, as determined by the ability to antagonise histamine-induced weals and flares in the skin, is within 1 to 2 hours. Peak effects occur at about 3 hours and, although activity declines thereafter, significant inhibition of histamine-induced weals and flares still occurs 8 hours after the dose.

5.2 Pharmacokinetic properties

After the administration of 2.5 mg tripolidine hydrochloride and 60 mg pseudoephedrine hydrochloride to healthy adult volunteers, the peak plasma concentration (C_{max}) of tripolidine is approximately 5.5 ng/ml - 6.0 ng/ml occurring at about 1.5 - 2.0 hours (T_{max}) after drug administration. Its plasma half-life is approximately 3.2 hours. The C_{max} of pseudoephedrine is approximately 180 ng/ml with T_{max} approximately 1.5 - 2.0 hours after drug administration. The plasma half-life is approximately 5.5 hours (urine pH maintained between 5.0 - 7.0). The plasma half-life of pseudoephedrine is increased in subjects with alkaline urine and decreased in subjects with acid urine.

Genetically controlled O-demethylation is the main determinant of dextromethorphan pharmacokinetics in human volunteers. It appears that there are two distinct phenotypes for this oxidation process resulting in highly variable pharmacokinetics between subjects.

5.3 Preclinical safety data

It has been estimated that 0.5 to 0.7% of a single dose of pseudoephedrine ingested by a mother will be excreted in the breast milk over 24 hours.

In rats and rabbits, systemic administration of tripolidine up to 75 times the human daily dosage did not produce teratogenic effects.

Systemic administration of pseudoephedrine up to 50 times the human daily dosage in rats, and up to 35 times the human daily dosage in rabbits did not produce teratogenic effects.

There is insufficient information available to determine whether dextromethorphan has teratogenic potential.

No studies have been conducted in animals to determine whether pseudoephedrine, dextromethorphan or tripolidine have the potential to impair fertility.

The active ingredients of BENYLIN Dual Action Dry Syrup are well-known constituents of medicinal products and their safety profiles are well documented. The results of pre-clinical studies do not add anything of relevance for therapeutic purposes.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sorbitol solution (70%)
 Sucrose
 Sodium benzoate (E211)
 Methyl parahydroxybenzoate (E218)
 Ponceau 4R (E124)
 Ethanol
 Blackberry flavour
 Levomenthol
 Vanillin
 Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 25°C. Do not refrigerate. Keep the bottle in the outer carton.

6.5 Nature and contents of container

Benylin Dual Action Dry Syrup is stored in 30ml, 40ml, 50ml, 100ml and 200ml amber glass bottles closed with metal roll-on closures or HDPE screw caps fitted with saran - or steran (PVDC)-faced wads.

Alternatively the product is available in amber glass bottles with a three piece plastic child resistant tamper evident closure fitted with a polyvinylidene chloride (PVDC) faced wad or polyethylene expanded polyethylene laminated wad.

Not all pack sizes may be marketed.

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

McNeil Healthcare (Ireland) Ltd.
Airton Road
Tallaght
Dublin 24

8 MARKETING AUTHORISATION NUMBER

PA 823/1/2

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15th March 1984

Date of last renewal: 15th March 2004

10 DATE OF REVISION OF THE TEXT

June 2008