SUMMARY OF PRODUCT CHARACTERISTICS

a) Proprietary name of a medicine

Hedon Tablets

b) Approved generic name(s)

ASPIRIN,PARACETAMOL,CAFFEINE tablets

c) Qualitative and quantitative composition

Each Tablet contains: Aspirin BP 300mg; Paracetamol BP 250mg & Caffeine Anhydrous BP 30mg.

d) Dosage form

Tablets

e) Clinical particulars

i. Therapeutic indication(s)

Hedon tablets are indicated for mild to moderate pain, headaches, inflammatory pyrexia, acute and chronic rheumatic disease and musculoskeletal disorders.

ii. Route of administration

For oral use

To be taken every 3-4 hours

- Adults and children over 12 years: 1-2 tablets
- Maximum daily dosage of 8 tablets.

If symptoms persist, seek medical advice.

iii. Contra-indication

Hypersensitivity to any of the ingredients.
Hypoprothrombinaemia, haemophilia and active peptic ulceration.

-

i. Special warnings and precautions for use

Hedon should be used with caution in patients with a history of peptic ulceration, coagulation abnormalities, impaired renal or hepatic function, or in dehydrated patients.

Hedon may enhance the effects of anti-coagulants, oral hypoglycaemic agents, phenytoin and sodium valproate. It may inhibit the uricosuric action of probenecid and increase the toxicity of sulphonamides.

Hedon may precipitate bronchospasm or induce attacks of asthma in susceptible patients.

Hedon should be avoided in the last 3 months of pregnancy.

Hedon should not be given to children below 12 years.

ii. Interactions

Aspirin:
Other NSAIDS and corticosteroids: Concurrent use of other NSAIDS or corticosteroids may increase the likelihood of GI side effects.
Diuretics: Antagonism of the diuretic effect.
Anticoagulants: Increased risk of bleeding due to antiplatelet effect.
Metoclopramide: Metoclopramide increases the rate of absorption of aspirin. However, concurrent use need not be avoided.
Phenytoin : The effect of phenytoin may be enhanced by aspirin. However, no special precautions are needed.
Valproate: The effect of valproate may be enhanced by aspirin.
Methotrexate: Delayed excretion and increased toxicity of methotrexate.
Paracetamol:
Cholestyramine: The speed of absorption of paracetamol is reduced by cholestyramine. Therefore, the cholestyramine should not be taken within one hour if maximal analgesia is required.
Metoclopramide and Domperidone : The speed of absorption of paracetamol is increased by metoclopramide and domperidone. However, concurrent use need not be avoided.
Warfarin: 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.
Chloramphenicol: Increased plasma concentration of chloramphenicol

iii. Pregnancy and lactation

There is clinical and epidemiological evidence of safety of aspirin in pregnancy, but it may prolong labour and contribute to maternal and neonatal bleeding, and so should not be used in late pregnancy.
Aspirin appears in breast milk, and regular high doses may affect neonatal clotting. Not recommended while breast-feeding due to possible risk of Reye's Syndrome as well as neonatal bleeding due to hypoprothrombinaemia.
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 the doctor regarding its use. Paracetamol is excreted in breast milk but not in a significant amount. Available published data do not contraindicate breast feeding.
Caffeine appears in breast milk. Irritability and poor sleeping pattern in the infant have been reported.

iv. Effects on the ability to drive and operate machinery

None stated

v. Undesirable effects

Side effects are mild and infrequent, but there is a high incidence of gastro-intestinal irritation with slight asymptomatic blood loss. Increased bleeding time. Aspirin may precipitate bronchospasm and induce asthma attacks or other hypersensitivity reactions, such as skin reactions (including angioedema and face oedema) in susceptible individuals.
Aspirin may induce gastro-intestinal haemorrhage, occasionally major. It may precipitate gout in susceptible individuals. Possible risk of Reye's Syndrome in children under 16 years.
Adverse effects of paracetamol are rare. Very rare cases of serious skin reactions have been reported. There have been reports of blood dyscrasias including thrombocytopenia purpura and agranulocytosis, but these were not necessarily causality related to paracetamol.
High doses of caffeine can cause tremor and palpitations.

Overdose This product contains both paracetamol and aspirin, and as such, any overdose events should be assessed using information available on both active substances.
Liver damage is possible in adults who have taken 10g or more of paracetamol. Adults who have consumed more than 5g of paracetamol, may experience liver damage if they have one of the following risk factors:
• long term treatment with either anti-infectives, anti-epileptics or St John's Wort, or any other drugs that induce

liver enzymes
• regular consumption of ethanol in excess of recommended amounts
• likely to be glutathione deplete e.g. eating disorder, cystic fibrosis, HIV infection, starvation, cachexia.
Salicylate poisoning is usually associated with plasma concentrations >350 mg/L (2.5 mmol/L). Most adult deaths occur in patients whose concentrations exceed 700 mg/L (5.1 mmol/L). Single doses less than 100 mg/kg are unlikely to cause serious poisoning.
Symptoms
Common features exist for both active substances when taken in overdose, but these can be tabulated as follows:

