Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Kapake 30mg/500mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Ingredient	mg per tablet
Paracetamol (As Paracetamol DC 96% and Povidone 4%)	500.0mg
Codeine Phosphate	30.0mg

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

Product imported from the UK:
Oblong white uncoated tablets marked ‘Kapake’ and bearing a scoreline on one side, the other side is plain and unmarked. The scoreline is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the treatment of severe pain.

4.2 Posology and method of administration

For oral administration.

Adults:
One or two tablets to be taken every four hours as required up to a maximum of eight tablets in any 24 hour period.

Children:
Not recommended for children under 12 years of age.

Elderly:
The dosage may need to be reduced and should be titrated to the individual’s need and overall medical condition.

4.3 Contraindications

Kapake 30mg/500mg Tablets should not be used in patients hypersensitive to codeine phosphate, paracetamol or any of the other ingredients. This product is contraindicated in patients with raised intracranial pressure or head injury, respiratory depression, acute asthma and acute alcoholism. Kapake 30mg/500mg Tablets are also contraindicated in patients receiving monoamine oxidase inhibitors or who have received these agents within the previous two weeks. It is not recommended for children under 12 years of age.

4.4 Special warnings and precautions for use

Codeine is partially metabolised by CYP2D6. If a patient has a deficiency or is completely lacking this enzyme they will not obtain adequate analgesic effects. Estimates indicate that up to 7% of the caucasian population may have this deficiency. However, if the patient is an ultra-rapid metaboliser there is an increased risk of developing side effects of opioid toxicity even at low doses. General symptoms of opioid toxicity include nausea, vomiting, constipation, lack of appetite and somnolence. In severe cases this may include symptoms of circulatory and respiratory depression. Estimates indicate that up to 1 to 2% of the caucasian population may be ultra-rapid metabolisers.

It should be used with caution in the elderly and debilitated as these patients may be more sensitive to the effects of opioids, those with prostatic hypertrophy, inflammatory or obstructive bowel disorders or Addison's disease. 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. Dependence of the morphine type may be produced especially with prolonged use of high doses of codeine.

The risk-benefit of continued use should be assessed regularly by the prescriber.

Immediate medical advice should be sought in the event of an overdose, even if the patient feels well, because of the risk of delayed serious liver damage. Patients should be advised not to take other paracetamol-containing products concurrently.

Do not exceed the recommended dose. If symptoms persist, consult your doctor. Keep out of the reach of children.

The leaflet will state in a prominent position in the 'before taking' section:

• Do not take for longer than directed by your prescriber

• Taking codeine regularly for a long time can lead to addiction, which might cause you to feel restless and irritable when you stop the tablets

• Taking a painkiller for headaches too often or for too long can make them worse.

The label will state (to be displayed prominently on outer pack – not boxed):

Do not take for longer than directed by your prescriber as taking codeine regularly for a long time can lead to addiction.

Codeine is partially metabolised by CYP2D6. If a patient has a deficiency or is completely lacking this enzyme they will not obtain adequate analgesic effects. Estimates indicate that up to 7% of the caucasian population may have this deficiency. However, if the patient is an ultra-rapid metaboliser there is an increased risk of developing side effects of opioid toxicity even at low doses. General symptoms of opioid toxicity include nausea, vomiting, constipation, lack of appetite and somnolence. In severe cases this may include symptoms of circulatory and respiratory depression. Estimates indicate that up to 1 to 2% of the caucasian population may be ultra-rapid metabolisers.

4.5 Interaction with other medicinal products and other forms of interaction

The depressant effects of codeine may be enhanced by other central nervous system depressants : anxiolytics, hypnotics, antidepressants, antipsychotics and alcohol. If combined therapy is necessary, the dose of one or both agents should be reduced. Alcohol should be avoided.

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.

4.6 Fertility, pregnancy and lactation

This product should not be used during pregnancy.

At normal therapeutic doses codeine and its active metabolites may be present in breast milk at very low doses and is unlikely to adversely affect the breast fed infant.

However, if the patient is an ultra-rapid metaboliser of CYP2D6, higher levels of the active metabolites may be present in breast milk and on very rare occasions may result in symptoms of opioid toxicity in the infant.

