Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Paracetamol 500 mg, Guaifenesin 200 mg, Phenylephrine Hydrochloride 10 mg, Powder for Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One sachet contains:
500mg Paracetamol
200mg Guaifenesin
10mg Phenylephrine hydrochloride

Excipients with known effect:
Sucrose 2000 mg
Aspartame 6 mg
Sodium 157 mg

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for oral solution, sachet
Off-white powder
Appearance after reconstitution: Opalescent yellow coloured solution with characteristics citrus/menthol odour and taste.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Short term symptomatic relief of mild to moderate pain, fever, nasal congestion with an expectorant effect on chesty cough, associated with colds, chills and influenza.

4.2 Posology and method of administration

Posology
Adults, the Elderly and children aged 12 years and over: One sachet
Repeat every four hours as required, but do not exceed four doses (sachets) in any 24 hours.
Do not give to patients with hepatic or severe renal impairment (see Section 4.3).
Seek medical advice if symptoms persist for more than 3 days

Paediatric population
Paracetamol 500 mg, Guaifenesin 200 mg, Phenylephrine HCl 10 mg, Powder for oral solution is contraindicated in children under 12 years old (see section 4.3).

Method of administration:
Dissolve the contents of one sachet in a standard mug of hot, but not boiling, water (approx. 250 ml). Allow to cool to a drinkable temperature.

4.3 Contraindications

- Hypersensitivity to active substances paracetamol, guaifenesin, phenylephrine hydrochloride or any of the excipients listed in section 6.1.
- Hepatic or severe renal impairment
- Hypertension
- Hyperthyroidism
- Diabetes

- Heart disease
- Narrow-angle glaucoma
- Porphyria
- Use in patients taking tricyclic antidepressants
- Use in patients who are currently taking or have taken monoamine oxidase inhibitors (MAOIs) within the last 2 weeks Use in patients taking beta-blocking drugs
- Use in patients who are currently taking other sympathomimetic drugs
- Children under 12 years

4.4 Special warnings and precautions for use

Long term use of the product is not recommended.

Patients should be advised not to take with other paracetamol-containing products or other products containing the same active ingredients as this preparation. They should also be advised not to take other cough, cold or decongestant products concurrently, or alcohol. 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).

This medicine should only be recommended if all symptoms (pain and/or fever, nasal congestion and chesty cough) are present.

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

Use with caution in patients receiving digitalis, beta-adrenergic blockers, methyldopa or other anti-hypertensive agents (see section 4.5).

Use with caution in patients with prostatic hypertrophy as they may be susceptible to urinary retention. Sympathomimetic-containing products should be used with great care in patients receiving phenothiazines. Use in patients with Raynaud's phenomenon.

Ask a doctor before use if you have persistent or chronic cough such as occurs with smoking, asthma, chronic bronchitis, or emphysema.

Precaution shall be observed when paracetamol is administered in patients withsevere haemolytic anaemia, glucose-6-dehydrogenase deficit, dehydrated patients, and patients with chronic malnutrition disorders.

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

Contains sodium 157 mg per dosage unit, equivalent to 7.85% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Contains aspartame (E951) a source of phenylalanine. May be harmful for people with phenylketonuria.

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.

4.5 Interaction with other medicinal products and other forms of interaction

The hepato-toxicity of paracetamol may be potentiated by excessive intake of alcohol. The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and the extent of absorption is reduced by colestyramine.

Drugs which induce hepatic microsomal enzymes, such as alcohol, barbiturates, monoamine oxidase inhibitors and tricyclic antidepressants, may increase the hepatotoxicity of paracetamol, particularly after overdosage.

Isoniazid reduces the paracetamol clearance, with possible potentiation of its action and/or toxicity, by inhibition of its metabolism in the liver.

Probenecid causes an almost 2-fold reduction in clearance of paracetamol by inhibiting its conjugation with glucuronic acid. A reduction in the paracetamol dose should be considered if it is to be used concomitantly with probenecid.

Regular use of Paracetamol possibly reduces metabolism of Zidovudine (increased risk of neutropenia).

Hypertensive interactions occur between sympathomimetic amines such as phenylephrine and monoamine oxidase inhibitors. Phenylephrine may adversely interact with sympathomimetic agents and may reduce the efficacy of beta-blocking drugs, methyldopa and other antihypertensive drugs (see section 4.4). Conditions where these drugs are used are contraindications for the product.

