PROFESSIONAL INFORMATION

SCHEDULING STATUS: S2

1. NAME OF THE MEDICINE

DILINCT DRY COUGH SYRUP

15 mg, syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains:	
Dextromethorphan hydrobromide	15 mg

Excipients with known effect:

Preservative: Sodium benzoate 0,20 % $^{m}/_{v}$

Contains sweeteners: 350 mg sorbitol and 9 mg saccharin sodium.

Alcohol and sugar free

Tartrazine free

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Syrup.

A clear, red syrup with an odour of raspberry

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

For the symptomatic relief of a dry, non-productive cough.

4.2 Posology and method of administration

Posology

Adults: One medicine measure (5 ml) every four hours, or two medicine measures (10 ml) every six to eight hours.

Children 5 to 12 years: Half (2,5 ml) to one medicine measure (5 ml) every six to eight hours.

Children below 5 years: Not recommended (see section 4.3)

Method of administration

For oral use only

Shake the bottle before use.

4.3 CONTRAINDICATIONS

- Known hypersensitivity to dextromethorphan hydrobromide or any of the other excipients listed in section 6.1.
- Not to be given to children under 5 years of age (See section 4.2)
- In asthma and hepatic dysfunction.
- Patients at risk of developing respiratory failure.
- Not to be taken for a productive cough.
- Patients taking monoamine oxidase inhibitors (MAOIs), or for 2 weeks after stopping the MAOI medicine. There is risk of serotonin syndrome with the concomitant use of DILINCT DRY COUGH SYRUP and MAOIs and the concomitant use of these medicines may cause a rise in blood pressure and/or hypertensive crisis (see section 4.5).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

- DILINCT DRY COUGH SYRUP should not be taken for a persistent respiratory condition, which occurs with smoking, bronchial asthma, emphysema, chronic bronchitis or where cough is accompanied by excessive secretions, except under the advice and supervision of a doctor. A persistent cough may be a sign of a serious condition. If cough persists for more than one week, tends to recur or is accompanied by high fever, rash or persistent headache, consult a doctor. Persistent coughs should be investigated by a doctor for the possible underlying cause.
- Cases of dextromethorphan abuse and associated dependence have been reported. Caution with DILINCT DRY COUGH SYRUP is particularly recommended for adolescents and young adults, as well as in patients with a history of drug abuse or use of psychoactive substances.
- 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 with DILINCT DRY COUGH SYRUP should therefore be exercised in patients who are slow metabolisers of CYP2D6 or use CYP2D6 inhibitors (see section 4.5). If a patient is a known slow metaboliser of CYP2D6, or is using any other medicines (such as serotonergic medicines, including selective serotonin re-uptake inhibitors (SSRIs), medicines which impair the metabolism of serotonin (including MAOIs - see section 4.3) or CYP2D6 Inhibitors), a doctor or pharmacist should be consulted prior to taking DILINCT DRY COUGH SYRUP. Serotonergic effects, including the development of a potentially life-threatening serotonin syndrome, have been reported for dextromethorphan with concomitant administration of serotonergic medicines.

- DILINCT DRY COUGH SYRUP contains 50 mg propylene glycol in each 5 ml which is equivalent to 10 mg/ml.
    - If your child is less than 5 years old, talk to your doctor or pharmacist before giving them this medicine, in particular if they use other medicines that contain propylene glycol or alcohol.
    - If you are pregnant or breastfeeding, do not take this medicine unless recommended by your doctor. Your doctor may carry out extra checks while you are taking this medicine.
    - If you suffer from a liver or kidney disease, do not take this medicine unless recommended by your doctor. Your doctor may carry out extra checks while you are taking this medicine.
- DILINCT DRY COUGH SYRUP contains 350 mg sorbitol in 5 ml which is equivalent to 70 mg/ml.
    - Sorbitol is a source of fructose. If your doctor has told you that you (or your child) have an intolerance to some sugars or if you have been diagnosed with hereditary fructose intolerance (HFI), a rare genetic disorder in which a person cannot break down fructose, talk to your doctor before you (or your child) take or receive this medicine.
- DILINCT DRY COUGH SYRUP contains 10 mg sodium benzoate in 5 ml which is equivalent to 2 mg/ml.
    - Sodium benzoate may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old).

4.5 Interaction with other medicines and other forms of interaction

- Concurrent use of DILINCT DRY COUGH SYRUP with monoamine oxidase inhibitors, or use of *monoamine oxidase inhibitors* within two to three weeks of DILINCT DRY COUGH SYRUP may cause hypertension, hyperpyrexia and excitation
- Concurrent administration with other *central nervous system (CNS) depressants* may enhance the CNS depressant effects of these medications.
- DILINCT DRY COUGH SYRUP is metabolised by CYP2D6 and has an extensive first-pass metabolism. Concomitant use of potent CYP2D6 enzyme inhibitors can increase the dextromethorphan concentrations in the body. This increases the risk of the patient 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 increases the CNS
  adverse effects of the medicine. *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 DILINCT DRY COUGH SYRUP is necessary, the patient should be monitored and the DILINCT DRY COUGH SYRUP dose may need to be reduced.
- *Isavuconazole* is a moderate inhibitor of CYP3A4 and a mild inducer of CYP2B6. When administered concomitantly with dextromethorphan, the area under the curve (AUC) and Cmax of dextromethorphan has been observed to increase by 18 % and 17 %, respectively.
- Concomitant use of DILINCT DRY COUGH SYRUP with *SSRI medicines* may lead to serotonin syndrome.

