

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ilvico Cold and Flu film-coated tablets
Paracetamol 325 mg
Caffeine 30 mg
Brompheniramine maleate 3 mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains:

Paracetamol 325mg

Caffeine 30mg

Brompheniramine maleate 3mg

For a full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the relief of symptoms associated with the common cold, influenza and upper respiratory tract infections.

4.2 Posology and method of administration

For Oral Use

Adults and children older than 12 years

One or two tablets taken orally with water three times daily.

Not recommended for children under the age of 12 years

4.3 Contraindications

1. Hypersensitivity to any of the ingredients.
2. Ilvico must not be used in the presence of narrow-angle glaucoma.
3. Ilvico must not be used in patients who have brain damage or epilepsy.
4. Use in children less than 12 years old.
5. Use in patients with tachyarrhythmias.
6. Use in patients with Peptic ulcers.

7. Use in patients with Severe renal impairment.
8. Use in patients with Severe hepatic impairment (including viral hepatitis).
9. Use in patients with haemophilia.

4.4 Special warnings and precautions for use

This product contains paracetamol and should be administered with care to patients with impaired liver or renal function.

Paracetamol must be administered with precaution, avoiding prolonged treatment on patients with anaemia, cardiac or pulmonary afflictions or renal dysfunction (in the latter case, occasional use is acceptable, but the prolonged administration of high doses may increase the risk of appearance of adverse renal effects).

The use of Paracetamol in patients who habitually consume alcohol (three or more alcoholic beverages (e.g. beer, wine, liquor) per day) may cause hepatic damage.

In chronic alcoholics, no more than 2g/day must be administered of Paracetamol.

Caution is advised with asthmatic patients sensitive to acetylsalicylic acid, because light bronchospastic reactions have been described with Paracetamol (cross reaction) in these patients, although they were only manifested in less than 5% of those tested.

The hazards of overdose are greater in those with non-cirrhotic liver disease.

The stated dose should not be exceeded.

Patients should be advised not to take other paracetamol-containing products or other cough and cold medicines concurrently.

If symptoms persist the doctor should be consulted Prolonged use except under medical supervision may be harmful.

This product should only be used when clearly necessary.

Immediate medical advice should be sought in the event of overdosage even if patient feels well due to the risk of irreversible liver damage.

Keep out of the reach and sight of children.

Ilvico film-coated tablets contain Brompheniramine, which must be administered with caution in patients with vesical neck obstruction, prostatic symptomatic hypertrophy or urinary retention (the anti-cholinergic effects of Brompheniramine may precipitate it or aggravate it).

As this product contains an antihistamine, it may act as a cerebral stimulant in children and occasionally in adults giving rise to insomnia, nervousness, hyperpyrexia, tremors and epileptiform convulsions.

4.5 Interaction with other medicinal products and other forms of interaction

In simultaneous use with drugs which cause enzyme induction in the liver, e.g. certain hypnotics and anti-epileptics, liver damage may be caused with paracetamol doses which would otherwise not be harmful. The same applies to alcohol abuse. When gastric emptying is slowed, e.g. due to propantheline, the rate of paracetamol absorption may be reduced, resulting in later onset action.

When gastric emptying is accelerated, e.g. after administration of metoclopramide, the rate of absorption is increased. The half life of chloramphenicol may be prolonged in combinations of chloramphenicol with the risk of increased toxicity. Paracetamol may potentiate the anticoagulant effect of warfarin and coumarin derivatives slightly.

The clinical relevance, however, cannot yet be assessed. Patients undergoing treatment with oral anticoagulants should, therefore, only receive paracetamol over long periods under medical supervision.

Simultaneous administration of paracetamol and AZT enhances the tendency to develop neutropenia. Therefore, the agent is to be administered simultaneously with AZT only if recommended by a physician.

Paracetamol has been associated with a diminution of its plasmatic levels when taken with oestrogen based drugs, leading to a possible inhibition of its effect through possible induction of its metabolism.

Ilvico may potentiate the effect of agents with central depressant action, e.g. analgesics and tranquillisers, alcohol and vice versa. If MAOIs and tricyclic antidepressants are administered simultaneously, the adrenergic or anticholinergic effects may be potentiated.

Paracetamol is metabolised at hepatic level, giving rise to hepatotoxic metabolites and thus may interact with medicines which utilise the metabolic pathways.

These medicines are:

Oral Anticoagulants (Coumarol, warfarin)

The administration of Paracetamol during prolonged periods at doses higher than 2 g/day with these types of product may provoke an increase of the anti-coagulant effect, possibly due to a diminution of the hepatic synthesis of the factors favouring coagulation.

Ethyl Alcohol

Potentialisation of the toxicity of Paracetamol, through possible induction of the hepatic production of the hepatotoxic products derived from Paracetamol.

Anticonvulsants (phenitoin, phenobarbital, methylphenobarbital, primidone)

Diminution of the bioavailability of the Paracetamol as well as potentiation of the hepatic toxicity in overdosage, due to the induction of hepatic metabolism.

