Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Non-drowsy Sinutab Tablets Paracetamol 500mg Pseudoephedrine hydrochloride 30mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 30 mg Pseudoephedrine hydrochloride and 500 mg Paracetamol.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet
White round biconvex tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Non-drowsy Sinutab is indicated for the short term symptomatic relief of conditions where congestion of the mucous membranes of the upper respiratory tract, especially nasal mucosa and sinuses, is accompanied by mild to moderate pain or pyrexia, eg the common cold, influenza, sinusitis and nasopharyngitis.

4.2 Posology and method of administration

Posology:

Adults and Children aged 16 years and over
Two tablets to be taken every four to six hours, up to four times a day.
Maximum daily dose: 8 tablets (240 mg pseudoephedrine and 4 g paracetamol).

Children aged 12 to 15 years:
One tablet every four to six hours, up to four times a day.
Maximum daily dose: 4 tablets (i.e. 120 mg pseudoephedrine hydrochloride, 2 g paracetamol).

Children under 12 years:
This medicine is contraindicated in children under the age of 12 years (see section 4.3).

Hepatic Impairment:
In patients with hepatic impairment or Gilbert's Syndrome, the dose should be reduced or the dosing interval prolonged.

The daily dose should not exceed 2g paracetamol/day unless directed by a physician.

Renal Impairment:
Caution should be exercised when administering Non-drowsy Sinutab to patients with mild to moderate renal impairment.

It is recommended, when giving paracetamol to patients with renal impairment, to reduce the dose and to increase the minimum interval between each administration to at least 6 hours unless directed otherwise by a physician. See Table below:

Adults:

Glomerular filtration rate	Dose
10-50 ml/min	500mg every 6 hours
<10ml/min	500mg every 8 hours

Use in the Elderly
Experience has indicated that normal adult dosage is usually appropriate. However, in frail, immobile, elderly subjects or in elderly patients with renal or hepatic impairment, a reduction in the amount or frequency of dosing may be appropriate. The maximum daily dose should not exceed 60mg/kg/day (up to a maximum of 2g paracetamol per day) in the following situations, unless directed by a physician:

- Weight less than 50kg
- Chronic alcoholism
- Dehydration
- Chronic malnutrition

Duration of use:
Patients should be advised not to use this product for more than 5 days and to seek medical advice if symptoms persist.

Method of administration:
For oral use.

4.3 Contraindications

Hypersensitivity to paracetamol, pseudoephedrine or to any of the excipients listed in section 6.1

This product is contra-indicated in patients with:

- Cardiovascular disease including hypertension
- Diabetes mellitus
- Phaeochromocytoma
- Hyperthyroidism
- Closed angle glaucoma
- Severe acute or chronic kidney disease/renal failure

This product should not be used concomitantly with (see section 4.5):

- Monoamine oxidase inhibitors (MAOIs), or within 14 days of stopping MAOIs. The concomitant use of pseudoephedrine and these products may cause a rise in blood pressure and/or hypertensive crisis.
- Other sympathomimetic decongestants
- Beta-blockers

This medicine is contraindicated in patients at risk of developing respiratory failure.

This medicine is contra-indicated in children under 12 years of age.

4.4 Special warnings and precautions for use

<u>Paracetamol</u>
Paracetamol should be administered with caution under the following circumstances (see section 4.2):

- Hepatic impairment
- Chronic alcoholism
- Renal impairment (GFR ≤ 50ml/min)
- Gilberts syndrome (familial non-haemolytic jaundice)
- Concomitant treatment with medicinal products affecting hepatic function
- Glucose-6-phosphate dehydrogenase deficiency
- Haemolytic anaemia
- Glutathione deficiency
- Dehydration
- Chronic malnutrition
- Weight less than 50kg
- Elderly patients

In general, medicinal products containing paracetamol should be taken for only a few days without the advice of a physician or dentist and not at high doses.

If high fever or signs of secondary infection occur or if symptoms persist for longer than 3 days, a physician should be consulted.

Prolonged or frequent use is discouraged.

Patients should be advised not to take other paracetamol-containing medicines concurrently.

