SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Solpa Headache 500mg/65mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

INGREDIENT	QTY	UNIT	DOSE
Paracetamol	500	mg	tablet
Caffeine	65	mg	tablet

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Tablet
White capsule shaped tablets with no marks and plain on both sides.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of mild to moderate pain including headache, migraine, neuralgia, toothache, sore throat, period pains, symptomatic relief of sprains, strains, rheumatic pains, sciatica, lumbago, fibrositis, muscular aches and pains, joint swelling and stiffness, influenza, feverishness and feverish colds.

4.2 Posology and method of administration

Route of administration: Oral.

For all indications:

Adults, the elderly and children over 16 years of age:

Two tablets every 4-6 hours when necessary to a maximum of 4 doses in 24 hours.

Children from 12 to 15 years:
One tablet every 4-6 hours when necessary to a maximum of 4 doses in 24 hours.

Not recommended for children under 12 years of age.

Dosage should not be continued for longer than 3 days without consulting a doctor.

As caffeine is found naturally in tea, coffee and chocolate, and in some carbonated drinks there is the potential for users to take more than the recommended 520 mg/day of caffeine (8 tablets) per day. Therefore users should take account of dietary and other medicinal sources of caffeine and ensure that they do not exceed the stated dose.

Typical amounts of caffeine available from dietary sources are
Brewed coffee; 50-100mg/100ml*
Instant coffee and tea: 20-73mg/100ml*
Carbonated drinks (cola) 9-19mg/100ml*
Chocolate 5-20mg/100ml
(*100ml is equivalent to about 1 small cup of fluid)

4.3 Contraindications

Hypersensitivity to paracetamol, caffeine and/or other constituents.

This medicine should not be used by people who have been diagnosed with hypertension or who are receiving antihypertensive medication, or who have a history of cardiac arrhythmia.

This medicine should not be used by patients recovering from chronic alcoholism who are taking disulfiram.

This medicine should not be used if antidepressants (including lithium carbonate), anxiolytics (including clozapine) and sedatives are being used , or by persons with anxiety disorders.

This medicine should not be used by any persons who are also taking ephedrine (see also section 4.5).

Caffeine shares the same metabolic pathway as theophylline and therefore this medicine should not be used concurrently with theophylline.

4.4 Special warnings and precautions for use

- Patients should be advised to consult their doctor if their headaches become persistent.
- Do not take anything else containing paracetamol while taking this medicine.
- Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.
- Excessive intake of caffeine (e.g. coffee, tea and some canned drinks) should be avoided while taking this product.
- 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.

Pack Label

- **Talk to a doctor at once if you take too much of this medicine even if you feel well.**
- **Do not take anything else containing paracetamol while taking this medicine.**
- Do not take more medicine than the label tells you to.
- Keep out of the sight and reach of children.

Patient Information Leaflet

- Talk to a doctor at once if you take too much of this medicine even if you feel well. This is because too much paracetamol can cause delayed, serious liver damage.
- Keep this medicine out of the sight and reach of children.

4.5 Interaction with other medicinal products and other forms of interaction

As caffeine is found naturally in tea, coffee and chocolate, and in some carbonated drinks there is the potential for users to take more than the recommended 520 mg/day of caffeine (8 tablets) per day. Therefore users should take account of dietary and other medicinal sources of caffeine and ensure that they do not exceed the stated dose (See section 4.2).

Xanthine derivatives such as caffeine can weaken the vasodilating effect of substances used for myocardial imaging such as adenosine and dipyridamole. Therefore, caffeine should be avoided for 24 hours before myocardial imaging.

Caffeine, a CNS stimulant, has an antagonistic effect towards the action of sedatives and tranquilizers.

Caffeine may enhance the tachycardic effect of phenylpropanolamine.

Caffeine exerts a competitive inhibition of the metabolism of clozapine. Therefore clozapine and caffeine must not be used concurrently (see contraindications).

Caffeine can increase blood pressure and counters the hypotensive action of beta blockers such as atenolol, metoprolol, oxprenolol and propranolol. This medicine should not be used at the same time as beta blockers.

Disulfiram increases caffeine clearance by up to 50%. Concomitant use of disulfiram and caffeine should be avoided (see contraindications).

Use of lithium carbonate and caffeine may cause a small to moderate rise in serum lithium levels. Concomitant use should be avoided (see contraindications).

Monoamine oxidase inhibitors may increase the stimulant effects of caffeine.

Methoxsalen reduces clearance of caffeine and may increase the effects of caffeine.

Phenytoin doubles caffeine clearance, although caffeine does not affect the metabolism of phenytoin.

Pipemidic acid reduces caffeine clearance, enhancing the effects of caffeine.

Theophylline and caffeine share the same metabolic pathway, leading to increased clearance times for theophylline when used concurrently with caffeine. Concomitant use should be avoided (see contraindications).

Levothyroxine, like caffeine can increase blood pressure, and therefore these two active ingredients should not be used concurrently.

Ephedrine and caffeine interact to produce significant cardiovascular effects. Therefore caffeine should be avoided when ephedrine is being taken.

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

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.

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

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.

However, paracetamol-caffeine is not recommended for use during pregnancy due to the possible increased risk of lower birth weight and spontaneous abortion associated with caffeine consumption.

Lactation

Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding.

Caffeine appears in breast milk. Irritability and poor sleeping pattern in the infant have been reported. Caffeine in breast milk may potentially have a stimulating effect on breast fed infants.