If symptoms of opioid toxicity develop in either the mother or the infant, then all codeine containing medicines should be stopped and alternative non-opioid analgesics prescribed. In severe cases consideration should be given to prescribing naloxone to reverse these effects.

4.7 Effects on ability to drive and use machines

Patients receiving this medication should be advised not to drive or operate machinery if affected by dizziness or sedation.

4.8 Undesirable effects

Adverse effects of paracetamol are rare but hypersensitivity including skin rash may occur. There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis associated with the use of paracetamol.

The most common adverse effects to codeine are dizziness, drowsiness, nausea and vomiting. These effects are often more common in the ambulatory patient and thus may be alleviated if the patient lies down. Other side-effects to codeine which may occur include constipation, urinary retention, light-headedness, confusion, euphoria, dysphoria, miosis, bradycardia, abdominal pain (rarely codeine-induced pancreatitis has been reported in patients with a history of cholecystectomy), allergic reactions and pruritus.

Regular prolonged use of codeine is known to lead to addiction and tolerance. Symptoms of restlessness and irritability may result when treatment is then stopped.

Prolonged use of a painkiller for headaches can make them worse.

4.9 Overdose

Paracetamol Overdose

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 of Paracetamol Overdose

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 of Paracetamol Overdose

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.

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 National Poisons Information Centre (NPIC) or a liver unit.

Codeine Overdose

The effects in overdosage will be potentiated by simultaneous ingestion of alcohol and psychotropic drugs.

Symptoms of Codeine Overdose

Central nervous system depression, including respiratory depression, may develop but is unlikely to be severe unless other sedative agents have been co-ingested, including alcohol, or the overdose is very large. The pupils may be pin-point in size, nausea and vomiting are common. Hypotension and tachycardia are possible but unlikely.

Management of Codeine Overdose

This should include general symptomatic and supportive measures including a clear airway and monitoring of vital signs until stable. Consider activated charcoal if an adult presents within one hour of ingestion of more than 350mg or a child more than 5mg/kg.

Give naloxone if coma or respiratory depression is present. Naloxone is a competitive antagonist and has a short half-life so large and repeated doses may be required in a seriously poisoned patient. Observe for at least four hours after ingestion, or eight hours if a sustained release preparation has been taken.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Natural opium alkaloids, ATC Code NO2A A59

Paracetamol has analgesic and antipyretic effects that do not differ significantly from that of aspirin. Its anti-inflammatory action is weak and it has practically no anti-platelet effect. The mechanism of action is unclear although it is believed to exert its action by inhibition of prostaglandin synthesis.

Codeine is an analgesic with uses similar to those of morphine although it is much less potent as an analgesic and has only mild sedative effects. It is used for the relief of cough and pain. Codeine has a low affinity for opioid receptors, the analgesic effect of codeine may be due to its conversion to morphine; approximately 10% of administered codeine is demethylated to form morphine.

5.2 Pharmacokinetic properties

Paracetamol is readily absorbed from the GI tract with peak plasma concentrations occurring about 30 minutes to two hours after oral administration. 90-100% of administered drug can be recovered in the urine within the first day. Practically none is excreted unchanged, most is conjugated in the liver with glucuronic acid or sulphuric acid.

Codeine and its salts are rapidly absorbed from the GI tract with peak plasma levels occurring about one hour after oral administration. Codeine is metabolised in the liver and excreted in the urine mainly as a conjugate of glucuronic acid. Approximately 10% of administered codeine is demethylated to form morphine.

Concurrent administration of both drugs does not interfere with the normal metabolic processes of each agent.

5.3 Preclinical safety data

None stated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Sodium starch glycollate (Type A)
Magnesium stearate
Povidone

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The shelf-life expiry date of this product is the date shown on the blister strips and outer carton of the product on the market in the country of origin.

6.4 Special precautions for storage

Store below 25˚c. Store in the original package.

6.5 Nature and contents of container

Cardboard outer containing blister strips.
Pack size: 100 tablets

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements

7 PARALLEL PRODUCT AUTHORISATION HOLDER

Imbat Limited
Unit L2, North Ring Business Park
Santry
Dublin 9

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA 1151/135/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16th April 2010

10 DATE OF REVISION OF THE TEXT

April 2012