SUMMARY OF PRODUCT CHARACTERISTICS FOR XPEL COUGH EXPECTORANT

1. **Name of the medicinal product**
Xpel cough Expectorant

2. **Qualitative and quantitative composition**

Each 5 ml contains:

Diphenhydramine hydrochloride	14.0 mg
Ammonium Chloride B.P	135mg
Sodium Citrate	57mg
Menthol	1.1 mg

For a full list of excipients, see section 6.1.

3. **Pharmaceutical form**
Syrup.

A Brown coloured syrupy liquid with characteristic odour

4. Clinical particulars

4.1 **Therapeutic indications**
Xpel Cough Expectorant is indicated for the relief of cough and associated congestive symptoms.

4.2 Posology and method of administration
For oral use

Adults and Children aged 12 years and over:

One 10 ml dose of syrup 4 times a day.

Maximum daily dose: 40 ml syrup.

Children under 12 years:

Xpel Cough Expectorant is contraindicated in children under the age of 12 years (see section 4.3).

The Elderly:

As for adults above (see Pharmacokinetics - The elderly).

Hepatic dysfunction

Caution should be exercised if moderate to severe hepatic dysfunction is present (see Pharmacokinetics - Hepatic dysfunction).

Renal dysfunction

It may be prudent to increase the dosage interval in subjects with moderate to severe renal failure (see Pharmacokinetics - Renal dysfunction).

Do not exceed the stated dose.

Keep out of the sight and reach of children.

4.3 Contraindications
Xpel Cough Expectorant is contraindicated in individuals with known hypersensitivity to Diphenhydramine or menthol or to any of the excipients listed in section 6.1.

Xpel Cough Expectorant should not be administered to patients currently receiving monoamine oxidase inhibitors (MAOIs) or within 14 days of stopping treatment (see section 4.5).

Not to be used in children under the age of 12 years.

4.4 Special warnings and precautions for use
This product may cause drowsiness. If affected individuals should not drive or operate machinery.

This product should not be used to sedate a child.

Diphenhydramine may enhance the sedative effects of central nervous system depressants including alcohol, sedatives, opioid analgesics, antipsychotics and tranquilizers. Alcoholic beverages should be avoided while taking this medicine (see section 4.5).

Do not use with any other product containing diphenhydramine, including topical formulations used on large areas of skin.

Subjects with hepatic disease or moderate to severe renal dysfunction should exercise caution when using this product (see Pharmacokinetics - Renal/Hepatic Dysfunction).

Patients with the following conditions should be advised to consult a physician before using this medicine:

• A chronic or persistent cough such as occurs with chronic bronchitis or emphysema, acute or chronic asthma, or where cough is accompanied by excessive secretions

• Susceptibility to angle-closure glaucoma

• Prostatic hypertrophy and/or urinary retention

Contains 3.5 g of glucose and 1 g of sucrose per 5 ml. This should be taken into account in patients with diabetes mellitus.

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

This product contains caramel coloured which does not may cause any allergic reactions.

This medicine contains 16.62 mg sodium (main component of cooking/table salt) in each 5 ml. This is equivalent to 0.83% of the recommended maximum daily dietary intake of sodium for an adult.

This medicine contains 0.22 mg benzyl alcohol in each 5ml. Benzyl alcohol may cause allergic reactions.

Ask your doctor or pharmacist for advice if you are pregnant or breast- feeding. This is because large amounts of benzyl alcohol can build-up in your body and may cause side effects (called “ metabolic acidosis”). High volumes should be used with caution and only if necessary, especially in subjects with liver or kidney impairment because of the risk of accumulation and toxicity (metabolic acidosis).

This medicine contains 10 mg sodium benzoate (E 211) in each 5 ml.

This medicine contains 197 mg of alcohol (ethanol) in each 5 ml. The amount in 5 ml of this medicine is equivalent to less than 5 ml beer or 2 ml wine.

The small amount of alcohol in this medicine will not have any noticeable effects.

4.5 Interaction with other medicinal products and other forms of interaction
Diphenhydramine

CNS depressants: may enhance the sedative effects of CNS depressants including barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives, antipsychotics and alcohol.

Antimuscarinic drugs: may have an additive muscarinic action with other drugs, such as atropine and some antidepressants.