Therefore, due to caffeine content of this product it should not be used if you are pregnant or breast feeding.

4.7 Effects on ability to drive and use machines

None stated.

4.8 Undesirable effects

Adverse events from historical clinical trial data are both infrequent and from small patient exposure. Accordingly, events reported from extensive post-marketing experience at therapeutic/labelled dose and considered attributable are listed below by system class. Due to limited clinical trial data, the

frequency of these adverse events is not known (cannot be estimated from available data), but post-marketing experience indicates that adverse reactions to paracetamol are rare and serious reactions are very rare.

Post marketing data

Paracetamol

Body System	**Undesirable effect**
Blood and lymphatic system disorders	Thrombocytopenia, agranulocytosis
	Agranulocytosis
Immune system disorders	Anaphylaxis
	Cutaneous hypersensitivity reactions including skin rashes, angioedema, Stevens Johnson syndrome / toxic epidermal necrolysis
Metabolism and nutrition disorders	High anion gap metabolic acidosis
Respiratory, thoracic and mediastinal disorders	Bronchospasm
Hepatobiliary disorders	Hepatic dysfunction

Description of selected adverse reactions

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.

* There have been cases of bronchospasm with paracetamol, but these are more likely in asthmatics sensitive to aspirin or other NSAIDs.

Very rare cases of serious skin reactions have been reported.

Caffeine

Body System	**Undesirable effect**
Central nervous system	Nervousness, Dizziness
When the recommended paracetamol-caffeine dosing regimen is combined with dietary caffeine intake, the resulting higher dose of caffeine may increase the potential for caffeine-related adverse effects such as restlessness and palpitations.	
Undesirable effects are not normally observed in healthy individuals taking caffeine at doses up to 520 mg per day. However some users who are caffeine naïve, have abstained from caffeine for a period or who are more sensitive to caffeine may experience effects more commonly seen at higher doses. These	

include tremor, insomnia, nervousness, irritability, anxiety, headache, tinnitus, arrhythmia, and tachycardia, diuresis, gastrointestinal disturbances and elevated respiration. Individuals who experience these effects must stop taking this medicine (and any others containing caffeine) and any other dietary caffeine.
Following regular use of caffeine, cessation of intake may lead to withdrawal symptoms which may last for up to a week and which include headache, tiredness and decreased alertness.

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.

4.9 Overdose

PARACETAMOL

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, 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 24h from ingestion should be discussed with the NPIS or a liver unit.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: N02BE51

Paracetamol

ANALGESIC:

The mechanism of analgesic action has not been fully determined. Paracetamol may act predominantly by inhibiting a prostaglandin synthesis in the central nervous system (CNS) and to a lesser extent through a peripheral action by blocking pain-impulse generation. The peripheral action may also be due to inhibition of prostaglandin synthesis or to inhibition of the synthesis or actions of other substances that sensitise pain receptors to mechanical or chemical stimulation.

ANTIPYRETIC:

Paracetamol probably produces antipyresis by acting centrally on the hypothalamic heat-regulating centre to produce peripheral vasodilation resulting in increased blood flow through the skin, sweating, and heat loss. The central action probably involves inhibition of prostagalandin synthesis in the hypothalamus.

Caffeine

Central nervous system stimulant - Caffeine stimulates all levels of the CNS, although its cortical effects are milder and of shorter duration than those of amfetamines.

ANALGESIA ADJUNCT:

Caffeine constricts cerebral vasculature with an accompanying decrease in cerebral blood flow and in the oxygen tension of the brain. It is believed that caffeine helps to relieve headache by providing a more rapid onset of action and/or enhanced pain relief with lower doses of analgesic. Recent studies with ergotamine indicate that the enhancement of effect by the addition of caffeine may also be due to improved gastrointestinal absorption of ergotamine when administered with caffeine.

5.2 Pharmacokinetic properties

PARACETAMOL

Absorption and Fate

Paracetamol is readily absorbed from the gastro-intestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion. It is metabolised in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half-life varies from about 1 to 4 hours. Plasma-protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.

A minor hydroxylated metabolite which is usually produced in very small amounts by mixed-function oxidases in the liver and which is usually detoxified by conjugation with liver glutathione may accumulate following paracetamol overdosage and cause liver damage.

CAFFEINE

Absorption and Fate

Caffeine is absorbed readily after oral administration and is widely distributed throughout the body. Caffeine is metabolised almost completely via oxidation, demethylation, and acetylation, and is excreted in the urine as 1-methyluric acid, 1-methylxanthine, 7-methylxanthine, 1,7-dimethylxanthine (paraxanthine), 5-acetylamino-6-formylamino-3-methyluracil (AFMU), and other metabolites with only about 1% unchanged.

5.3 Preclinical safety data

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

Maize Starch
Methylcellulose
Povidone
Talc
Calcium Stearate

6.2 Incompatibilities

None stated

6.3 Shelf life

3 years

6.4 Special precautions for storage

None required.

6.5 Nature and contents of container

UPVC/aluminium foil blisters in cartons of 8, 12, 16 tablets.

35gsm Glassine (Pergamin) paper/9 micron soft temper Aluminium foil/250 micron PVC blister

6.6 Special precautions for disposal

None

7 MARKETING AUTHORISATION HOLDER

Omega Pharma Ltd Wrafton

Braunton

North Devon EX33 2DL

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PL 02855/0338

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