SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Robitussin Dry Cough Medicine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Ingredient
Dextromethorphan Hydrobromide Ph Eur 7.5mg per 5ml

Excipients with known effect
Amaranth (E123) – 0.33 mg of amaranth in each 10 ml dose
Ethanol: 219.3 mg of alcohol (ethanol) in each 10 ml dose
Maltitol (E965): 484 mg of maltitol in each 10 ml dose
Sodium: 21.94 mg of sodium in each 10 ml dose
Sodium benzoate (E211): 12.0 mg of sodium benzoate in each 10 ml dose
Sorbitol (E420): 2094 mg sorbitol in each 10 ml dose

For full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Clear red colour liquid with a characteristic odour and taste of cherry for oral administration.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of persistent dry irritant coughs

4.2 Posology and method of administration

Oral administration.

Adults, the elderly and children over 12 years: One 10ml measure up to four times daily.

Children under 12 years: Do not use

Medical advice should be sought before use in patients with severe renal impairment. See Warnings and Precautions.

4.3 Contraindications

Hypersensitivity to any of the ingredients.

Taking a prescription selective serotonin reuptake inhibitor (SSRI), or other medications for depression, psychiatric, or emotional conditions, or Parkinson's disease. Do not use if you are taking or have taken in the past two weeks, monoamine oxidase inhibitors (MAOI's), usually used to treat depression. If you are not sure if your prescription medication contains one of these medicines, ask a doctor or pharmacist before taking this product. (See section 4.5).

Use in children under 12 years.

Patients with, or at risk of developing, respiratory failure (e.g. those with chronic obstructive airways disease or pneumonia, or during an asthma attack or an exacerbation of asthma).

4.4 Special warnings and precautions for use

Should not be used with other cough and cold medicines.

Patients suffering from chronic cough as occurs with smoking, asthma or patients suffering from an acute asthma attack, chronic bronchitis, and emphysema, or where cough is accompanied by excessive secretions should be advised to consult a Healthcare Professional before use.

Causes of chronic cough should be excluded if symptoms are persistent. Any accompanying symptoms should be actively sought and appropriately investigated/ treated. Stop use and ask your healthcare professional if your cough lasts more than 7 days, comes back or is accompanied by a fever, rash or persistent headache. These could be signs of serious conditions.

Medical advice should be sought before taking dextromethorphan in patients with: severe renal impairment.

Concomitant use of other cough and cold medicines should be avoided.

Concomitant use of alcohol should be avoided.

Drug dependence, tolerance and potential for abuse
For all patients, prolonged use of this product may lead to drug dependence (addiction), even at therapeutic doses. The risks are increased in individuals with current or past history of substance misuse disorder (including alcohol misuse) or mental health disorder (e.g., major depression). Caution is particularly recommended

for adolescents and young adults as well as in patients with a history of drug abuse or psychoactive substances.

Drug withdrawal syndrome
The drug withdrawal syndrome is characterised by some or all of the following: restlessness, lacrimation, rhinorrhoea, yawning, perspiration, chills, myalgia, mydriasis and palpitations. Other symptoms may also develop including irritability, agitation, anxiety, hyperkinesia, tremor, weakness, insomnia, anorexia, abdominal cramps, nausea, vomiting, diarrhoea, increased blood pressure, increased respiratory rate or heart rate.

Dextromethorphan is metabolised by hepatic cytochrome P450 2D6. The activity of this enzyme is genetically determined. About 10% of the general population are poor metabolisers of CYP2D6. Poor metabolisers and patients with concomitant use of CYP2D6 inhibitors may experience exaggerated and/or prolonged effects of dextromethorphan. Caution should therefore be exercised in patients who are slow metabolizers of CYP2D6 or use CYP2D6 inhibitors (see also section 4.5).

Keep out of the sight and reach of children.

Do not exceed recommended dose.

Excipient warnings:
- Patients with rare hereditary problems of fructose intolerance should not take this medicine because this product contains Sorbitol and Maltitol.
- This product contains Amaranth (E123), which may cause allergic reactions.
- This medicine contains 219.3 mg of alcohol (ethanol) in each 10 ml dose which is equivalent to 22 mg/ml (2.08% w/v). The amount in 10 ml of this medicine is equivalent to less than 6 ml beer or 3ml wine. Harmful for those suffering from alcoholism. To be taken into account in pregnant or breast-feeding women and high-risk groups such as patients with liver disease, or epilepsy.
- This medicine contains 12.0 mg sodium benzoate in each 10 ml dose which is equivalent to 1.2 mg/ml.
- This medicine contains 2094 mg sorbitol per 10 ml dose which is equivalent to 209.4 mg/ml. Sorbitol may cause gastrointestinal discomfort and mild laxative effect.
- This medicine contains less than 1 mmol sodium (23 mg) per 10 ml.