Taking multiple daily doses in one administration can severely damage the liver. In such cases, medical assistance should be sought immediately

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

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment and sepsis, or in patients with malnutrition or other sources of glutathione deficiency (e.g. chronic alcoholism) who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If HAGMA due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring, is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.

Serious skin reactions such as acute generalised exanthematous pustulosis (AGEP), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN), have been reported very rarely in patients receiving paracetamol. Patients should be informed about the signs of serious skin reactions, and use of the product should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

Pseudoephedrine

Although pseudoephedrine has virtually no pressor effects in normotensive patients, this medicine should be used with caution in patients taking antihypertensive agents, tricyclic antidepressants or other sympathomimetic agents (such as appetite suppressants and amphetamine-like psychostimulants). The effects of a single dose on the blood pressure of these patients should be observed before recommending repeated or unsupervised treatment.

The physician or pharmacist should check that sympathomimetic containing preparations are not simultaneously administered by several routes i.e. orally and topically (nasal, aural and eye preparations) (see sections 4.3 and 4.5)

Patients with difficulty in urination and/or enlargement of the prostate should be advised to consult a physician before using this product

Patients with thyroid disease who are receiving thyroid hormones should not take pseudoephedrine unless directed by a physician.

A variety of allergic skin reactions, with or without systemic features such as bronchospasm, angioedema have been reported following use of pseudoephedrine (see section 4.8).

Severe Skin reactions

Severe skin reactions such as acute generalized exanthematous pustulosis (AGEP) may occur with pseudoephedrine-containing products. This acute pustular eruption may occur within the first 2 days of treatment, with fever, and numerous, small, mostly non-follicular pustules arising on a widespread oedematous erythema and mainly localized on the skin folds, trunk, and upper extremities. Patients should be carefully monitored. If signs and symptoms such as pyrexia, erythema, or many small pustules are observed, administration of this medicine should be discontinued and appropriate measures taken if needed.

Ischaemic colitis

Some cases of ischaemic colitis have been reported with pseudoephedrine. Pseudoephedrine should be discontinued and medical advice sought if sudden abdominal pain, rectal bleeding or other symptoms of ischaemic colitis develop.

Ischaemic optic neuropathy

Cases of ischaemic optic neuropathy have been reported with pseudoephedrine. Pseudoephedrine should be discontinued if sudden loss of vision or decreased visual acuity such as scotoma occurs.

Posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS)
Cases of PRES and RCVS have been reported with the use of pseudoephedrine-containing products (see section 4.8). The risk is increased in patients with severe or uncontrolled hypertension, or with severe acute or chronic kidney disease/renal failure (see section 4.3).
Pseudoephedrine should be discontinued and immediate medical assistance sought if the following symptoms occur: sudden severe headache or thunderclap headache, nausea, vomiting, confusion, seizures and/or visual disturbances. Most reported cases of PRES and RCVS resolved following discontinuation and appropriate treatment.

This product may act as a cerebral stimulant giving rise to hyperpyrexia, tremor and epileptiform convulsions. Care should be taken when used in epileptic patients
If any of the following occur, this product should be stopped:

- Hallucinations
- Restlessness
- Sleep disturbances Use with caution in occlusive vascular disease Pseudoephedrine may induce positive results in certain anti-doping tests. Risks of abuse Pseudoephedrine carries the risk of abuse. Increased doses may ultimately produce toxicity. Continuous use can lead to tolerance resulting in an increased risk of overdosing. The recommended maximum dose and treatment duration should not be exceeded (see section 4.2).

4.5 Interaction with other medicinal products and other forms of interaction

Pseudoephedrine
MAOIs and/or RIMAs: Pseudoephedrine exerts its vasoconstricting properties by stimulating α-adrenergic receptors and displacing noradrenaline from neuronal storage sites. Since MAOIs impede the metabolism of sympathomimetic amines and increase the store of releasable noradrenaline in adrenergic nerve endings, MAOIs may potentiate the pressor effect of pseudoephedrine. This medicine should not be given to patients treated with monoamine inhibitors or within 14 days of stopping treatment as there is an increased risk of hypertensive crisis.

Moclobemide: risk of hypertensive crisis

Sympathomimetic agents: Concomitant use of this medicine with tricyclic antidepressants (TCAs) or with sympathomimetic agents (such as appetite suppressants and amphetamine-like psychostimulants) may cause a rise in blood pressure.