Paracetamol	Aspirin	Caffeine
Within the first 24 hours: Pallor Nausea Vomiting Anorexia Abdominal pain After 12-48 hours: Liver damage Abnormalities of glucose metabolism and metabolic acidosis Severe poisoning: Hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema and death. With or without severe liver damage: Acute renal failure with acute tubular necrosis strongly suggested by loin pain haematuria and proteinuria. Cardiac arrhythmias Pancreatitis	Common: Vomiting, Dehydration, Tinnitus Vertigo, Deafness, Sweating Warm extremities with bounding pulses Increased respiratory rate Hyperventilation Acid base disturbance Mixed respiratory alkalosis and metabolic acidosis with normal or high arterial pH (normal or reduced hydrogen ion concentration) in adults and children aged over 4 years. In children aged 4 years or less, a dominant metabolic acidosis with low arterial pH (raised hydrogen ion concentration) is common. Acidosis can increase salicylate transfer across the blood brain barrier. Uncommon: Haematemesis Hyperpyrexia Hypoglycaemia Hypokalaemia Thrombocytopenia Increased INR/PTR Intravascular coagulation Renal failure Non-cardiac pulmonary oedema Confusion, disorientation, coma and convulsions are more common in children than adults.	Other symptoms of overdosage, associated with the caffeine component include: CNS stimulation; anxiety, nervousnes restlessness, insomnia, excitemer muscle twitching, confusion, convulsic Cardiac: tachycardi cardiac arrhythmia Gastric: Abdominal stomach pains Other: diuresis, faci flushing

f) Pharmacological properties

Orally ingested aspirin is absorbed rapidly, partly from the stomach but mostly from the upper small intestines. Appreciable concentrations are found in plasma in less than 30 minutes: after a single dose, a peak value is reached in about 2 hours and then gradually declines. Rate of absorption is determined by many factors, particularly the disintegration and dissolution rates if tablets are given, the pH at the mucosal surfaces, and gastric emptying time. After absorption, aspirin is distributed throughout most body tissues and most transcellular fluids, primarily by pH-dependant passive processes. Aspirin is actively transported by a low-capacity, saturable system out of the CSF across the choroids plexus.

The drug readily crosses the placental barrier. The biotransformation of aspirin takes place in many tissues, but particularly in the hepatic endoplasmic reticulum and mitochondria. The three chief

metabolic products are salicyluric acid the glycine conjugate), the ether or phenolic glucuronide, and the ester or acyl glucuronide. IN addition, a small fraction is oxidized to gentisic acid (2,5-dihydroxybenzoic acid) and to 2,3-dihydroxybenzoic and 2,3,5-trihydroxibenzoic acids; gentisuric acid, the glycine conjugate of gentisic acid, is also formed. Aspirin is excreted in the urine as free salicylic acid (10%), salicyluric acid (75%), salicylic phenolic (10%) and acyl (5%) glucuronides, and gentisic acid (<1%). However, excretion of free salicylate is extremely variable and depends upon both the does and the urinary pH. In alkaline urine, more than 30% of the ingested drug may be eliminated as free salicylate, whereas in acidic urine this may be as low as %. The plasma half-life for aspirin is approximately 15 minutes.

Paracetamol is metabolized primarily by the hepatic microsomal enzymes. Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. The concentration in plasma reaches a peak in 30 to 60 minutes, and the half-life in plasma is about 2 hours after therapeutic doses. Paracetamol is relatively uniformly distributed throughout most body fluids. Binding of the drug to plasma proteins is variable; only 20 to 50% may be bound at the concentrations encountered during acute intoxication. After therapeutic doses, 90 to 100% of the drug may be recovered in the urine within the first day, primarily after hepatic conjugation with glucuronic acid (about 60%), sulfuric acid (about 35%), or cysteine (about 3%); small amounts of hydroxylated and deacetylated metabolies have also been detected. Children have less capacity for glucuronidation of the drug than do adults.

Caffeine is readily absorbed after oral administration, and maximum plasma concentrations are achieved within 1 hour. Caffeine is distributed into all body compartments. It is eliminated primarily by metabolism in the liver. Less than 5% of the amount administered is recovered in the urine unchanged. Caffeine has a half-life of 3 to 7 hours.

i. **Preclinical safety data** – Not applicable.

g) Pharmaceutical particulars

i. List of excipients

- Starch
- Sodium Benzoate
- Potassium Sorbate
- Stearic acid
- Talcum powder Purified
- Guar gum
- Aerosil
- Povidone

ii. **Incompatibilities** - None known.

iii. **Shelf-life** -

a. **In the original unopened container**; 36 months

b. **After reconstitution (where appropriate)** NA

c. **Shelf-life after first opening:** 36 months

iv. **Special precautions for storage:** Store below 25°C in a dry place. Protect from light.

Nature and composition of containers 50 x 2 Strip Pack

v. **Instruction for use/handling** – Not applicable

vi. **Restriction on sale / distribution:** General sale

h) Administrative data

i. Name and address of holder of a registration.

Regal Pharmaceuticals Limited

Phone: 8564211/2/3/4

Fax: 8560946/8564093

Email: info@regalpharmaceuticals.com

Plot No.: 7879/18, Off Baba Dogo Road, Ruaraka,

P.O. Box 44421-00100, Nairobi, Kenya

i. **Registration number**. H2006/468

ii. **Date of first registration**- 22/08/06