Serotonin Syndrome
Serotonergic effects, including the development of a potentially life-threatening serotonin syndrome, have been reported for dextromethorphan with concomitant administration of serotonergic agents, such as selective serotonin re-uptake inhibitors (SSRIs), drugs which impair metabolism of serotonin (including monoamine oxidase inhibitors (MAOIs)) and CYP2D6 inhibitors.
Serotonin syndrome may include mental-status changes, autonomic instability, neuromuscular abnormalities, and/or gastrointestinal symptoms. If serotonin syndrome is suspected, treatment with Robitussin Dry Cough should be discontinued.

4.5 Interaction with other medicinal products and other forms of interaction

Do not use if you are now taking a prescription selective serotonin reuptake inhibitor (SSRI), tricyclic antidepressants (TCAs) or other medications for depression, psychiatric, or emotional conditions, or Parkinson's disease. Do not use if you are taking or have taken in the past two weeks, monoamine oxidase inhibitors (MAOI's), usually used to treat depression. If you are not sure if your prescription medication contains one of these drugs, ask a doctor or pharmacist before taking this product.

CYP2D6 inhibitors
Dextromethorphan is metabolized by CYP2D6 and has an extensive first-pass metabolism. Concomitant use of potent CYP2D6 enzyme inhibitors can increase the dextromethorphan concentrations in the body to levels multifold higher than normal. This increases the patient's risk for toxic effects of dextromethorphan (agitation, confusion, tremor, insomnia, diarrhoea and respiratory depression) and development of serotonin syndrome. Potent CYP2D6 enzyme inhibitors include fluoxetine, paroxetine, quinidine and terbinafine. In concomitant use with quinidine, plasma concentrations of dextromethorphan have increased up to 20-fold, which has increased the CNS adverse effects of the agent. Amiodarone, flecainide and propafenone, sertraline, bupropion, methadone, cinacalcet, haloperidol, perphenazine and thioridazine also have similar effects on the metabolism of dextromethorphan. If concomitant use of CYP2D6 inhibitors and dextromethorphan is necessary, the patient should be monitored and the dextromethorphan dose may need to be reduced.

Alcohol
A dose of 10ml of this medicine administered to an adult weighing 70 kg would result in exposure to 2.8 mg/kg of ethanol which may cause a rise in bloodalcohol concentration (BAC) of about 0.4mg/100 ml.

A dose of 10ml of this medicine administered to a child over 12 years of age and weighing 40 kg would result in exposure to 4.9 mg/kg of ethanol which may cause a rise in blood alcohol concentration (BAC) of about 0.8 mg/100 ml

For comparison, for an adult drinking a glass of wine or 500 ml of beer, the BAC is likely to be about 50 mg/100 ml. Co-administration with medicines containing e.g. propylene glycol or ethanol may lead to accumulation of ethanol and induce adverse effects, in particular in young children with low or immature metabolic capacity.

4.6 Fertility, pregnancy and lactation

Fertility

There are no relevant clinical data available regarding effects on fertility from patients taking dextromethorphan. Studies in rats have demonstrated a lack of adverse effect on fertility (see section 5.3). Therefore, no adverse effects on human fertility are expected at therapeutically relevant doses.

Pregnancy

There are no relevant clinical data available regarding effects on pregnancy from patients taking dextromethorphan. Animal studies do not indicate embryofetal toxicity (see section 5.3). Dextromethorphan should not be used during pregnancy without medical advice.

Breastfeeding

Avoid the use of the product during lactation, unless the benefits to the mother outweigh the risks to the infant. If used, the lowest effective dose and shortest duration of treatment should be considered.

Dextromethorphan is excreted in breast milk in minor quantities. There is a lack of data available on the effect of infant exposure through breast milk.

4.7 Effects on ability to drive and use machines

This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When taking this medicine, patients should be told:

- The medicine is likely to affect your ability to drive
- Do not drive until you know how the medicine affects you
- It is an offence to drive while under the influence of this medicine
- However, you would not be committing an offence (called 'statutory defence') if:
  - The medicine has been prescribed taken to treat a medical problem and
  - You have taken it according to the information provided with the medicine and
  - It was not affecting your ability to drive safely

4.8 Undesirable effects

The following convention has been utilised for the classification of the frequency of adverse reactions: 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 available data).