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

Pharmacological interactions involving paracetamol with a number of other drugs have been reported. These are considered to be of unlikely clinical significance in acute use at the dosage regimen proposed.

Salicylates/aspirin may prolong the elimination $T_{1/2}$ of paracetamol.

Paracetamol may decrease the bioavailability of lamotrigine, with possible reduction of its effect, due to a possible induction of its metabolism in the liver

There is a possibility that digitalis may sensitise the myocardium to effects of sympathomimetic drugs.

Paracetamol may affect phosphotungstate uric acid tests and blood sugar tests.
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).

Paediatric population
Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

Fertility:
The effects of this product on fertility have not been specifically investigated. Preclinical studies with paracetamol do not indicate special hazard to fertility at therapeutically relevant doses. There are no adequate reproductive toxicology studies with phenylephrine and guaifenesin.

Pregnancy:
This product should be used only if the benefit outweighs the risks where other safer treatments are not available. It should be used only upon advice of a doctor or a pharmacist.

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 effective dose for the shortest possible time and at the lowest possible frequency.

Phenylephrine:
There are limited data on the use of phenylephrine in pregnant women. Vasoconstriction of uterine vessels and reduced uterine blood flow associated with use of phenylephrine may result in foetal hypoxia.

Guaifenesin:

The safety of guaifenesin in pregnancy has not been fully established. Currently available studies do not provide conclusive results on associations of guaifenesin with foetal malformations. Guaifenesin should only be used in pregnancy when considered essential by the doctor.

Breast-feeding:
This product should not be used without medical advice and only if the benefit outweighs the risks. Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding. There are no data available on whether phenylephrine is released into breast milk and no reports on the effects of phenylephrine on the nursing infant. Until more data are available, use of phenylephrine should be avoided in breast-feeding women, unless considered essential by the physician. Guaifenesin is excreted in breast milk in small amounts. There is insufficient information on the effects of guaifenesin in breastfed infants.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. When performing these activities, the possibility of adverse effects, such as dizziness and confusion should be taken into account.

4.8 Undesirable effects

The frequency of occurrence of undesirable effect is usually classified as follows:
Very common (> 1/10)
Common (> 1/100 to < 1/10)
Uncommon (> 1/1,000 to < 1/100)
Rare (> 1/10,000 to < 1/1,000)
Very rare (< 1/10,000)
Not known (incidence cannot be assessed on the basis of the available data).

Blood and lymphatic system disorders
Very rare: blood dyscrasias e.g. thrombocytopenia, agranulocytosis, haemolytic anaemia, neutropenia, leucopenia, pancytopenia have been reported with paracetamol, but these were not necessarily causally related.

Immune system disorders
Rare: allergic or hypersensitivity reactions with both phenylephrine and paracetamol, including skin rashes, urticaria, anaphylaxis and bronchospasm.

Nervous system disorders
As with other sympathomimetic amines insomnia, nervousness, tremor, anxiety, restlessness, confusion, irritability and headache may rarely occur.
Headache and dizziness are also known to occur rarely with Guaifenesin.

Cardiac disorders
Phenylephrine may rarely be associated with tachycardia.

Vascular disorders
High blood pressure with headache, vomiting and palpitations may occur rarely with phenylephrine.

Gastrointestinal disorders
Anorexia, nausea and vomiting are common with sympathomimetics and may occur with phenylephrine.

Gastrointestinal discomfort, nausea, vomiting and diarrhoea are the most common side effects associated with Guaifenesin but these occur rarely.

Gastro-intestinal effects of paracetamol are very rare but there have been reports of acute pancreatitis after ingestion of above normal dosage.

Hepatobiliary disorders
Rare: Liver function test abnormal (increase in hepatic transaminases).

Skin and subcutaneous disorders
Hypersensitivity reactions including skin rash and urticaria may occur rarely. Very rare cases of serious skin reactions have been reported with paracetamol.

Renal and urinary disorders
Interstitial nephritis has been reported incidentally after prolonged use of high doses of paracetamol.