Oestrogens:

Diminution of the plasmatic levels of Paracetamol, with possible inhibition of its effects, through possible induction of its metabolism.

Loop Diuretics

The effects of the diuretics may be reduced, given that the Paracetamol may reduce renal excretion of prostaglandins and the activity of the plasmatic rennin.

Isoniazid:

Diminution of the Paracetamol clearance, with possible potentiation of its action and/or toxicity, through inhibition of its hepatic metabolism.

Lamotrigine:

Diminution of the area under the curve (20%) and of the half life (15 % of Lamotrigine), with possible inhibition of its effect, through possible induction of its hepatic metabolism.

Probenecid:

May slightly increase the therapeutic efficacy of Paracetamol.

Propanolol:

Propanolol inhibits the enzymatic system responsible for the glucuronidation and oxidation of Paracetamol. Therefore, it may strengthen the action of Paracetamol.

Rifampicin:

Increase of the clearance of Paracetamol through possible induction of its hepatic metabolism.

Chloramphenicol:

Prolongation of its half-life, increasing the risk of chloramphenicol toxicity.

Anti-cholinergics: (glycopyrrone, propanteline)

Diminution in the absorption of Paracetamol, with possible inhibition of its effect, through diminution of the gastric draining speed.

Ionic Exchange Resins (cholestyramine):

Diminution in the absorption of Paracetamol with possible inhibition of its effect, through fixation of Paracetamol in the intestine.

Zidovudine:

It may provoke a diminution of the pharmacological effects of zidovudine through an increase in the clearing of this substance.

Brompheniramine interacts with anti-cholinergic medications in a manner that the anti-cholinergic effects may strengthen, also Brompheniramine may increase the effects of other CNS depressors, such as alcohol, monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants, barbiturates, anaesthetics, maybe provoking overdose symptoms.

Interactions with Diagnostic Tests

Paracetamol may alter the values of the following diagnostic tests:

Blood (biological) increase of transaminases (ALT and AST), alkaline phosphatase, ammonium, bilirubin, creatinine, lactate dehydrogenase (LDH) and urea.

Increase (analytical interference) of glucose, theophylline and uric acid.

Increase of the prothrombin time (in patients with warfarin maintenance dosages, although without clinical significance).

Reduction (analytical interference) of glucose when oxidase-peroxidase method is used.

Urine: falsely increased values of metadrenalin and uric acid may appear.

Pancreatic function tests with bentiromide: Paracetamol, as does bentiromide, metabolises in the form of arylamine, thus increasing the apparent recovered quantity of Para-Amino Benzoic Acid (PABA). **It is recommended to interrupt treatment with Paracetamol for at least three days before the administration of bentiromide.**

5-hydroxyindoleacetic acid (5-HIAA) determination in urine: in qualitative diagnostic detection tests that use nitrosonaphthol as reagent, Paracetamol may produce falsely positive results. The quantitative tests are not altered.

Antihistamines: may interfere in cutaneous tests made with allergenic extracts. It is recommended to suspend the medication for at least 3 days prior to the commencement of cutaneous allergenic testing.

4.6 Fertility, pregnancy and lactation

Paracetamol crosses the placental barrier and may be found in maternal milk in quantities similar to those of maternal plasma.

Brompheniramine is suspected to cause a risk of congenital defects if used during pregnancy.

Pregnant women are advised to restrict their caffeine intake to no more than 200 mg per day (the approximate amount provided by two cups of instant coffee).

Therefore, do not take this product when pregnant or breastfeeding unless advised by a doctor.

4.7 Effects on ability to drive and use machines

This product may cause drowsiness, therefore, if affected patients, should refrain from driving or operating machinery.

4.8 Undesirable effects

The most serious adverse reactions which may occur are due to paracetamol and are: agranulocytosis, leucopenia, pancytopenia, thrombocytopenia and haemolytic anaemia, all of which are very rare adverse reactions, with an estimated frequency of less than 1 case in every 10,000 patients.

The most frequently occurring adverse reactions are: sedation and dry mouth, which are due to the brompheniramine and drowsiness, ataxia, headache, restlessness and dizziness, none of which can be specifically attributed to any particular active ingredient or excipient.

Hypersensitivity reactions may occur after administration of drugs containing paracetamol (very rare skin reactions, thrombocytopenia or leucopenia have been described). Agranulocytosis or pancytopenia have also been observed; bronchospasms have been triggered in predisposed persons (analgesic asthma). Quinke’s oedema, dyspnoea, sweating, nausea and a drop in blood pressure to the point of shock have also been described for the active constituent paracetamol. The antihistamine component may produce sedation, dry mouth and, in rare cases, excitation.

