

## PACKAGE INSERT TEMPLATE FOR PARACETAMOL AND CAFFEINE

### Brand or Product Name

[Product name] Tablet

### Name and Strength of Active Substance(s)

Paracetamol.....500mg

Caffeine.....65mg

### Product Description

[Visual description of the appearance of the product (eg colour etc)]

Eg: White, film-coated, capsule shaped tablets with 'P' debossed on one side.

### Pharmacodynamics

#### Paracetamol

Paracetamol is a centrally acting analgesic and antipyretic with minimal anti-inflammatory properties.

#### *Analgesic*

The mechanism of analgesic action has not been fully determined. Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the central nervous system (specifically cyclooxygenase (COX)-2) 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 sensitize pain receptors to mechanical or chemical stimulation

#### *Antipyretic*

Paracetamol act centrally on the hypothalamic heat-regulating center to produce peripheral vasodilatation resulting in increase blood flow through the skin, sweating and heat loss.

Paracetamol reduces fever by inhibiting the formulation and release of prostaglandins in the CNS and by inhibiting endogenous pyrogens at the hypothalamic thermoregulator center

#### Caffeine

Caffeine is a central nervous system stimulant . It stimulates all levels of the CNS, although its cortical effects are milder and of shorter duration than those of amphetamines.

#### *Analgesia adjunct*

Caffeine constricts cerebral vasculature with an accompanying decrease in the cerebral blood flow and in the oxygen tension of the brain. It is believed that caffeine helps to relieve headache by providing more rapid onset of action and/or enhancing pain relief with lower doses of analgesic.

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

## Pharmacokinetics

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.

## Indication

Paracetamol-caffeine is indicated for the treatment of most painful and febrile conditions eg, headache, including migraine, backache, toothache, rheumatic pain and dysmenorrhoea. Relief of the symptoms of colds, influenza and sore throat.

## Recommended Dosage

### *Adult, elderly and children Dosage*

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

### *Children under 12 years*

Not recommended for children under 12 years.

## Mode of Administration

Oral

## Contraindications

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

## Warnings and Precautions

Avoid other caffeine containing products. Too much caffeine may cause rapid heart rate, nervousness or sleeplessness.

Ask a doctor or pharmacist before use if you have high blood pressure, glaucoma, or overactive bladder syndrome.

Do not exceed 8 tablets in 24 hours.

Do not take more than the recommended dose unless advised by your doctor. Use the smallest effective dose. Taking more than the maximum daily dose may cause **severe or possibly fatal liver damage**.

Do not use with other drugs containing **paracetamol**.

Not recommended for children under 12 years

Care is advised in the administration of paracetamol to patients with renal or hepatic impairment. The hazard or overdose is greater in those with non-cirrhotic alcohol liver disease.

Excessive intake of caffeine (e.g: coffee, tea and some canned drinks) should be avoided while taking this product.

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

Keep medicine out of reach of children

### **Interactions with Other Medicaments**

The speed of absorption of paracetamol may be increased by metaclopramide 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.

### **Statement on Usage During 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.

### **Adverse Effects / Undesirable Effects**

Adverse reactions of paracetamol-caffeine are rare when taken in recommended doses, but some of undesirable effect has been reported such as skin rash or itching, sometimes with breathing problems or swelling of the lips, tongue, throat or face. Bruising or bleeding

#### *Paracetamol adverse effect*

These are very rare side effect that has been reported according to the body system; Thrombocytopenia and Agranulocytosis (*Blood and lymphatic system disorders*), Anaphylaxis, cutaneous hypersensitivity reactions including skin rashes, angiodema and Stevens Johnson syndrome/toxic epidermal necrolysis(Immune system disorders), Bronchospasm (respiratory, thoracic and mediastinal disorders), Hepatic dysfunction(hepatic effects).

#### *Caffeine adverse effect*

Nervousness and dizziness has been reported for the central nervous system.

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 insomnia, restlessness, anxiety, irritability, headaches, gastrointestinal disturbances and palpitations.

## **Overdose and Treatment**

### Paracetamol

#### *Symptoms*

Symptoms of paracetamol overdose 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.

#### *Treatment*

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 the overdose or the risk of organ damage.

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 or cardiac arrhythmia, CNS stimulation (insomnia, restlessness, excitement, agitation, jitteriness, tremors and convulsions).

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.

#### *Treatment*

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.

**Storage Conditions**

*[ Store below 30° C, Protect from light and moisture ]*

**Dosage Forms and Packaging Available**

*[ Packaging type & pack size ]*

**Name and Address of Manufacturer**

*[ Name & full address of manufacturer ]*

**Name and Address of Marketing Authorization Holder**

*[ Name & full address of marketing authorization holder ]*

**Date of Revision of Package Insert**

*[ day/month/year ]*