MAOIs: Not be used in patients taking MAOIs or within 14 days of stopping treatment as there is a risk of serotonin syndrome.

Menthol

There are no known drug interactions associated with menthol.

4.6 Fertility, pregnancy and lactation
This product should not be used during pregnancy or breastfeeding unless the potential benefit of treatment to the mother outweighs the possible risks to the developing fetus or breastfeeding infant.

Diphenhydramine

Pregnancy

Diphenhydramine has been in widespread use for many years without any apparent ill consequence. Diphenhydramine is known to cross the placenta and, therefore, should only be used during pregnancy if considered essential by a doctor.

Breastfeeding

Diphenhydramine is excreted into human breast milk, but levels have not been reported. Although the levels are not thought to be sufficiently high enough after therapeutic doses to affect the infant, the use of diphenhydramine during breast-feeding is not recommended.

Menthol

There are no adequate and well-controlled studies in pregnant women for menthol. Menthol is excreted in breast milk; when 100 mg of menthol was ingested, there was up to 5.87 ug/L of menthol in breast milk.

4.7 Effects on ability to drive and use machines
This product may cause drowsiness. If affected, the patient should not drive or operate machinery.

4.8 Undesirable effects
Diphenhydramine

Adverse drug reactions (ADRs) identified during clinical trials and post- marketing experience with Diphenhydramine are included in the table below by System Organ Class (SOC). The frequencies are provided according to the following convention:

Very common	≥ 1/10
Common	≥ 1/100 and < 1/10
Uncommon	≥ 1/1,000 and <1/100
Rare	≥ 1/10,000 and <1/1,000
Very rare	<1/10,000
Not known	(cannot be estimated from the available data)

System Organ Class (SOC)	**Frequency***	**Adverse Drug Reaction**
Blood and Lymphatic System Disorders	Rare	Blood disorders
Immune System Disorders	Rare	Hypersensitivity reactions
Psychiatric Disorders	Uncommon	Irritability Hallucination Nervousness
	Rare	Confusional state
Nervous System Disorders	Very common	Somnolence (usually diminishes within a few days)
	Common	Dizziness Headache Paradoxical stimulation Psychomotor impairment
	Uncommon	Agitation Paraesthesia Sedation
	Rare	Convulsion Depression Extrapyramidal effects Insomnia Tremor

Eye Disorders	Common	Vision blurred
Ear and Labyrinth Disorders	Uncommon	Tinnitus
Cardiac Disorders	Uncommon	Tachycardia
	Rare	Arrhythmia Palpitations
Vascular Disorders	Rare	Hypotension
Respiratory, Thoracic and Mediastinal Disorders	Common	Thickened respiratory tract secretions
	Uncommon	Chest discomfort Nasal dryness
Gastrointestinal Disorders	Common	Dry mouth Nausea Vomiting
Hepatobiliary Disorders	Rare	Liver dysfunction
Skin and Subcutaneous Tissue Disorders	Uncommon	Pruritus Rash Urticaria
Renal and Urinary Disorders	Common	Urinary retention
General Disorders and Administration site conditions	Common	Asthenia

(*) Frequency category based on clinical trials with single-ingredient diphenhydramine

Menthol

Adverse reactions to menthol at the low concentration present in XPEL COUGH EXPECTORANTCOUGHS (ORIGINAL) are not anticipated.

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

Diphenhydramine

Mild to Moderate Symptoms:

Drowsiness, anticholinergic syndrome (mydriasis, flushing, fever, dry mouth, urinary retention, decreased bowel sounds), tachycardia, mild hypertension, nausea and

vomiting are common after overdose. Agitation, confusion and hallucinations may develop after moderate poisoning.

Severe Symptoms:

Effects may include delirium, psychosis, seizures, coma, hypotension, QRS widening, and ventricular dysrhythmias (including torsades de pointes), but are generally only reported in adults after large ingestions. Rhabdomyolysis and renal failure may rarely develop in patients with prolonged agitation, coma or seizure. Death may occur as a result of respiratory failure or circulatory collapse.

In children, CNS excitation, including hallucinations and convulsions may appear; with larger doses, coma or cardiovascular collapse may follow.

Menthol

Excessive use of menthol may lead to abdominal pain, vomiting, flushed face, dizziness, weakness, tachycardia, stupor, and ataxia.

