Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Paracodin 10 mg/g Oral Drops, Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each drop contains 0.5 mg of dihydrocodeine hydrorhodanide.
1 g of Paracodin drops (=20 drops) contains 10 mg of dihydrocodeine hydrorhodanide.
Excipients: benzoic acid (E201) 2mg per 20-drop dose For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral drops, solution.

Clear, brown solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Paracodin is indicated in the management of non-productive cough.

4.2 Posology and method of administration

For oral administration.

Adults: 14-20 drops taken up to three times daily.

Children (aged 6-12 years): 6-12 drops taken up to three times daily.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Opiate addiction, mental clouding, disturbances of the breathing centre and respiratory function, head injuries and conditions in which intracerebral pressure is elevated (at high doses), hypotension and hypovolaemia.

Do not give Paracodin to children below the age of 6 years.

Do not give to patients who are receiving monoamine oxidase inhibitors or who have received these within the previous 14 days.

4.4 Special warnings and precautions for use

As dihydrocodeine may bring about histamine release, Paracodin should not be given during an attack of asthma and it should be administered with care to persons liable to such attacks.

Paracodin Drops contains Benzoic Acid

This medicine contains 2 mg benzoic acid in each 20-drop dose
Dosage should be reduced in the elderly, in hypothyroidism, in chronic hepatic disease and in renal insufficiency. Prolonged regular use, except under medical supervision, may lead to physical and psychological dependence
(addiction) and result in withdrawal symptoms such as restlessness and irritability, once the drug is stopped.

Patients with pre-existing seizure disorders should be observed with caution when prescribed this product.

Patients should take Paracodin until a relief in the cough and for no longer than the maximum of 7 days for children (6 – 12 years).

CYP2D6 Metabolism

Dihydrocodeine is a semi-synthetic analogue of codeine. There are similarities between the metabolism of codeine and dihydrocodeine in the formation of (O-demethylated) metabolites catalysed by CYP2D6. There are genetic differences in the expression of the CYP2D6 enzyme. For codeine, this results in a risk of lack of efficacy in poor metabolisers and a risk of opioid toxicity in patients who are ultra rapid metabolisers. The clinical implications of CYP2D6 genetic polymorphisms have not been sufficiently elucidated for dihydrocodeine (see section 5.2).

4.5 Interaction with other medicinal products and other forms of interactions

As with all other drugs acting on the central nervous system, the consumption of alcohol should be avoided under Paracodin therapy.

Paracodin should not be administered to patients who are receiving monoamine oxidase inhibitors or who have received these within the previous 14 days.

The effects of DHC on central nervous system may be enhanced by other drugs acting on central nervous system such as:
• Anxiolytics or hypnotics may increase CNS depression, particularly respiratory depression;
• Triciclic antidepressants (e.g. imipramine, amitriptyline) may enhance CNS depressive effects when taken with dihydrocodeine
• Antipsychotic may enhance hypotensive and sedative effects.

The efficacy of analgesics is enhanced.

Cimetidine and other drugs (e.g. quinidine, fluoxetine) may inhibit hepatic metabolism of dihydrocodeine but no change of the clinical effects of dihydrocodeine have been noted.

4.6 Fertility, pregnancy and lactation

All the narcotic analgesics are able to traverse the placenta and are also excreted in milk. They should not be used during pregnancy or lactation unless considered essential by the physician.

4.7 Effects on ability to drive and use machines

Paracodin may induce drowsiness. Patients receiving Paracodin Drops should not drive or operate machinery if affected.

4.8 Undesirable effects

At the usual recommended doses the most frequent side effects are nausea and constipation and less frequently headache and dizziness.

Psychiatric disorders.
Confusion, euphoria

Nervous system disorders
Dizziness, headache, vertigo, drowsiness

Eye disorders
Miosis, visual disturbances

Respiratory, thoracic and mediastinal disorders
Dyspnea, respiratory depression (large doses). Laryngeal oedema has been reported very rarely.

Gastrointestinal disorders
Nausea, vomiting, gastrointestinal complaints and constipation.

Cardiovascular disorders
Bradycardia, hypotension, palpitations, facial flushing

Skin and subcutaneous tissue disorders
Rash, urticaria, pruritus. Angioedema (Quincke's edema)

Renal and urinary disorders
Urinary retention.

General disorders and administration site conditions
Fatigue.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

In the case of overdosage, conservative management is recommended. Severe respiratory depression can be treated with naloxone hydrochloride 0.4 to 2 mg subcutaneously, repeated as required at 2 or 3 minute intervals.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Paracodin is a centrally-acting anti-tussive. Dihydrocodeine works on the cough centre to lessen the incidence and intensity of coughing fits. Dihydrocodeine inhibits troublesome, unproductive cough but does not impair the expectoration of bronchial mucus. The analgesic action of DHC may be helpful in patients with painful cough. Dihydrocodeine also exerts dose-dependent sedative effects.

Opiates may cause depression of the respiratory centre and thereby reduce its sensitivity to normal respiratory stimuli (CO_2 partial pressure in the blood).
It depresses the respiratory centre in a dose-dependent fashion.

Opiates increase for instance the tone of gastrointestinal smooth muscle. Thus, the transit time of food through the gastrointestinal tract is prolonged and intestinal peristalsis reduced. Constipation occurs as a result of inhibited peristalsis and defaecation as well as an increase in the tone of the sphincter ani.

5.2 Pharmacokinetic properties

Dihydrocodeine is readily absorbed after oral administration, has a duration of action of 4 to 6 hours, is extensively metabolised in the liver and is excreted mainly via the kidney.

The biological availability of dihydrocodeine is three times higher than that of codeine. In comparative studies in healthy volunteers, 35% of the orally-applied dose of dihydrocodeine was eliminatedin the urine in the course of 24 hours. After oral administration of dihydrocodeine, the highest concentration was found in the plasma after 1.7 hours. The elimination half-life was 4 hours.

The metabolism of dihydrocodeine shows important similarities with metabolism of codeine. Dihydrocodeine is also a substrate of the polymorphic enzyme CYP2D6. This enzyme catalyses the conversion of dihydrocodeine to dihydromorphine by the O-demethylation pathway (see section 4.4).

5.3 Preclinical safety data

The mean lethal dose (LD50) of dihydrocodeine hydrogen tartrate was determined on mice and rats after oral and intraperitoneal administration. The following 24-hour values, related to the base, were obtained:

Animal	Route	Sex	Dihydrocodeine base LD50 (mg/kg bodyweight)
Mouse	Oral	m/f	417/544
Rat	Oral	m/f	139/129
Mouse	Intraperitoneal	m/f	160/155
Rat	Intraperitoneal	m/f	69/73

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Purified water
Benzoic acid (E210)
Glycerol (85 per cent)
Saccharin sodium
Sodium chloride
Caramel (E150)
Thyme flavour
Eucalyptus flavour

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years.

6.4 Special precautions for storage

Do not store above 30°C.
Store in the original package in order to protect from light.

6.5 Nature and contents of container

Amber glass bottle (type III) with polyethylene dropper and polypropylene screw cap containing 15 gof solution.

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

Teofarma S.R.L.
Valle Salimbene (PV)
Via F. LLI Cervi
8 CAP 27010
Italy

8 MARKETING AUTHORISATION NUMBER

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 04 October 1991

Date of last renewal: 04 October 2006

10 DATE OF REVISION OF THE TEXT

August 2020