

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Covonia Original Bronchial Balsam Syrup

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Dextromethorphan Hydrobromide	7.5mg/5ml (Recommended dose is 10ml)
Menthol	2.5mg/5ml (Recommended dose is 10ml)

Excipients with known effect

This medicine contains, per 10ml dose: 13.7mg Ethanol, 8.8g Sucrose, 5mg Sodium benzoate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Syrup

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the symptomatic relief of non-productive coughs such as those associated with the common cold and bronchitis.

4.2 Posology and method of administration

Oral.

Recommended doses

Adults and children over 12 years: 10ml.

Elderly: as adults dose with caution.

Dosage schedule

The dose may be repeated after 4 hours if required.

4.3 Contraindications

Contraindicated in patients with liver disease and/or known hypersensitivity to dextromethorphan hydrobromide, and menthol. Patients being treated with monoamine oxidase inhibitors should avoid using the product. Persistent or productive cough. Dextromethorphan should not be administered to patients in or at risk of developing respiratory failure or during an acute asthma attack. Do not use within 2 weeks of discontinuation of MAOI use.

Children under 12 years of age.

4.4 Special warnings and precautions for use

Warning: Do not take more medicine than the label tells you to.

Keep all medicines away from children.

If symptoms persist consult your doctor.

Covonia normally works without causing drowsiness, but care should be taken initially as rare exceptions can occur.

Use with caution in a history of asthma.

Label states: Consult a doctor or pharmacist before use if you have a history of asthma.

Do not give to children under 12 years.

Can cause addiction.

This medicine may cause opioid-like effects when used at high doses.

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).

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).

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.

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 Covonia Original Bronchial Balsam Syrup should be discontinued.

Ingredients with specified warnings

This medicine contains 14mg of alcohol (ethanol) in each 10ml dose. The amount in 10ml of this medicine is less than 1ml of beer or 1ml of wine. The small amount of alcohol in this medicine will not have any noticeable effects.

This medicine contains less than 1mmol sodium (23mg) in each 10ml dose, that is to say essentially 'sodium-free'.

Contains 8.8g sucrose per 10ml dose, to be taken into account in people with diabetes mellitus. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.

This medicine contains 5mg Sodium benzoate in each 10ml dose.

4.5 Interaction with other medicinal products and other forms of interaction

Cimetidine may delay the elimination of dextromethorphan. It is therefore imperative that the dose of Covonia is not exceeded when it is taken with other medicines. Dextromethorphan interacts with MAOI's.

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, diarrhea 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.

4.6 Fertility, pregnancy and lactation

There is no evidence of safety in human pregnancy. However, the drugs in the formulation have been widely used for many years without apparent ill consequence. No information is available on the excretion of dextromethorphan or its metabolites in breast milk. It is therefore best avoided during breastfeeding.

4.7 Effects on ability to drive and use machines

At the stated dose, no evidence has been found that the formulation has any effect on the ability to drive or use machinery however dextromethorphan hydrobromide may cause dizziness and drowsiness rarely.

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 prescribing 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 to treat a medical or dental problem and
 - You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and
 - It was not affecting your ability to drive safely

4.8 Undesirable effects

At the stated dose constipation, gastrointestinal discomfort, nausea, vomiting, dizziness and drowsiness may occur rarely.

Drug dependence and drug withdrawal syndrome may also occur (frequency unknown).

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

Serious overdoses have been reported with other dextromethorphan containing products. Taken in large doses, may cause drowsiness, dizziness, excitation, nausea, vomiting, gastro intestinal disturbance, blurred vision, nystagmus, ataxia, urinary retention, stupor, coma, facial oedema and urticaria. Very large doses may produce respiratory depression and some patients may be particularly sensitive to this. This may be combatted with trial small doses (1.5 - 3UG/KG to be repeated only if there is a response) of morphine antagonists such as naloxone. Symptoms arising from oral poisoning with menthol are,

severe abdominal pain, nausea, vomiting, vertigo, ataxia, drowsiness and coma.

Treatment of overdose: acutely, gastric lavage: otherwise, general supportive measures should be used.

Dependence has been reported occasionally with dextromethorphan.

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

Pharmacotherapeutic Group: Cough suppressant and expectorants, Combinations

ATC Code: R05F

Dextromethorphan acts as a non-narcotic cough suppressant. The drug acts centrally to elevate the threshold for coughing.

Menthol relieves irritation, diminishes congestion, and checks excessive secretion of mucous membranes in the upper respiratory tract and is used for the treatment of the symptoms of bronchitis.

5.2 Pharmacokinetic properties

Dextromethorphan is fully absorbed from the gastro-intestinal tract and passes via the portal vein to the liver before entering the general circulation.

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-Nmethylmorphinan), 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.

Dextromethorphan is not metabolised to either morphine or codeine. In general, approximately 50% of dextromethorphan plus metabolites is excreted in the urine within 24 hours. Plasma levels of therapeutic doses are very low, due to metabolism in the liver. Plasma levels of the principal metabolite, dextrorphan, are higher than dextromethorphan, plasma levels reaching a peak 2 hours after administration. The plasma half life of dextrorphan has been determined as approximately 0.5-1.0 hour in the dog.

After absorption menthol is excreted in the urine and bile as a glucuronide.

5.3 Preclinical safety data

None

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water purified

Citric acid monohydrate

Peppermint oil

Anise oil

Capsicum tincture (Contains Ethanol)

Macrogol cetostearyl ether

Caramel

Glycerol (E422)

Cineole

Sodium benzoate (E211)

Syrup (Contains Sucrose)

6.2 Incompatibilities

No major incompatibilities are known.

6.3 Shelf life

150ml: 36 months unopened

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

150ml flat sloping shoulder amber glass bottle, with 28mm tamper evident child resistant closure with EPE/ Saranex liner.

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Thornton & Ross Ltd
Huddersfield
HD7 5QH
England

8 MARKETING AUTHORISATION NUMBER(S)

PL 00240/5033R

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

29/05/1990

10 DATE OF REVISION OF THE TEXT

19/06/2020