Anticholinergic drugs: The effects of anti-cholinergics e.g., some psychotropic drugs (such as tricyclic antidepressants) and atropine, may be potentiated by this product giving rise to tachycardia, mouth dryness, gastrointestinal disturbances, e.g., colic, urinary retention and headache.

Antihypertensives: Pseudoephedrine may antagonise the hypotensive action of antihypertensive drugs which interfere with sympathetic activity including bretylium, betanidine, reserpine, guanethidine, debrisoquine, methyldopa, adrenergic neurone blockers - and beta- blockers (see sections 4.3 and 4.4).
Because of its pseudoephedrine content, concomitant use of this medicine with oxytocin or cardiac glycosides may cause of a risk of hypertension or an increased risk of dysrhythmias, respectively.

When used concurrently with ergot alkaloids (ergotamine & methysergide), this product can increase the risk of ergotism.

Anaesthetic agents: Concurrent use with halogenated anaesthetic agents such as chloroform, cyclopropane, halothane, enflurane or isoflurane may provoke or worsen ventricular arrhythmias.

Paracetamol
Chronicalcohol can increase the hepatotoxicity of paracetamol overdosage and may have contributed to the acute pancreatitis reported in one patient who had taken an overdose of paracetamol. Acute alcohol intake may diminish an individual's ability to metabolise large doses of paracetamol, the plasma half-life of which can be prolonged.

The use of drugs which induce hepatic microsomal enzymes, such as anticonvulsants and oral contraceptive steroids, may increase the extent of metabolism of paracetamol, resulting in reduced plasma concentrations of the drug and a faster elimination rate.

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by cholestyramine.

Because of its paracetamol content, the anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of this medicine with increased risk of bleeding; occasional doses have little or no significant effect.

Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis due to pyroglutamic acidosis, especially in patients with risks factors (see section 4.4).

4.6 Fertility, pregnancy and lactation

There are no adequate and well controlled clinical studies in pregnant or breast feeding women for the combination of paracetamol and pseudoephedrine.

Pregnancy

This medicine should not be used during pregnancy unless the potential benefit of treatment to the mother outweighs the possible risks to the developing foetus.

Paracetamol

A large amount of data on pregnant women indicate neither malformative, nor feto/neonatal toxicity.
Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results.
If clinically needed, paracetamol can be used during pregnancy however it should be used at the lowest possible dose, for the shortest possible time at the lowest possible frequency.

When given to the mother in therapeutic doses, paracetamol crosses the placenta into the foetal circulation as early as 30 minutes after ingestion and is effectively metabolised by foetal sulphate conjugation.

Pseudoephedrine

Although pseudoephedrine has been in widespread use for many years without apparent ill consequence, there are no specific data on its use during pregnancy. Caution should therefore be exercised by balancing the potential benefit of treatment to the mother against any possible hazards to the developing foetus.

Breast-feeding

This medicine should not be used during lactation unless the potential benefit of treatment to the mother outweighs the possible risks to the nursing infant.

Paracetamol
Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding. A pharmacokinetic study of paracetamol in 12 nursing mothers revealed that less than 1% of a 650 mg oral dose of paracetamol appeared in the breast-milk. Similar findings have been reported in other studies, therefore maternal ingestion of therapeutic doses of paracetamol does not appear to present a risk to the infant.

Pseudoephedrine
Pseudoephedrine is excreted in breast milk in small amounts but the effect of this on breast-fed infants is not known. It has been estimated that approximately 0.4 to 0.7% of a single 60 mg dose of pseudoephedrine ingested by a nursing mother will be excreted in the breast milk over 24 hours. Data from a study of lactating mothers taking 60 mg pseudoephedrine every 6 hours suggests that from 2.2 to 6.7% of the maximum daily dose (240 mg) may be available to the infant from a breastfeeding mother.

Fertility

There is no information on the effects of this medicine on human fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

This product may have a minor influence on the ability to drive and use machines.

This product may cause dizziness. Patients should be cautioned about engaging in activities such as driving a car or operating machinery, until they have established their own response to the drug.