4.6 Fertility, pregnancy and lactation

The safety in pregnant and lactating woman has not been established. No fertility data available.

4.7 Effects on ability to drive and use machines

DILINCT DRY COUGH SYRUP may lead to drowsiness and impaired concentration that may be

aggravated by the simultaneous intake of alcohol or other central nervous system depressants. Patients should be advised, particularly at the initiation of therapy, against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of concentration could lead to accidents.

4.8 Undesirable effects

System Organ Class	*Frequency*	*Undesirable effect*
Immune system disorders	Less frequent	Angioedema
Nervous system disorders	Less frequent	Dizziness, mild drowsiness, headache, psychomotor hyperactivity
Psychiatric disorders	Less frequent	Confusion, insomnia
Gastrointestinal disorders	Less frequent	Constipation, abdominal pain, nausea and vomiting
Skin and subcutaneous tissue disorders	Less frequent	Pruritus, rash, urticaria

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who- umc.org) found on SAHPRA website. You may also report to Adcock Ingram Limited using the following email:

Adcock.AEReports@adcock.com

4.9 Overdose

Symptoms of overdose may include excitation, agitation, confusional state, conversion disorder, mixed hallucinations, ataxia, clumsiness, coma, depressed levels of consciousness, dysarthria, dystonia, lethargy, nystagmus, seizure, serotonin syndrome, tremor, miosis, mydriasis, respiratory depression,

urinary retention, tachycardia, ischaemic colitis, and hypertension. Bromide intoxication has been observed during concomitant use with bromide-containing over-the counter medicines or with overdose of dextromethorphan hydrobromide.

Treatment is symptomatic and supportive. Assisted respiration, vital sign monitoring and intravenous naloxone may be used to treat an overdosage.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 10.1 Antitussives and expectorants

Pharmacotherapeutic group: Cough Suppressant, Opium alkaloids and derivatives

ATC code: R05DA09

Dextromethorphan hydrobromide is a cough suppressant. It acts centrally on the cough centre in the medulla by elevating the threshold for coughing.

Dextromethorphan is the dextrorotatory isomer of 3-methoxy-N-methylmorphinan. It is a synthetic morphine derivative that, in contrast to its levoisomer, has no significant analgesic, respiratory depressant or physical dependency properties at recommended The major metabolite of dextromethorphan, dextrorphan, binds with high affinity to s-receptors to produce the antitussive activity without exhibiting the classic opiate effects that occur from binding into μ- and d-receptors. Dextrorphan also exhibits binding activity at serotonergic receptors and has shown to enhance serotonin activity by inhibiting the reuptake of serotonin. In larger than therapeutic doses, dextrorphan is also an antagonist of N-methyl-D-aspartate (NMDA) receptors.

5.2 Pharmacokinetic properties

Absorption: Dextromethorphan is rapidly absorbed from the gastrointestinal tract with peak plasma concentrations reached in approximately 2 to 2.5 hours. The low plasma levels of dextromethorphan suggest low oral bioavailability secondary to extensive first-pass (pre-systemic metabolism) in the liver. The maximum clinical effects occur 5 to 6 hours after ingestion of dextromethorphan.

Distribution: Dextromethorphan is widely distributed in the human body. Dextromethorphan and its

active metabolite, dextrorphan, are actively taken up and concentrated in brain tissue. It is not known whether dextromethorphan or dextrorphan are excreted in breast milk or cross the placenta.

Metabolism: 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.

Elimination: Dextromethorphan is primarily excreted via the kidney as unchanged parent compound and its active metabolite, dextrorphan. Dextrorphan and 3-hydroxymorphinan are further metabolised by glucuronidation and are eliminated via the kidneys. The elimination half-life of the parent compound is between 1,4 to 3,9 hours and that of dextrorphan is between 3,4 to 5,6 hours. The half-life of dextromethorphan in poor metabolisers is extremely prolonged, and is in the range of 45 hours. Dextromethorphan syrup has a terminal plasma elimination half-lives of 3,3 ± 0,63 h.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Polyvinylpyrrolidone [E1201],
- Acid Citric Monohydrate [E330],
- Saccharin Sodium [E954],
- Xanthan Gum [E415],
- Colour Raspberry Red [E30b5d],
- Levomenthol,
- Propylene Glycol [E1520],
- Glycerol [E422],
- Sorbitol 70 % [E420],

- Sodium benzoate [E210]
- Essence Raspberry.
- Purified water

6.2 Incompatibilities

None.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 ºC in a well-closed container.

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

A clear, red syrup with an odour of raspberry.

Amber glass bottles of 50 ml, 100 ml and 200 ml with a white polypropylene screw on cap.

6.6 Special precautions for disposal and other handling

No special requirements.

7 HOLDER OF THE CERTIFICATE OF REGISTRATION

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8 REGISTRATION NUMBER

38/10.1/0239

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 07 April 2006

10. DATE OF REVISION OF THE TEXT

30 April 2026

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