Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Panadol Fever and Congestion Film-coated Tablets Paracetamol 500mg Pseudoephedrine Hydrochloride 30mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains paracetamol 500 mg and pseudoephedrine hydrochloride 30 mg. For the full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Form: Film coated tablet.
Description: A bilayer (white/blue) film coated capsule shaped tablet. The tablet is debossed with the number 2 in a circle on one face.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Panadol Fever and Congestion is indicated in adults and adolescents aged 12 to 18 years.
Symptomatic relief of nasal congestion when combined with fever and/or pain such as sore throat, sinus pain or headache in the common cold or influenza.

4.2 Posology and method of administration

Posology
The lowest dose necessary to achieve efficacy should be used for the shortest duration of treatment.

Adults, including the elderly
Two tablets up to three times daily as required for relief of symptoms.
The dose should not be repeated more frequently than every four hours nor should more than three doses be given in any 24 hour period.

Paediatric Population

Adolescents aged 16 to 18 years old
One to two tablets up to three times daily as required for relief of symptoms.
The dose should not be repeated more frequently than every four hours nor should more than three doses be given in any 24 hour period.
Adolescents aged 12 to 15 years old
One tablet up to three times daily as required for relief of symptoms.
The dose should not be repeated more frequently than every four hours nor should more than three doses be given in any 24 hour period.

Panadol Fever and Congestion is contraindicated in children aged under 12 years and below (see section 4.3).

Patients with renal impairment
Pseudoephedrine is primarily excreted renally. Pseudoephedrine should not be used by those with severe renal impairment GFR<30mL/min (see section 4.3) and should be used with caution in those with moderate renal impairment GFR 30-59 mL/min (see sections 4.4 and 5.2).
Patients with hepatic impairment
Patients who have been diagnosed with hepatic impairment must seek medical advice before taking this medication. The

restrictions related to the use of such combinations in patients with hepatic impairment are primarily a consequence of the paracetamol content of the product (see section 4.4).

Method of administration
For oral use.
Patients should be advised not to use this product for more than 5 days and to seek medical advice if symptoms persist.
Do not exceed the stated dose.
The tablets should be taken with water.

4.3 Contraindications

Hypersensitivity to paracetamol, pseudoephedrine or any of the excipients listed in section 6.1.
Not to be used by patients taking moclobemide or monoamine oxidase inhibitors (MAOIs) or for two weeks after stopping the MAOI drug.
The oxazolidinone class of antibiotics (including furazolidone and linezolid) should not be taken with Panadol Fever and Congestion (see section 4.5).
Not to be used by patients with the following conditions:
· Hypertension
· Cardiovascular disease
· Hyperthyroidism
· Prostatic hypertrophy
· Glaucoma
· Severe renal impairment (GFR<30mL/min)
Not to be used by patients currently receiving other sympathomimetics (such as decongestants, tricyclic antidepressants, appetite suppressants and amphetamine-like psychostimulants see section 4.5).
Not to be used by patients taking beta-blockers (see section 4.5).
Paediatric Population
Not to be used by children under 12 years of age.

4.4 Special warnings and precautions for use

Contains paracetamol.
Do not use with any other paracetamol-containing products. The concomitant use with other products containing paracetamol may lead to an overdose. Paracetamol overdose may cause liver failure which may lead to liver transplant or death.

Use with caution in patients with hepatic impairment or mild to moderate renal impairment.

Use with caution in patients with glutathione depletion due to metabolic deficiencies.

Use with caution in patients with psychosis.

Concomitant use of other cold and flu medicines should be avoided.

The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease.

Use with caution in patients with diabetes mellitus, arrhythmias or phaeochromocytoma.

Use with caution in patients taking antihypertensives or vasoconstrictive agents such as ergot alkaloids (see section 4.5 Interaction with other medicinal products and other forms of interaction).

Use with caution in patients over the age of 60 years. Patients in this age group are at greater risk of adverse reactions due to decreased renal function, and unwanted reactions when using oral sympathomimetic agents.

This product may give rise to insomnia and nervousness.

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

There have been rare cases of posterior reversible encephalopathy (PRES) /reversible cerebral vasoconstriction syndrome (RCVS) reported with sympathomimetic drugs, including pseudoephedrine. Symptoms reported included sudden onset of severe headache, nausea, vomiting, and visual disturbances. Most cases improved or resolved within a few days following appropriate treatment. Pseudoephedrine should be discontinued immediately and medical advice sought if signs/ symptoms of PRES/RCVS develop.

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 localised 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 Panadol Fever and Congestion should be discontinued and appropriate measures taken if needed.

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.

Care is advised in the administration of Panadol Fever and Congestion to patients who will be undergoing general anaesthesia. Acute perioperative hypertension may occur if volatile halogenated anaesthetics are used simultaneously with indirect sympathomimetic agents. It is recommended that pseudoephedrine treatment is stopped 24 hours before anaesthesia.