4.8 Undesirable effects

Adverse drug reactions (ADRs) identified during clinical trials and post-marketing experience with paracetamol, pseudoephedrine, or the combination are listed below by System Organ Class (SOC).
The frequencies are defined 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)

ADRs identified are presented by frequency category based on 1) incidence in adequately designed clinical trials or epidemiology studies, if available, or 2) when incidence cannot be estimated, frequency category is listed as 'Not known'.

System Organ Class (SOC)	***Product***	***Frequency***	***Adverse Drug Reaction (Preferred Term)***
Blood and Lymphatic System Disorders	*Paracetamol*	*Not known*	*Agranulocytosis* *Haemolytic anaemia* *Thrombocytopenic purpura*
Immune System Disorders	*Paracetamol* *Pseudoephedrine and Paracetamol single actives*	*Not known* *Rare*	*Anaphylactic reaction* *Hypersensitivity(cross-sensitivity may occur with other sympathomimetics)*
Psychiatric Disorders	*Pseudoephedrine*	*Common*	*Insomnia* *Nervousness*
	Pseudoephedrine	*Rare*	*Hallucination*
	Pseudoephedrine	*Not known*	*Agitation* *Anxiety* *Delusion* *Euphoric mood* *Hallucination, visual* *Irritability* *Restlessness* *Sleep disorder*
Nervous System Disorders	*Pseudoephedrine*	*Very common*	*Headache*
	Pseudoephedrine	*Common*	*Dizziness*
	Pseudoephedrine	*Not known*	*Cerebrovascular accident* *Paraesthesia* *Posterior reversible encephalopathy syndrome (PRES) (see sectio* *syndrome (RCVS) (see section 4.4)* *Psychomotor hyperactivity* *Somnolence* *Tremor*
Eye Disorders	*Pseudoephedrine*	*Not known*	*Ischaemic optic neuropathy*
Cardiac Disorders	*Pseudoephedrine*	*Not known*	*Arrhythmia* *Myocardial infarction/Myocardial ischaemia* *Palpitations*

			Tachycardia
Vascular Disorders	*Pseudoephedrine*	*Not known*	*Hypertension*
Gastrointestinal Disorders	*Pseudoephedrine*	*Common*	*Dry mouth* *Nausea*
	Pseudoephedrine / Paracetamol combination *Pseudoephedrine*	*Not known*	*Abdominal pain* *Diarrhoea* *Vomiting, Ischaemic colitis*
Hepato-biliary Disorders	*Paracetamol*	*Not known*	*Hepatic function abnormal* *Hepatic necrosis*
Skin and Subcutaneous Tissue Disorders	*Pseudoephedrine* *Paracetamol* *Pseudoephedrine / Paracetamol combination* *Pseudoephedrine and Paracetamol single actives*	*Not known* *Not known* *Rare*	*Severe skin reactions, including acute generalised exanthematous pustulosis (AGEP)* *Fixed eruption* *Rash pruritic* *Uriticaria* *Angioedema* *Pruritus* - *Rash* *Rash pruritic* -
Renal and Urinary Disorders	*Paracetamol*	*Uncommon*	*Nephropathy toxic*
	Pseudoephedrine *Paracetamol*	*Not known*	*Dysuria* *Urinary retention (in men* - prostatic enlargement could have been an important predisposing factor*)* *Renal papillary necrosis (after prolonged administration)*
Investigations	*Paracetamol*	*Not known*	*Transaminases increased*
Metabolism and nutrition disorders	*Paracetamol*	*Not known*	*High anion gap metabolic acidosis*

No differences between adult and paediatric safety profiles have been identified.

Liver damage has been reported after daily ingestion of excessive amounts of paracetamol. A review of a group of patients with chronic active hepatitis failed to reveal differences in the abnormalities of liver function in those who were long-term users of paracetamol nor was the control of their disease improved after paracetamol withdrawal.

Low level transaminase elevations may occur in some patients taking therapeutic doses of paracetamol; these elevations are not accompanied with liver failure and usually resolve with continued therapy or discontinuation of paracetamol

Very rare cases of serious skin reactions have been reported.

High anion gap metabolic acidosis

Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4).
Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.

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, Website: www.hpra.ie.

4.9 Overdose

Paracetamol

Please refer to local guidelines for the treatment of paracetamol overdose.

Paracetamol overdose can result in liver damage which may be fatal.