Whenever possible, adverse reactions observed in clinical trials and those reported from post-marketing experience at therapeutic/labelled doses have been presented separately. These reactions are tabulated by MedDRA System Organ Class (SOC). The following adverse events have been observed in clinical trials with dextromethorphan.

Gastrointestinal Disorders:

Gastrointestinal upset, nausea, vomiting, abdominal discomfort

Nervous System Disorders:
Dizziness, drowsiness, mental confusion

Adverse reactions identified during post-marketing use are listed below. As these reactions are reported voluntarily from a population of uncertain size, the frequency of these reactions is unknown.

Immune System Disorders:
Hypersensitivity

Psychiatric Disorders:
Frequency unknown: Drug dependence (see section 4.4)

Skin and Subcutaneous Disorders:
Allergic reactions (e.g. rash, urticaria, angioedema)

General Disorders and Administration Site Conditions:
Frequency unknown: drug withdrawal syndrome

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms and signs:
Dextromethorphan overdose may be associated with nausea, vomiting, dystonia, agitation, confusion, somnolence, stupor, nystagmus, cardiotoxicity (tachycardia, abnormal ECG including QTc prolongation), ataxia, toxic psychosis with visual hallucinations, hyperexcitability.
In the event of massive overdose the following symptoms may be observed: coma, respiratory depression, convulsions.

Management:
-Activated charcoal can be administered to asymptomatic patients who have ingested overdoses of dextromethorphan within the preceding hour.
-For patients who have ingested dextromethorphan and are sedated or comatose, naloxone, in the usual doses for treatment of opioid overdose, can be considered. Benzodiazepines for seizures and benzodiazepines and external cooling measures for hyperthermia from serotonin syndrome can be used.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Dextromethorphan hydrobromide is a cough suppressant which has a central action on the cough centre in the medulla. It has no analgesic properties.

Dextromethorphan
Pharmacotherapeutic group: Cough suppressant
ATC code: R05DA09

5.2 Pharmacokinetic properties

Dextromethorphan hydrobromide is well absorbed from the gastrointestinal tract.

Dextromethorphan undergoes rapid and extensive first-pass metabolism in the liver after oral administration. Genetically controlled O-demethylation (CYD2D6) is the main determinant of dextromethorphan pharmacokinetics in human volunteers.

It appears that there are distinct phenotypes for this oxidation process resulting in highly variable pharmacokinetics between subjects. Unmetabolised dextromethorphan, together with the three demethylated morphinan metabolites dextrorphan (also known as 3-hydroxy-N-methylmorphinan), 3-hydroxymorphinan and 3-methoxymorphinan have been identified as conjugated products in the urine.

Dextrorphan, which also has antitussive action, is the main metabolite. In some individuals metabolism proceeds more slowly and unchanged dextromethorphan predominates in the blood and urine.

5.3 Preclinical safety data

Non-clinical safety data on dextromethorphan obtained from the literature and in-house have not revealed findings which are of relevance to the recommended dosage and use of the product.

Reproductive and developmental toxicity

No adverse effects on male and female fertility or postnatal development were observed rats following oral administration of up to 50 mg/kg/day dextromethorphan. No effects on embryofetal development were observed in both rats and rabbits following oral administration of up to 50 mg/kg/day dextromethorphan during pregnancy. A 50 mg/kg/day dose in rats and rabbits is approximately 5- and 11-times

the maximum human equivalent therapeutic dose (based on the body weight of 12-year-old child of 40 kg), respectively.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerol
Sodium Carboxymethyl Cellulose
Sodium Benzoate
Disodium Edetate
Maltitol (E965)
Ethanol (96%)
Citric Acid Anhydrous
Amaranth (E123)
Caramel (E150)
Levomenthol
Cherry/Grenadine Flavour
Sorbitol Solution 70%
Sodium Cyclamate
Acesulfame Potassium Salt
Purified Water

6.2 Incompatibilities

None stated

6.3 Shelf life

33 months

6.4 Special precautions for storage

Do not store above 25^{o}C

Keep out of the sight and reach of children

6.5 Nature and Contents of Container

Brown glass bottle, hydrolytic class 3, containing 100 ml or 200ml with child resistant caps.
A transparent polypropylene measuring cap is also included.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

Haleon UK Trading Limited
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Weybridge
Surrey
KT13 0NY
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 44673/0207

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01/09/1993 / 18/05/2010

10 DATE OF REVISION OF THE TEXT

26/11/2024