PRODUCT INFORMATION LEAFLET

1. Product Name

Brand Name: Crocin Pain Relief
Generic Name: Paracetamol and Caffeine Tablets I.P.

2. Qualitative & Quantitative Composition

Each uncoated tablet contains:
Paracetamol I.P. 650 mg
Caffeine Anhydrous I.P. 50 mg

3. Dosage Form

Oral Uncoated Tablets

4. Clinical Particulars

4.1. Indications/Uses

Crocin Pain Relief contains paracetamol, which is an analgesic and antipyretic, and caffeine, which acts as an adjuvant to the analgesic effect of paracetamol.
Crocin Pain Relief is used for symptomatic relief from mild to moderate pain eg., headache, migraine, toothache, pain after dental procedures/ tooth extraction, ear ache, period pain, pain of osteoarthritis and musculoskeletal pain.

4.2. Posology and method of administration

Dosage for Adults and children over 12 years: 1 tablet every 4 to 6 hours.
Do not take more frequently than every 4 hours and not more than 6 tablets per 24 hours. Do not exceed the stated dose.

Always use the lowest effective dose to relieve your symptoms. Use the smallest dose that you need to treat your symptoms and use the medicine for the shortest period necessary.

Crocin Pain Relief is not recommended in children under 12 years of age. Please see your doctor if your symptoms do not improve.

4.3. Contra-indications

Crocin Pain Relief is contraindicated in patients with a previous history of hypersensitivity to paracetamol, caffeine or any of the other ingredients in the product.

4.4. Warnings and Precautions

Crocin Pain Relief contains Paracetamol. Taking too much paracetamol can cause serious harm to your liver. Do not take this medicine if you are taking any other prescription or non-prescription medicines containing paracetamol to treat pain, fever, symptoms of cold and flu or any other indication.

Always read and follow the label

Check with your doctor before use if you:

- have liver or kidney problems.
- have a severe infection, are severely malnourished, severely underweight or are a chronic heavy alcohol user as this may increase the risk of metabolic acidosis. Signs of metabolic acidosis include:
  - deep, rapid, difficult breathing,
  - feeling sick (nausea), being sick (vomiting),
  - loss of appetite.

  Contact a doctor immediately if you get a combination of these symptoms.

  You may also need to avoid using the product altogether or limit the amount of paracetamol that you take.

  This medicine contains caffeine. Avoid drinking too many caffeine containing drinks (eg. tea, coffee and caffeine containing canned drinks) when taking this medicine. High caffeine intake can result in difficulty sleeping, shaking and an uncomfortable feeling in the chest caused by palpitations.

  Please see your doctor if your symptoms do not improve.

4.5. Interaction with other medicaments and other forms of interaction

Before taking this medicine, make sure you consult your doctor if you are taking warfarin or similar medicines used to thin the blood.
This product is not recommended if you are taking lithium.

4.6. Pregnancy and lactation

Pregnancy: Not recommended for use during pregnancy.

Lactation: Not recommended for use during lactation.

4.7. Effects on ability to drive and use machines, if contra-indicated

None

4.8. Undesirable effects/side effects

Stop taking this medicine and tell your doctor immediately if:

- you experience allergic reactions such as skin rash or itching, sometimes with breathing problems or swelling of the lips, tongue, throat or face.
- you experience a skin rash or peeling, or mouth ulcers.
- you have previously experienced breathing problems with aspirin or non-steroidal anti-inflammatory drugs, and experience a similar reaction with this product.
- you experience unexplained bruising or bleeding.

These reactions are rare.

4.9. Overdose

In case of over dosage, seek medical advice from a doctor immediately even if you do not have any symptoms because of the risk of liver failure.

In case of over dosage, you may also contact the **National Poisons Information Centre of India. Details of the same are as below:**

Department of Pharmacology
All India Institute of Medical Sciences
New Delhi-110029
Toll Free No. - 1800 116 117
Tel No.- 26589391, 26593677

5. Pharmacological Properties

5.1. Pharmacodynamic properties & mechanism of action

ATC code: N02B E01
Pharmacotherapeutic group: Paracetamol: Anilides
Caffeine: Methylxanthine

Paracetamol is an antipyretic and analgesic. Its mechanism of action is believed to include inhibition of prostaglandin synthesis, primarily within the central nervous system. The lack of peripheral prostaglandin inhibition confers important pharmacological properties such as the maintenance of the protective prostaglandins within the gastrointestinal tract. Paracetamol, is therefore, particularly suitable for: patients with a history of disease, or patients taking concomitant medication, where peripheral prostaglandin inhibition would be undesirable (for example, those with a history of gastrointestinal bleeding or in the elderly).

Caffeine acts as an analgesic adjuvant which enhances the analgesic effect of paracetamol and shortens the time to onset of analgesic effect. The analgesic adjuvant effects of caffeine have been proposed to result from several mechanisms: (i) blockade of peripheral pronociceptive actions of adenosine; (ii) activation of central noradrenergic pathways that constitute an endogenous pain suppressing system; and (iii) CNS stimulation with a consequent modulation of the affective component of pain. Clinical data have demonstrated that paracetamol-caffeine provides superior pain relief compared to standard paracetamol tablets ($p<=0.05$). Caffeine is a methyl-xanthine and a non-selective adenosine receptor antagonist.

5.2. Pharmacokinetics

Paracetamol is rapidly almost completely absorbed from the gastrointestinal tract and is distributed into most body tissues. Binding to plasma proteins is minimal at therapeutic concentrations. Paracetamol is metabolised in the liver and excreted in

the urine mainly as glucuronide and sulphate metabolites - less than 5% is excreted as unmodified paracetamol.

Caffeine is completely and rapidly absorbed from the gastrointestinal tract with peak concentrations occurring between 5 and 120 minutes depending on the dose, health status, and co-medications in fasted subjects. There is no evidence of pre-systemic metabolism. Caffeine is widely distributed throughout the body. The mean plasma protein binding of caffeine is approximately 35%. Caffeine is metabolised almost completely (~99%) in the liver via oxidation and demethylation to various xanthine derivatives, which are excreted in the urine. Hepatic cytochrome P450 isoenzyme CYP1A2 is involved in caffeine enzymatic metabolism. Elimination is almost entirely by hepatic metabolism in adults. Only a small percentage (1 to 2%) of the ingested dose of caffeine in humans is excreted unchanged in the urine. In adults, marked individual variability in the rate of elimination occurs. The mean plasma half-life after oral administration is about 4.9 hours with a range of 1.9 - 12.2 hours.

Combination

No saturation of the elimination processes with the consequential risks of increased half-life and toxicity has been observed for paracetamol. The absorption of both active substances (i.e. paracetamol and caffeine) is quick as described in the individual pharmacokinetic properties. No interactions have been observed.

6. Pharmaceutical Particulars

6.1. List of Excipients

Pregelatinised Maize starch
Maize Starch
Povidone K-25
Croscarmellose Sodium
Potassium Sorbate
Magnesium stearate
Purified Water

6.2. Incompatibilities

Not applicable

6.3. Shelf life

24 months

6.4. Special storage conditions

Keep out of sight and reach of children.
Store at ambient room temperature protected from light and moisture.

6.5. Nature and specification of the container

15 tablets blister (Aluminium/ PVC).

6.6. Instructions for Use and Handling

No special instructions for use and handling.

6.7. Manufacturing License Holder

Remidex Pharma Pvt Ltd.
B- 249/250, Peenya II Stage, Bangaluru 560058, India

6.8. Marketed By

GlaxoSmithKline Asia Private Limited,
Patiala Road, Nabha- 147201, Punjab, India