After the administration of Ilvico the following adverse reactions may occur: frequent (estimated frequency >1/100, <1/10); rare (estimated frequency >1 / 10,000, <1/1,000); very rare, including isolated notifications (estimated frequency <1/10,000);

MedDRA System Organ Class	Active Ingredient	Adverse Reactions	Frequency
Blood and lymphatic system disorders	Paracetamol	Thrombocytopenia Leucopenia Agranulocytosis Pancytopenia Haemolytic- Anaemia Hypotension	Very rare Very rare Very rare Very rare Very rare Rare
	Not attributable to a specific active or excipient	Hypertension	Frequent
Nervous system disorders	Brompheniramine Maleate	Sedation	Frequent
	Not attributable to a specific active or excipient	Drowsiness Ataxia Headache Restlessness	Frequent Frequent Frequent Frequent
Ear and labyrinth disorders	Brompheniramine Maleate	Dizziness	Frequent
Respiratory, thoracic and mediastinal disorders	Paracetamol	Bronchospasms Dyspnoea	Very rare
Gastrointestinal disorders	Paracetamol	Nausea	Rare
	Brompheniramine Maleate	Dry mouth	Frequent
Skin and subcutaneous tissue disorders	Paracetamol	Skin reactions Quinke’s oedema Sweating	Very rare

4.9 Overdose

Immediate medical attention must be sought in the event of an overdose as there is a risk of permanent and irrevocable liver damage.

1. Acute symptoms and signs and potential sequelae

Symptomology for Paracetamol overdose includes dizziness, vomiting, loss of appetite, jaundice, abdominal pain and renal and hepatic insufficiency.

Symptoms of paracetamol overdosage in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema, and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

2. Management of overdose

* Monitoring

If an overdose has been ingested the patient must be treated immediately at a medical centre even if there are no symptoms or significant signs because, even though they may be fatal, often they are not manifested immediately after ingestion, but rather from the third day onwards. Death may occur through hepatic necrosis. Likewise, acute renal failure may occur.

Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable).

▪ Use of agonist/antagonist/antidote

Binding of the cytotoxic metabolite can be achieved by intravenous administration of SH donors such as cysteamine or N-acetylcysteine, if possible within 8 hours after intoxication. Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after this time.

If required, the patient should be given intravenous N-acetylcysteine, in line with established dosage schedule.

If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital.

Management of patients who present with serious hepatic dysfunction beyond 24 hours from ingestions, should be discussed with a liver unit.

▪ Method to increase elimination

If paracetamol intoxication is suspected, gastric lavage is indicated in the first 6 hours after overdose.

The paracetamol plasma concentration can be lowered by dialysis.

Treatment with activated charcoal should be considered if the overdosage has been taken within 1 hour.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group:- Other combined preparations for common cold Code ATC: R05X

Paracetamol is an analgesic pharmacopoeia that also possesses antipyretic properties. The mechanism of analgesic action has not been fully determined. Paracetamol may act predominantly inhibiting the synthesis of prostaglandin at the central nervous system level and to a lower degree blocking the generation of the pain impulse at peripheral level. The peripheral action may also be due to the inhibition of the prostaglandin synthesis or to the inhibition of the synthesis, or of the action, of other substances that sensitise the nociceptors to mechanical or chemical stimulations.

Probably Paracetamol produces the antipyretic effect acting at central level over the hypothalamic centre regulating temperature, to produce a peripheral vasodilatation that gives place to an increase of perspiration and to flow of blood in the skin and loss of heat. The action at central level probably is related with the inhibition of the prostaglandin synthesis in the hypothalamus.

Brompheniramine maleate: is a highly effective antagonist of the H1 receptors of Histamines. From the different studies in this field it is known that the antihistaminic effect reduces capillary permeability and the permeability of cellular membranes producing a diminution of the secretion and congestion of the inflamed mucous membranes of the superior respiratory tract. This diminution of permeability, that appears to be independent of the histamine and the allergic process, appears independently of whatever is the cause of the increase of permeability. The experimental use of Brompheniramine in animals has evidenced antitussive effects and stimulation of blood circulation. At the same time it has a slight sedative effect.

Caffeine stimulates circulation and strengthens the analgesic and antipyretic effects of Paracetamol.

5.2 Pharmacokinetic properties

It is quickly and completely absorbed after oral administration, reaching maximum plasmatic peak between 3-4 hours. Plasmatic bioavailability is 60-80%, linking with proteins at 10%. It metabolises mainly through the liver, being eliminated mainly through the kidney as inactive metabolites.

Average plasmatic life is between 1.5-2.5 hours, being completely eliminated after 24 hours. Maximum pharmacological effect is achieved at 4-6 hours.

5.3 Preclinical safety data

Studies of chronic toxicity in animals show that high Paracetamol doses produce testicular atrophy and inhibition of spermatogenesis; the importance of this fact in humans is unknown.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Sodium Carboxymethylstarch Type A
Crospovidone
Hypromellose
Cellulose powder
Magnesium stearate
Titanium dioxide E171
Glycerol
Macrogol 4000
Macrogol 6000
Talc
Colloidal anhydrous silica

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

PVC/Aluminium package blisters containing 20 film-coated tablets.

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

Seven Seas Ltd
Bedfont Cross
Stanwell Road
Feltham
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 417/18/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 5th November 2010

10 DATE OF REVISION OF THE TEXT

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