Symptoms generally appear within the first 24 hours and may comprise nausea, vomiting, anorexia, pallor, hyperhidrosis, malaise and abdominal pain or patients may be asymptomatic.

Overdose of paracetamol can cause liver cell necrosis likely to induce complete and irreversible necrosis, resulting in hepatocellular insufficiency, metabolic acidosis and encephalopathy which may lead to coma and death. Simultaneously, increased levels of hepatic transaminases (AST, ALT), lactate dehydrogenase and bilirubin are observed together with increased prothrombin levels that may appear 12 to 48 hours after administration.

Liver damage is likely in adults and adolescents who have taken more than the recommended amounts of paracetamol. It is considered that excess quantities of a toxic metabolite become irreversibly bound to liver tissue.

Some patients may be at increased risk of liver damage from paracetamol toxicity:

Risk factors include:

- Patients with liver disease
- Elderly patients
- Young children
- Patients receiving long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.
- Patients who regularly consume ethanol in excess of recommended amounts.
- Patients with glutathione depletion e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms

The following sequelae to acute hepatic failure associated with paracetamol overdose are considered expected and may be fatal.

Expected Sequelae to Acute Hepatic Failure Associated with Paracetamol Overdose

System Organ Class (SOC)	**Adverse event**
Infections and infestations	Bacterial infection Fungal infection Sepsis
Blood and lymphatic system disorders	*Coagulopathy* *Disseminated intravascular coagulation* *Thrombocytopenia*
Metabolism and nutrition disorders	Hypoglycaemia Hypophosphatemia Lactic acidosis Metabolic acidosis
Nervous system disorders	Brain oedema

	Coma (with massive paracetamol overdose or multiple drug overdose) Encephalopathy
Cardiac disorders	Cardiomyopathy Cardiac arrhythmias
Vascular disorders	Hypotension
Respiratory, thoracic and mediastinal disorders	Respiratory failure
Gastrointestinal disorders	Gastrointestinal haemorrhage Pancreatitis
Renal and urinary disorders	Acute renal failure * with acute tubular necrosis
General disorders and administration site conditions	Multi-organ failure

*Acute renal failure with acute tubular necrosis may also develop.

Cardiac arrhythmias and pancreatitis have also been reported.

Haemolytic anaemia (in patients with glucose-6-phosphate dehydrogenase [G6PD] deficiency): Haemolysis has been reported in patients with G6PD deficiency, with use of paracetamol in overdose.

Management

Immediate transfer to hospital.

Blood sampling to determine initial paracetamol plasma concentration. In the case of a single acute overdose, paracetamol plasma concentration should be measured 4 hours post ingestion. Administration of activated charcoal should be considered if the overdose of paracetamol has been ingested within the previous hour.

The antidote N-acetylcysteine, should be administered as soon as possible in accordance with national treatment guidelines.

Symptomatic treatment should be implemented.

Pseudoephedrine

Symptoms

Overdosage may result in:
Metabolism and nutrition disorders: hyperglycaemia, hypokalaemia
Psychiatric disorders: CNS stimulation, insomnia; irritability, restlessness, anxiety, agitation; confusion, delirium, hallucinations, psychoses
Nervous system disorders: seizures, tremor, intracranial haemorrhage including intracerebral haemorrhage, drowsiness in children
Eye disorders: mydriasis
Cardiac disorders: palpitations, tachycardia, reflex bradycardia, supraventricular and ventricular arrhythmias, dysrhythmias, myocardial infarction
Vascular disorders: hypertension, hypertensive crisis
Gastrointestinal disorders: nausea, vomiting, ischaemic bowel infarction
Musculoskeletal and connective tissue disorders: rhabdomyolysis
Renal and urinary disorders: acute renal failure, difficulty in micturition

Management

Measures should be taken to maintain and support respiration andcontrol convulsions. Catheterisation of the bladder may be necessary. If desired, the elimination of pseudoephedrine can be accelerated by acid diuresis or by dialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: R01BA02

Pseudoephedrine has direct and indirect sympathomimetic activity and is an effective upper respiratory tract decongestant. Pseudoephedrine is substantially less potent than ephedrine in producing both tachycardia and elevation in systolic blood pressure and considerably less potent in causing stimulation of the central nervous system.