If you are taking medication, or are under medical care consult your doctor or pharmacist.
Pseudoephedrine content of this product may result in a positive reaction during antidoping control tests.

Caution is advised if paracetamol is administered concomitantly with flucloxacillin due to increased risk of high anion gap metabolic acidosis (HAGMA), particularly in patients with severe renal impairment, sepsis, malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism), as well as those using maximum daily doses of paracetamol. Close monitoring, including measurement of urinary 5-oxoproline, is recommended.

Keep all medicines safely out of sight and reach of children.

Hepatotoxicity at therapeutic dose
Cases of paracetamol induced hepatotoxicity, including fatal cases, have been reported in patients taking paracetamol at doses within the therapeutic range. These cases were reported in patients with one or more risk factors for hepatotoxicity including low body weight (<50 kg), renal and hepatic impairment, chronic alcoholism, concomitant intake of hepatotoxic drugs and in acute and chronic malnutrition (low reserves of hepatic glutathione). Paracetamol should be administered with caution to patients with these risk factors. Caution is also advised in patients on concomitant treatment with drugs that induce hepatic enzymes and in conditions which may predispose to glutathione deficiency (see section 4.2 and 4.9).

Doses of paracetamol should be reviewed at clinically appropriate intervals and patients should be monitored for emergence of new risk factors for hepatotoxicity, which may warrant dosage adjustment.

4.5 Interaction with other medicinal products and other forms of interaction

The co-administration of Panadol Fever and Congestion with tricyclic antidepressants, the antidepressant moclobemide, decongestants, appetite suppressants and amphetamine-like psychostimulants or with monoamineoxidase inhibitors (MAOIs) (or within two weeks of stopping MAOIs) which interfere with the catabolism of sympathomimetic agents, may occasionally cause a rise in blood pressure and may lead to hypertensive crisis in the case ofmoclobemide or MAOIs.
The oxazolidinone class of antibiotic (including furazolidone and linezolid) are known to cause a dose-related inhibition of monoamineoxidase. Therefore, they should not be taken with Panadol Fever and Congestion as there is a potential to cause hypertensive crisis (see section 4.3).

Pseudoephedrine may antagonize the effect of certain classes of antihypertensives (e.g.,beta-blockers, methyldopa, reserpine, debrisoquine, guanethidine) (see sections4.3 and 4.4).

Pseudoephedrinemay interact with halogenated anaesthetics (see section 4.4).

Concomitant administration of vasoconstrictor agents (including ergot derivatives such asbromocriptine, pergolide, lisuride, cabergoline, ergotamine, dihydroergotamine and methylsergide) may cause an increased risk of ergotism (see section 4.4).

The rate of paracetamol absorption may be reduced by colestyramine. The interaction can be avoided by delaying administration of colestyramine by one hour, in order to maintain maximal analgesic effects.

The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of Panadol Fever and Congestion with increased risk of bleeding; occasional doses have no significant effect.

Sodium bicarbonate alkalinizes the urine and may reduce the renal elimination of pseudoephedrine, a reduction in dose may be necessary.

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

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

4.6 Fertility, pregnancy and lactation

Pregnancy

There are insufficient data from the use of the combination paracetamol and pseudoephedrine in pregnant women. Animal studies are insufficient with respect to reproductive toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. Panadol Fever and Congestion is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breastfeeding

Pseudoephedrine is excreted in human milk to such an extent that effects on the breastfed newborns/infants are likely. Panadol Fever and Congestion should not be used during breastfeeding.

Fertility

There are no relevant data available. See section 5.3.

4.7 Effects on ability to drive and use machines

Dizziness is one of the most frequent adverse effects. Thus, Panadol Fever and Congestion could have a major influence on the ability to drive and use machines.

4.8 Undesirable effects

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 and <1/10), uncommon (≥1/1000 and <1/100), rare (≥1/10,000 and <1/1000) and very rare (<1/10,000) and not known (cannot be estimated from the available date).

Paracetamol:

System Organ Class	Adverse Reaction	Frequency
Blood and lymphatic system disorders	Blood dyscrasia, including thrombocytopenia and agranulocytosis	Very rare
Immune system disorders	Hypersensitivity*	Rare
	Anaphylaxis Cutaneous hypersensitivity reactions including, among others, Toxic Epidermal Necrolysis, Stevens Johnson syndrome, angioedema and skin rashes.	Very rare
Hepatobiliary disorders	Hepatic dysfunction	Very rare
Respiratory, thoracic and mediastinal disorders	Bronchospasm – more likely in patients sensitive to aspirin or NSAIDs	Very rare

Pseudoephedrine:

System Organ Class	Adverse Reaction	Frequency
Psychiatric disorders	Nervousness, insomnia	Common
	Agitation, restlessness	Uncommon
	Hallucinations (particularly in children)	Rare
Nervous system disorders	Dizziness	Common
	Headache, tremor	Not known
Eye disorders	Ischaemic optic neuropathy	Not Known
Gastrointestinal disorders	Dry mouth, nausea, vomiting	Common
	Ischaemic colitis	Not known
Skin and subcutaneous disorders	Allergic dermatitis*, rash	Rare
	Severe skin reactions, including acute generalizes exanthematous pustulosis (AGEP)	Not known
Renal and urinary disorders	Urinary retention** Dysuria	Uncommon
Cardiac disorders	Minor tachycardia	Uncommon
	Palpitations	Rare
	Cardiac arrhythmias	Rare
Vascular disorders	Increased blood pressure	Rare

*A variety of allergic skin reactions, with or without systemic features such as bronchospasm and angioedema have been reported following use of pseudoephedrine.
**Urinary retention is most likely to occur in those with bladder outlet obstruction such as prostatic hypertrophy.
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

Liver damage is likely in patients who have taken more than the recommended amounts of paracetamol. It is considered that excess quantities of toxic metabolite become irreversibly bound to liver tissue. Some patients may be at increased risk of liver damage from paracetamol toxicity.

Risk factors: If the patient

a. Is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.

or

b. Regularly consumes ethanol in excess of recommended amounts.

or

c.Is likely to be glutathione deplete e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms

Paracetamol overdose may cause liver failure, which may lead to liver transplant and death.

Symptoms of paracetamol overdose usually occur within the first 24 hours and are pallor, nausea, vomiting, anorexia and abdominal pain.

Simultaneously, increased levels of hepatic transaminases (AST, ALT), lactate dehydrogenase and bilirubin are observed together with increased prothrombin time that may appear 12 to 48 hours after administration. Abnormalities of glucose metabolism and metabolic acidosis may occur. Clinical symptoms of liver damage are usually evident initially after 2 days, and reach a maximum after 4 to 6 days

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. Other non-hepatic symptoms that have been reported following paracetamol overdosage include myocardial abnormalities and pancreatitis.

In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema, and death.

Management

Immediate treatment is essential in the management of paracetamol overdose.

Despite a lack of symptoms, seek immediate advice from your Poison Centre and refer patients to hospital urgently for medical attention. Symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines.

Paracetamol concentrations in blood should be measured not less than 4 hours after overdose in order to be able to assess the risk of developing liver damage (using the paracetamol overdose nomogram). However, N-acetylcysteine (NAC) treatment should be started immediately when massive overdose is suspected.

The administration of activated charcoal may be beneficial when performed within one hour of the overdose but can be considered for up to four hours after the overdose.

Intravenous (IV) infusion (or oral administration if IV infusion is not possible) of the antidote N-acetylcysteine should be started if possible before the 8th hour. The effectiveness of the antidote declines sharply after this time. Nacetylcysteine can, however, give some degree of protection even after 8 hours, and up to 24hours, but in these cases prolonged treatment is given. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas,outside hospital.

Symptomatic treatment should be implemented.

Pseudoephedrine

Symptoms

As with other sympathomimetics pseudoephedrine overdose will result in symptoms due to central nervous system and cardiovascular stimulation e.g. excitement, irritability, restlessness, tremor, hallucinations, hypertension, palpitations, arrhythmias and difficulty with micturition. In severe cases, psychosis, convulsions, coma and hypertensive crisis may occur. Serum potassium levels may be low due to extracellular to intracellular shifts in potassium.

Management

Treatment should consist of standard supportive measures. Beta-blockers should reverse the cardiovascular complications and the hypokalaemia.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Paracetamol, combinations excl. psycholeptic ATC code: N02B E51

Panadol Fever and Congestion is a mild to moderate analgesic, antipyretic and decongestant.

Mechanism of action
The analgesic and antipyretic actions of paracetamol are believed to be due, at least in part, to inhibition of prostaglandin synthesis in the central nervous system. Pseudoephedrine acts on the alpha adrenergic receptors in the mucosa of the respiratory tract producing vasoconstriction which results is shrinkage of swollen nasal mucous membranes, reduction of nasal congestion and increase in nasal airway patency.

Pharmacodynamic effects
Paracetamol is an analgesic and antipyretic. Pseudoephedrine is a nasal decongestant.
Clinical efficacy and safety
Paracetamol 1 g has been shown to be an effective analgesic and antipyretic.

Pseudoephedrine 60 mg has been shown to be an effective nasal decongestant, as measured by nasal airflow, in patients with the common cold and rhinitis.

At therapeutic doses, pseudoephedrine has no clinically significant effect on blood pressure in normotensive patients. Studies in patients with controlled hypertension have demonstrated that pseudoephedrine 60 mg has no, or minimal, effect on blood pressure and does not have sedative effects.

