1. Name of the medicinal Product

KRISDREX TABLETS (Paracetamol 500mg + Caffeine 30mg)

2. Qualitative and Quantitative Composition

Each uncoated tablet contains:

Paracetamol USP----------500mg

Caffeine BP----------30mg

Excipients----------q.s.

Quantitative declaration

Excipients with known effect:

Maize Starch, Sodium Starch Glycolate, Methyl Paraben, Propyl Paraben, Magnesium Stearate, Purified Talc, Colloidal Silicon Dioxide (Aerosil), Croscarmellose Sodium, Dicalcium Phosphate, colour sunset yellow supra, & PVPK-90.

For a full list of excipients, see section 6.1

3. Pharmaceutical Form

Oral caplets

Flat, uncoated tablets, embossed with KRISHAT on white side and break-line on coloured side.

4. Clinical Particulars

4.1 Therapeutic Indications

A mild analgesic and antipyretic formulated to give extra pain relief. The caplets are recommended for the treatment of most painful and febrile conditions, for example, headache, including migraine, backache, toothache, rheumatic pain and dysmenorrhoea, and the relief of the symptoms of colds, influenza and sore throat.

4.2 Posology and Method of Administration

Oral use.

Adults (including the elderly), and children aged 16 years and over:

Two caplets up to four times daily. The dose should not be repeated more frequently than every 4 hours. Do not exceed 8 caplets in 24 hours.

Children aged 12-15 years: One caplet up to four times daily. The dose should not be repeated more frequently than every 4 hours. Do not exceed 4 caplets in 24 hours. Not recommended for children under 12 years.

4.3 Contraindications

Hypersensitivity to paracetamol, caffeine or any of the other constituents.

4.4 Special Warnings and Special Precautions for Use

Do not exceed stated dose.

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 require liver transplant or lead to death. Care is advised in the administration of paracetamol to patients with renal or hepatic impairment. The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease. Caution should be exercised in patients with glutathione depleted states, as the use of paracetamol may increase the risk of metabolic acidosis (see section 4.9). Excessive intake of caffeine (e.g. coffee, tea and some canned drinks) should be avoided while taking this product. If symptoms persist, medical advice must be sought. Keep out of the sight and reach of children.

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.

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.

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 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. Caffeine may increase clearance of lithium. Concomitant use is therefore not recommended.

4.6 Pregnancy and Lactation

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. Caffeine in breast milk may potentially have a stimulating effect on breast fed infants. 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 MedDRA System Organ Class. Adverse reactions identified during post-marketing use are reported voluntarily from a population of uncertain size, the frequency of these reactions is unknown but likely to be very rare (<1/10,000).

Post marketing data

PARACETAMOL

Body System	**Undesirable effect**
Blood and lymphatic system disorders	Thrombocytopenia Agranulocytosis
Immune system disorders	Very rare cases of serious skin reactions have been reported. Anaphylaxis Cutaneous hypersensitivity reactions including (amongst others) skin rashes
Respiratory, thoracic and mediastinal disorders	Bronchospasm – more likely in patients sensitive to aspirin and other NSAIDs
Hepatobiliary disorders	Hepatic dysfunction

CAFFEINE

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.

Body System	**Undesirable effect**
Central nervous system	Dizziness Headache
Cardiac disorders	Palpitation
Psychiatric disorders	Insomnia Restlessness Anxiety and irritability
Gastrointestinal disorders	Gastrointestinal disturbances

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.

4.9 Overdose

Liver damage is possible in adults who have taken 10 g or more of paracetamol. Ingestion of 5 g 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 Nacetylcysteine 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.

Caffeine

Symptoms Overdose of caffeine may result in epigastric pain, vomitting, diuresis, tachycardia or cardia arrhythmia, CNS stimulation (insomnia, restlessness, excitement, agitation, jitteriness, tremors and convulsions). Parakris Extra Caplets (Paracetamol B.P 500mg + Caffiene B.P 30mg) It must be noted that for clinically significant symptoms of caffeine overdose to occur with this product, the amount ingested would be associated with serious paracetamol related toxicity.

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 requires assessment of plasma paracetamol levels for antidote treatment, with signs and symptoms of caffeine toxicity being managed symptomatically.

5. Pharmacological Properties

5.1 Pharmacodynamics Properties

ATC code: N02B 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. 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 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, Sodium Starch Glycolate, Methyl Paraben, Propyl Paraben, Magnesium Stearate, Purified Talc, Colloidal Silicon Dioxide (Aerosil), Croscarmellose Sodium, Dicalcium Phosphate, color Sunset yellow supra & PVPK-90.

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

36 months

6.4 Special Precautions for Storage

Store below 30°C. Protect from light & moisture.

6.5 Nature and Contents of Container

The caplets are packed in Alu/PVC blister and inserted in a carton.

Pack sizes: 20x10 Caplets.

6.6 Special precaution for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

Keep the medicine out of reach of children.

7. Manufacturing By

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