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
There is a risk of poisoning, particularly in elderly patients, young children, in patients with liver disease, in case of chronic alcoholism, in patients with chronic malnutrition. Overdosing may be fatal in these cases.

Liver damage is possible in adults who have taken 10g or more of paracetamol. Ingestion of 5g or more of paracetamol may lead to liver damage if the patient has risk factors (see below).

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
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.

Management
Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate 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.

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable).

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 the 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 24h from ingestion should be discussed with the local National Poison Centre or a liver unit.

PHENYLEPHRINE HYDROCHLORIDE
Symptoms of phenylephrine overdose include irritability, headache, an increase in blood pressure and associated reflex bradycardia and arrhythmias.
Raised blood pressure should be treated with an alpha receptor antagonist such as intravenous phentolamine. Reduction of blood pressure should, by reflex mechanism, increase the heart rate but, if necessary, this can be facilitated by the administration of atropine.

GUAIFENESIN
Mild to moderate overdose may cause dizziness and gastrointestinal disturbances. Very high doses may produce excitation, confusion and respiratory depression. Urinary calculi have been reported in patients consuming large quantities of preparations containing guaifenesin.
Treatment is symptomatic, involving gastric lavage and general supportive measures.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Other cold combination preparations
ATC code: R05X

Paracetamol has both analgesic and antipyretic activity which is mediated principally through its inhibition of prostaglandin synthesis in the central nervous system.
Guaifenesin has an expectorant action. Expectorants are believed to alleviate cough discomfort by stimulating receptors in the gastric mucosa that initiate a reflex secretion of respiratory tract fluid, thereby increasing the volume and decreasing the viscosity of bronchial secretions. This facilitates removal of mucus and reduces irritation to the bronchial tissue.
Phenylephrine hydrochloride mainly acts directly on adrenergic receptors. It has predominantly α-adrenergic activity and is without significant stimulating effects on the central nervous system at usual doses. It has recognised decongestant activity and acts by vasoconstriction to reduce oedema of the nasal mucosa.

The active ingredients are not known to cause sedation.

5.2 Pharmacokinetic properties

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. Peak plasma concentrations are attained 10-60 minutes following oral dosing. Paracetamol is primarily metabolised in the liver via three pathways: glucuronidation, sulphation and oxidation. It is excreted in the urine, mainly as the glucuronide and sulphate conjugates. The elimination half-life ranges from 1 to 3 hours.

Guaifenesin is rapidly absorbed from the gastrointestinal tract after oral administration with maximum blood levels occurring within 15 minutes of administration. It is rapidly metabolised in the kidneys by oxidation to β-(2 methyoxy-phenoxy) lactic acid, which is excreted in the urine. The elimination half life is one hour.

Phenylephrine hydrochloride is irregularly absorbed from the gastrointestinal tract and undergoes first-pass metabolism by monoamine oxidase in the gut and liver; orally administered phenylephrine thus has reduced bioavailability. It is excreted in the urine almost entirely as the sulphate conjugate. Peak plasma levels occur between 1 and 2 hours and the plasma half life ranges from 2 to 3 hours.

5.3 Preclinical safety data

Preclinical safety data on these active ingredients in the literature have not revealed any pertinent and conclusive findings which are of relevance to the recommended dosage and use in the product and which have not already been mentioned elsewhere in this Summary. 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

Sucrose
Citric Acid
Tartaric Acid
Sodium Cyclamate
Sodium Citrate
Aspartame (E951)
Acesulfame Potassium (E950)
Powdered Menthol
Lemon Flavour
Lemon Juice Flavour
Quinoline Yellow (E104)

6.2 Incompatibilities

None known

6.3 Shelf life

3 years

Duration of storage after reconstitution: The reconstituted solution is stable for 90 minutes.

6.4 Special precautions for storage

Do not store above 25°C.

For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

The sachet laminate comprises:
Surlyn/aluminium foil/Low density polyethylene/paper (outer layer).

A pack size of five and ten sachets is available.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

WICK Pharma - Zweigniederlassung der Procter & Gamble GmbH
Sulzbacher Str. 40
65823 Schwalbach am Taunus
Germany

8 MARKETING AUTHORISATION NUMBER

PA2294/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 7th October 2011
Date of last renewal: 1st June 2015

10 DATE OF REVISION OF THE TEXT