SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Effervescent Paracetamol and Caffeine Granules

Resolve Extra

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains Paracetamol 1 g, Sodium Bicarbonate 1.408g and Caffeine 60mg.

Excipients with known effect:

Dextrose (glucose)

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Effervescent granules.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Recommended for the relief of headache, including tension headache and migraine, with gastric upset, particularly associated with over-indulgence in food or drink or both. Effervescent Paracetamol and Caffeine Granules contain an extra strength pain relieving formula with an antacid to settle the stomach. It is also recommended for the treatment of toothache, neuralgia, sore throat, period pains and symptomatic relief of rheumatic aches and pains, colds and influenza.

4.2 Posology and method of administration

Posology

Route of administration: oral.

Method of administration:
Dissolve the contents of the sachet in a glass of water (150 - 200 ml) before taking.

Adults aged 18 years and over:
One sachet every 4 hours as required. Do not take more than 4 sachets in any 24 hours.

The elderly may take the normal adult dose

Not to be given to children under 18 years of age

4.3 Contraindications

- Hypersensitivity to paracetamol, sodium bicarbonate, caffeine or to any of the excipients listed in section 6.1.
- Patients on sodium restricted diets.
- Patients with hypochloraemia.

4.4 Special warnings and precautions for use

Care is advised in the administration of this product to patients with severe renal or severe hepatic impairment. The hazards of overdose with paracetamol are greater in those with noncirrhotic, alcoholic liver disease.

Excessive intake of tea or coffee should be avoided while taking this product.

This product contains dextrose (glucose) and patients should consult their physician if they are suffering from diabetes before using this product.

Oral sodium bicarbonate may increase blood pressure or cause fluid retention and pulmonary oedema in those at risk. Sodium-containing salts should be given extremely cautiously to patients with heart failure, oedema, renal impairment, hypertension, pre-eclampsia and aldosteronism.

Patients with rare hereditary glucose-galactose malabsorption should not take this medicine.

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 and other sources of glutathione deficiency (e.g. chronic alcoholism) who were treated with paracetamol at a 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.

Resolve Extra® contains 454mg of sodium per sachet, equivalent to 23% of the WHO recommended daily intake of 2g sodium for an adult.

Do not exceed the stated dose.

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

If symptoms persist, consult your doctor.

Keep out of the sight and reach of children.

Consult your doctor if you are taking warfarin.

4.5 Interaction with other medicinal products and other forms of interaction

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

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

The hepatotoxicity of paracetamol may be potentiated by excessive intake of alcohol. These interactions are considered to be of unlikely clinical significance in acute use at the dosage regimen proposed.

As this product contains sodium bicarbonate, which has antacid properties, it is recommended that this product should not be taken simultaneously with other medications, but should be taken two hours later, as this product may impair drug absorption.

Medicinal products which induce hepatic microsomal enzymes, such as barbiturates, may increase the hepatotoxicity of paracetamol, particularly after overdose.

Caffeine undergoes extensive metabolism by hepatic microsomal cytochrome P450, factors known to alter the activity of this enzyme system may influence caffeine clearance. Thus, caffeine elimination is enhanced in cigarette smokers.

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

Pregnancy:
Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol used in the recommended dosage, and hence paracetamol is not contraindicated during pregnancy. During pregnancy, it appears that the half-life of caffeine is prolonged. Patients should follow the advice of their doctor regarding the use of this product during pregnancy.

Breast-Feeding:
Paracetamol is excreted in breast milk but not in clinically significant amounts. Available published data do not contraindicate breast-feeding.
Caffeine is excreted in breast milk but at levels which are not thought to present a hazard, although irritability and a poor sleeping pattern have been reported.

Fertility:
There is no information on the effects of this product on fertility.

4.7 Effects on ability to drive and use machines

None

4.8 Undesirable effects

Paracetamol:
Adverse effects of paracetamol are rare, but hypersensitivity including skin rashes and other allergies may occur. There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis, but these are not necessarily causally related to paracetamol.

Caffeine
The most commonly reported adverse events following dosing with caffeine are GI irritation and CNS stimulation. Adverse CNS effects include insomnia, restlessness, nervousness; adverse GI effects include nausea, vomiting and gastric irritation.

<u>Frequency not known:</u>

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 the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for 'MHRA Yellow Card' in the Google Play or Apple App Store.

4.9 Overdose

Liver damage is possible in adults who have taken 10g or more of paracetamol. It is considered that excess quantities of a toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested) become irreversibly bound to liver tissue. 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:

- Is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.
- Regularly consumes ethanol in excess of recommended amounts.
- 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 and 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, see BNF overdose section. 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 24 hours from ingestion should be discussed with the NPIS or a liver unit.

Caffeine
Symptoms: Overdose of caffeine may produce nervousness, restlessness, insomnia, emesis, convulsions, excitement, diuresis, facial flushing, muscle twitching, GI disturbance, tachycardia or cardiac arrhythmia, "rambling" flow of thought and speech, psychomotor agitation, or periods of inexhaustibility. No specific antidote. However, treatment is usually fluid therapy for mild to moderate toxicity and for correction of electrolyte imbalance. Fatal poisoning is rare.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: N02BE51

The combination of paracetamol and caffeine is a well-established analgesic combination.

5.2 Pharmacokinetic properties

Paracetamol is rapidly and almost completely absorbed from the gastro-intestinal tract. It is relatively uniformly distributed throughout most body fluids and exhibits variable protein binding. Excretion is almost exclusively renal, in the form of conjugated metabolites.

Caffeine is absorbed readily after oral administration, maximal plasma concentrations are achieved within one hour and the plasma half-life is about 3.5 hours. 65-80% of administered caffeine is excreted in the urine as I -methyluric acid and l-methylxanthine.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to
that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric Acid (anhydrous)

Sodium Carbonate (anhydrous)

Sodium Lauryl Sulphate

Polyvinylpyrrolidone K25

Saccharin Sodium

Dextrose (anhydrous)

Lemon Durarome

Purified Water

6.2 Incompatibilities

None

6.3 Shelf life

60 months.

6.4 Special precautions for storage

None.

6.5 Nature and contents of container

Polythene/foil laminate sachets in cardboard carton outers containing 1, 5, 6 or 10
sachets

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

Risolv Health Limited

Clifton House
Bunnian Place
Basingstoke
RG21 7JE

8 MARKETING AUTHORISATION NUMBER(S)

PL 58255/0002

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