Treatment

Treatment of overdose should be symptomatic and supportive. The benefit of gastric decontamination is uncertain. Consider activated charcoal (charcoal dose: 50 g for adults; 1 g/kg for children) only if the patient presents within 1 hour of ingestion of a potentially toxic amount Seizures may be controlled with Diazepam or Thiopental Sodium. The intravenous use of Physostigmine may be efficacious in antagonising severe antichoinergic symptoms.

5. **Pharmacological properties**

5.1 Pharmacodynamic properties

Diphenhydramine possesses antitussive, antihistaminic and anticholinergic properties. Experiments have shown that the antitussive effect (resulting from an action on the brainstem) is discrete from its antihistaminic effect.

The duration of activity of diphenhydramine is between 4 and 8 hours.

Menthol has mild local anaesthetic and decongestant properties.

5.2 Pharmacokinetic properties

Absorption

Diphenhydramine and menthol are well absorbed from the gut following oral administration. Peak serum levels of diphenhydramine following a 50 mg oral dose are reached at between 2 and 2.5 hours.

Distribution

Diphenhydramine is widely distributed throughout the body, including the CNS. Following a 50 mg oral dose of diphenhydramine, the volume of distribution is in the range 3.3 - 6.8 l/kg, and it is some 78% bound to plasma proteins.

Metabolism and Elimination

Diphenhydramine undergoes extensive first pass metabolism. Two successive N-demethylations occur, with the resultant amine being oxidised to a carboxylic acid. Values for plasma clearance of a 50 mg oral dose of diphenhydramine lie in the range 600-1300 ml/min and the terminal elimination half-life lies in the range 3.4 - 9.3 hours. Little unchanged drug is excreted in the urine. Menthol is hydroxylated in the liver by microsomal enzymes to p-methane-3,8 diol. This is then conjugated with glucuronide and excreted both in urine and bile as the Glucuronide.

The Elderly

Pharmacokinetic studies indicate no major differences in distribution or elimination of Diphenhydramine compared to younger adults.

Renal Dysfunction

The results of a review on the use of Diphenhydramine in renal failure suggest that in moderate to severe renal failure, the dose interval should be extended by a period dependent on Glomerular filtration rate (GFR).

Hepatic Dysfunction

After intravenous administration of 0.8 mg/kg Diphenhydramine, a prolonged half-life was noted in patients with chronic liver disease which correlated with the severity of the disease. However, the mean plasma clearance and apparent volume of distribution were not significantly affected.

5.3 Preclinical safety data
Mutagenicity

The results of a range of tests suggest that neither diphenhydramine nor menthol have mutagenic potential.

Carcinogenicity

There is insufficient information to determine the carcinogenic potential of diphenhydramine or menthol, although such effects have not been associated with these drugs in animal studies.

Teratogenicity

The results of a number of studies suggest that the administration of either diphenhydramine or menthol does not produce any statistically significant teratogenic effects in rats, rabbits and mice.

Fertility

There is insufficient information to determine whether diphenhydramine has the potential to impair fertility, although a diminished fertility rate has been observed in mice in one study.

6. **Pharmaceutical particulars**

6.1 List of excipients

Propylene Glycol B.P., Polysorbate 80 B.P. Sodium Methyl Hydroxy benzoate B.P., Sodium Propyl Hydroxy benzoate B.P., Glycerine B.P., Citric Acid B.P., Colour Caramel B.P., Flavour Butter scotch, Flavour Vanilla, Sorbitol Solution 70 % B.P. (Non-crystalizing), Purified Water B.P.

6.2 Incompatibilities

None known

6.3 Shelf life

Unopened: 3 years

Opened: Discard the bottle 4 months after opening, even if there is syrup remaining.

6.4 **Special precautions for storage**

store below 30° C and protect from sunlight

6.5 **Nature and contents of container**

100ml amber pet bottles

6.6 Special precautions for disposal and other handling

No special requirements.

7. **Marketing authorisation holder**

Dana Pharmaceuticals Ltd

Shiroro Dam Road,

Maitumbi, Mianna

8. **Marketing authorisation number(s)**

A4 - 2757

9. **Date of first authorisation/renewal of the authorisation**

21st of March, 2018

10. **Date of revision of the text**

22nd June, 2023