GlaxoSmithKline has conducted a clinical study in patients with symptoms of cold and flu to assess relief of pain and nasal congestion. The study compared Panadol Fever and Congestion (taken three times daily as required for three days) with paracetamol alone, pseudoephedrine alone and placebo. Results demonstrated that Panadol Fever and Congestion gives significantly ($p<0.05$) greater pain relief than either placebo or pseudoephedrine and that Panadol Fever and Congestion has a significantly ($p<0.05$) greater decongestant effect than either placebo or paracetamol. Panadol Fever and Congestion demonstrated an additive effect for relief of pain and nasal congestion compared to paracetamol or pseudoephedrine. For a single dose of Panadol Fever and Congestion there was significantly greater ($p<0.05$) relief of pain and nasal congestion (nasal airflow) compared to placebo at one hour post dose.

5.2 Pharmacokinetic properties

Paracetamol:

Absorption: The absorption of paracetamol by the oral route is rapid and complete. Maximum plasma concentrations are reached 30 to 60 minutes following ingestion.
Distribution: Paracetamol is distributed rapidly throughout all tissues. Concentrations are comparable in blood saliva and plasma. Protein binding is low.
Biotransformation: Paracetamol is metabolised mainly in the liver, following two major metabolic pathways: Glucuronic acid and sulfuric acid conjugates. The latter route is rapidly saturated at doses higher than the therapeutic dosages. A minor route, catalyzed by the Cytocrome P 450 (mostly CYP2E1), results in the formation of an intermediate reagent (N-acetyl-p-benzoquinoneimine) which under normal conditions of use, is rapidly detoxified by glutathione and eliminated in the urine, after conjugation with cysteine and mercapturic acid.
Conversely, when massive intoxication occurs, the quantity of this toxic metabolite is increased.
Elimination: Elimination is essentially through the urine. 90% of the ingested dose is eliminated via the kidneys within 24 hours, principally as glucuronide (60-80%) and sulphate conjugates (20-30%). Less than 5% is eliminated in unchanged form. Elimination half life is about 2 hours.
Physiopathological variations
Renal Insufficiency: In cases of severe renal insufficiency (creatinine clearance lower than 10ml/min) the elimination of paracetamol and its metabolites is delayed.
Elderly subjects: Conjugation capacity is not modified.

Pseudoephedrine:

Absorption: Pseudoephedrine is rapidly and completely absorbed from the gastrointestinal tract after oral administration with no presystemic metabolism. Peak plasma levels are achieved after 1-2 hours.
Distribution: Pseudoephedrine is rapidly distributed throughout the body. No protein binding data are available. The volume of distribution ranges from 2.64 to 3.51 l/kg in both single and multiple dose studies.
Metabolism: There is little metabolism of pseudoephedrine in man with approximately 90% being excreted in the urine unchanged. Approximately 1% is eliminated by hepatic metabolism, by N-demethylation to norpseudoephedrine.
Elimination: The plasma half-life varies from 4.3-7.0 hours in adults. As a weak base the extent of renal excretion is dependent on urinary pH. At low pH tubular resorption is minimal and urine flow rate will not influence clearance of the drug. At high pH (>7.0) pseudoephedrine is extensively reabsorbed in the renal tubule and renal clearance will depend on urine flow rate.
Physiopathological variations
Renal Insufficiency: Renal impairment will result in increased plasma levels.
Elderly subjects: Elimination capacity is not modified.
A steady state pharmacokinetic interaction study in healthy volunteers has demonstrated that the rate (C_{max}, t_{max}) and extent ($AUC_{0\text{-}6hours}$) of absorption from Panadol Cold and Flu tablet is equivalent to those of paracetamol alone and of pseudoephedrine alone.
In the same study the median t_{max} values for the paracetamol and pseudoephedrine components of Panadol Cold and Flu were 0.7 hours and 1.2 hours, respectively.

5.3 Preclinical safety data

There are no preclinical data considered relevant to clinical safety beyond data included in other sections of the SPC. Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cellulose microcrystalline E 460
Silica, Colloidal anhydrous E 551
Stearic acid E 570
Magnesium stearate E 572
Starch pregelatinised
Povidone
Crospovidone
Croscarmellose sodium E 468
Hypromellose E 464
Macrogol
Carnauba wax E 903
Indigo carmine E132

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

Opaque blister strips of PVC/ PE/ PVDC heat-sealed to a bilayer of Aluminium foil/PET
. Blisters are packed into cartons and each carton contains 2, 5, 6, 10, 12, 16, 18, 24, 30 or 32 tablets (not all pack sizes may be marketed).

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

Haleon Ireland Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0678/094/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28 November 2003
Date of last renewal: 2 December 2012

10 DATE OF REVISION OF THE TEXT

April 2023