ATC Code: N02BE01
Paracetamol has analgesic and antipyretic actions but only weak anti-inflammatory properties. This may be explained by the presence of cellular peroxides at sites of inflammation which prevent inhibition of cyclo-oxygenase by paracetamol at other sites associated with low levels of cellular peroxides, eg pain, fever, paracetamol and successfully inhibit prostaglandin biosynthesis.

5.2 Pharmacokinetic properties

Pseudoephedrine
Pseudoephedrine is partly metabolised in the liver by N-demethylation to norpseudoephedrine, an active metabolite. Pseudoephedrine and its metabolite are excreted in the urine: 55% to 75% of a dose is excreted unchanged. The rate of urinary excretion of pseudoephedrine is accelerated when the urine is acidified. Conversely as the urine pH increases, the rate of urinary excretion is slowed.

In a limited study, three mothers nursing healthy infants were given an antihistamine-decongestant preparation containing 60 mg of pseudoephedrine and 2.5 mg of triprolidine. Milk concentrations of pseudoephedrine were higher than plasma levels in all three patients, with peak milk concentrations occurring at 1.0–1.5 hours. The investigators calculated that 1000 ml of milk produced during 24 hours would contain approximately 0.5%–0.7% of the maternal dose. However, following a single-blind, crossover study of a single dose of pseudoephedrine 60 mg vs. placebo conducted in 8 lactating mothers, and assuming maternal intake of 60 mg pseudoephedrine hydrochloride four times daily, the estimated infant dose of pseudoephedrine based on AUC and an estimated milk production rate of 150 ml/kg/day was 4.3% (95% CI, 3.2, 5.4%; range 2.2 to 6.7%) of the weight-adjusted maternal dose.

Paracetamol
Peak plasma paracetamol concentration usually occurs between 30 and 90 minutes after oral ingestion. Paracetamol is distributed uniformly throughout most body fluids and is only 15 to 25 per cent bound to plasma proteins. The plasma half life of paracetamol after therapeutic doses is in the range of 1 to 3 hours.

5.3 Preclinical safety data

Mutagenicity

Paracetamol
Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

Pseudoephedrine
The results of a wide range of tests indicate that pseudoephedrine does not post a mutagenic risk to man.

Carcinogenicity

Paracetamol
There is inadequate evidence to determine the carcinogenic potential of paracetamol in humans. A positive association between the use of paracetamol and cancer of the ureter (but not of other sites of the urinary tract) was observed in a case-control study in which approximate lifetime consumption of paracetamol (whether acute or chronic) was estimated. However, other similar studies have failed to demonstrate statistically significant association between paracetamol and cancer of the urinary tract, or paracetamol and renal cell carcinoma.

There is limited evidence for the carcinogenicity of paracetamol in experimental animals. Liver cell tumours can be detected in mice and liver and bladder carcinomas can be detected in rats, following chronic feeding 500 mg/kg/day paracetamol.

Pseudoephedrine
There is insufficient information available to determine whether pseudoephedrine has carcinogenic potential.

Teratogenicity

Paracetamol
Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

Pseudoephedrine
Systemic administration of pseudoephedrine, up to 50 times the human daily dosage in rats and up to 35 times the human daily dosage in rabbits did not produce teratogenic effects.

Fertility

Paracetamol
Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

Pseudoephedrine
Systemic administration of pseudoephedrine to rats, up to 7 times the human daily dosage in females and 35 times the human daily dosage in males, did not impair fertility or alter foetal morphological development and survival.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline Cellulose
Pregelatinised maize starch
Crospovidone
Sodium Starch Glycolate (type A)
Povidone
Stearic acid
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 25˚C. Store in the original package.

6.5 Nature and contents of container

Opaque white PVC and PVDC/Aluminium foil blister.
Packs of 4, 12, 15 and 24 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.
Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

JNTL Consumer Health I (Ireland) Limited

Office 5, 6 And 7
Block 5
High Street
Tallaght
Dublin 24
D24 YK8N
Ireland

8 MARKETING AUTHORISATION NUMBER

PA23490/020/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 06 February 1998

Date of last renewal: 06 February 2008

10 DATE OF REVISION OF THE TEXT

March 2025