SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Crescent Pharma Pain Relief 500 mg/65 mg Film-coated Tablets

Paracetamol and Caffeine 500 mg/65 mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains: Paracetamol 500 mg and Caffeine 65 mg.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

White, capsule-shaped, film-coated “MANDA+” embossed on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Crescent Pharma Pain Relief Film-coated Tablets/Paracetamol and Caffeine Film-coated Tablets is a mild analgesic and antipyretic. It is indicated in the treatment of most painful and febrile conditions, for example, headache, including migraine, toothache, neuralgia, rheumatic pain, muscular aches and pains, dysmenorrhoea, and relief of the symptoms of cold, influenza and sore throat.

4.2 Posology and method of administration

Posology

Children aged 12-15 years:

1 tablet every 4-6 hours

Do not take more than 4 tablets in any 24-hour period

Adults and children over 16 years of age:

One to two tablets every four to six hours.

Maximum of eight tablets daily.

Paediatric population

Not recommended for children under 12 years of age.

Elderly:

One to two tablets every four to six hours.

Maximum of eight tablets daily.

Reduce dosage if renal or hepatic function is impaired.

Method of administration

For oral administration.

Do not exceed the recommended dose.

Do not take with any other paracetamol-containing products. Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage.

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.

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

Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazard of overdose is 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.

Do not exceed the stated dose.

Patients should be advised to consult their doctor if their headaches become persistent.

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.

The pack label will state:

- Contains paracetamol
- Do not take more medicine than the label tells you to. If you do not get better talk to your doctor.
- Do not take anything else containing paracetamol while taking this medicine.
- Talk to a doctor at once if you take too much of this medicine, even if you feel well.

The patient information leaflet will state:

- 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.

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.

8.5 Interaction with other medicinal products and other forms of interaction

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

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.

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.

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

Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol used in the recommended dosage, but patients should follow the advice of their doctor regarding its use. ***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.

Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data on paracetamol do not contraindicate breast feeding but caffeine in breast milk may potentially have a stimulating effect on breast fed infants. Therefore, due to the 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.

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 tabulated 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

Body System	**Undesirable effect**
Blood and lymphatic system disorders	Thrombocytopenia
	Agranulocytosis

Immune system disorders	Anaphylaxis
	Cutaneous hypersensitivity reactions including skin rashes, angioedema and Stevens Johnson syndrome/toxic epidermal necrolysis
Respiratory, thoracic and mediastinal disorders	Bronchospasm*
Hepatobiliary disorders	Hepatic dysfunction

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

Caffeine	
Central Nervous System	Nervousness
	Dizziness
At doses up to 520 mg per day undesirable effects are not normally observed in healthy individuals. 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, elevated respiration, restlessness and palpitations. 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, phenobarbital, 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 24 h from ingestion should be discussed with the NPIS or a liver unit.

Caffeine

Symptoms

Overdose of caffeine may result in epigastric pain, vomiting, diuresis, tachycardia, nervousness, facial flushing, "rambling" flow of thought and speech or cardia arrhythmia, CNS stimulation (insomnia, restlessness, excitement, agitation, jitteriness, muscle twitching, tremors and convulsions).

Management

Patients should receive general supportive care (e.g. hydration and maintenance of vital signs). 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. The CNS effects of overdose may be treated with intravenous sedatives.

Summary

Treatment of overdose with Crescent Pharma Pain Relief Film-coated Tablets/Paracetamol and Caffeine Film-coated Tablets requires assessment of plasma paracetamol levels for antidote treatment, with signs and symptoms of caffeine toxicity being managed symptomatically.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics, ATC code: NO2B E51

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 with peak plasma levels occurring about 30 minutes to 2 hours after ingestion.

It is relatively uniformly distributed throughout most body fluids and exhibits variable protein binding. It is metabolised in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted unchanged.

The elimination half life of Paracetamol varies from about 1 to 4 hours.

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 1-methyluric acid and 1-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

Maize starch
Silica, colloidal anhydrous
Sodium starch glycollate (Type A)
Povidone
Potassium sorbate
Magnesium stearate
Talc
Hypromellose (Pharmacoat 606)
Hypromellose (Pharmacoat 615)
Macrogol 4000

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 25°C. Store in the original container. Keep container in outer carton.

6.5 Nature and contents of container

Aluminium/PVC blister.

16 tablets per carton, in 2 blister packs of 8 tablets.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Crescent Pharma Limited

Key House

Sarum Hill, Basingstoke

RG21 8SR

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 20416/0730

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

29/09/2005

10 DATE OF REVISION OF THE TEXT

26/01/2024