SUMMARY OF PRODUCT CHARACTERISITCS

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8. Marketing authorization number
9. Date of first registration/renewal of the registration
10. Date of revision of the text

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

Hedex Caplets

1.1 Strength

Each caplet contains: Aspirin 400mg, Paracetamol 200mg and Caffeine 50mg

1.2 Pharmaceutical Form

Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

2.1 Qualitative declaration

Aspirin BP, Paracetamol BP and Caffeine BP

2.2 Quantitative declaration

Each caplet contains: Aspirin 400mg, Paracetamol 200mg and Caffeine 50mg

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Pharmaceutical Form: Tablet

Description: White caplets free from any foreign particles, chips or cracks engraved HEDEX on both sides

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Hedex Caplets is indicated for the treatment of mild to moderate pain including headache, migraine, neuralgia, toothache, sore throat, period pains, symptomatic relief of sprains, strains, rheumatic pain, sciatica, lumbago, fibrositis, muscular aches and pains, joint swelling and stiffness, influenza, feverishness and feverish colds.

4.2 Posology

- Adults: 1 or 2 caplets every 3 to 4 hours. Total daily dose not to exceed 8 caplets

4.3 Method of Administration

Oral Administration

4.4 Contraindications

Hedex Caplets is contra indicated in patients with a previous history of hypersensitivity to Paracetamol. If you have been diagnosed with liver or kidney imparment seek medical advice before taking this medication.

4.5 Special Warnings and Precautions for Use

Children under 16 years should not use the medicine for chicken pox or flu symptoms before a doctor is consulted about Reye's syndrome, a rare but serious illness.

Do not use for pain for more than 5 days or for fever for more than 3 days.

Do not take with other products containing Paracetamol

Due to the Caffeine content of this product it should not be used if you are pregnant or breast feeding.

4.6 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.

4.7 Fertility, pregnancy and lactation

Pregnancy

Hedex Caplets is not recommended for use during pregnancy due to the possible increased risk of lower birth weight and spontaneous abortion associated with Caffeine consumption.

Lactation

Caffeine in breast milk may potentially have a stimulating effect on breast fed infants.

4.8 Effects on ability to drive and use machines

It does not affect the ability to drive and use machines

4.9 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 system class. Due to limited clinical trial data, the frequency of these adverse events is not known (cannot be estimated from available data), but post-marketing experience indicates that adverse reactions to Paracetamol are rare and serious reactions are very rare.

Post marketing data

Body System	**Undesirable effect**
Blood and lymphatic system disorders	Thrombocytopenia Agranulocytosis

Immune system disorders	Anaphylaxis Cutaneous hypersensitivity reactions including skin rashes, angiodema and Stevens Johnson syndrome/toxic epidermal necrolysis
Respiratory, thoracic and mediastinal disorders	Bromchospasm*
Hepatobiliary disorders	Hepatic dysfunction

* There have been cases of bronchospasm with paracetamol, but these are more likely in asthmatics sensitive to aspirin or other NSAIDs.

Caffeine	
Central Nervous system	Nervousness Dizziness
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.	

4.10 Overdose

Paracetamol

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, coma and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported. Liver damage is possible in adults who have taken 10g or more of paracetamol. It is considered that excess quantities of a toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested) become irreversibly bound to liver tissue.

Treatment for 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. Gastric lavage or 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. Antidotes such as N-acetylcysteine (NAC) and methionine protect the liver if administered within 12 hours of overdose. NAC is effective up to and possibly beyond 24 hours. General supportive measures must be available.

Caffeine

Overdose of caffeine may result in epigastric pain, vomitting, diuresis, tachycardia or cardia arrhythmia, CNS stimulation (insomnia, restlessness, excitement, agitation, jitteriness, tremors and convulsions).

Treatment for Caffeine Overdose

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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacological Properties

Pharmacotherapeutic group and ATC Code

Pharmacotherapeutic group: **Analgesics and Antipyretics**

ATC Code: **N02BA51**

Aspirin

Salicylate inhibits the activity of the enzyme cyclo-oxygenase to decrease the formation of precursors of prostaglandin's and thromboxanes from arachidonic acid. Although many of the therapeutic effects may result from inhibition of prostaglandin synthesis (and consequent reduction of prostaglandin activity) in various tissues, other actions may also contribute significantly to the therapeutic effects.

Analgesic: Produces analgesia through a peripheral action by blocking pain impulse generation and via a central action, possibly in the hypothalamus.

Anti-inflammatory (non-steroidal): Exact mechanisms have not been determined. Salicylates may act peripherally in inflamed tissue probably by inhibiting the synthesis of prostaglandins and possibly by inhibiting the synthesis and/or actions of other mediators of the inflammatory response.

Paracetamol

Analgesic:

The mechanism of analgesic action has not been fully determined. Paracetamol may act predominantly by inhibiting a prostaglandin synthesis in the central nervous system (CNS) 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 probably produces antipyresis by acting centrally on the hypothalamic heat-regulating centre to produce peripheral vasodilatation resulting in increased blood flow through the skin, sweating and heat loss. The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus.

Caffeine

Central nervous system stimulant – Caffeine 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 cerebral blood flow and in the oxygen tension of the brain. It is believed that caffeine helps to relieve headache by providing a more rapid onset of action and/or enhanced pain relief with lower doses of analgesic. Recent studies with ergotamine indicate that the enhancement of effect by the addition of caffeine may also be due to improved gastrointestinal absorption of ergotamine when administered with caffeine.

5.2 Pharmacokinetic Properties

Aspirin

Absorption is generally rapid and complete following oral administration. It is largely hydrolyzed in the gastrointestinal tract, liver and blood to salicylate which is further metabolized primarily in the liver.

Paracetamol

Paracetamol is readily absorbed from the gastro-intestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion. It is metabolized in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half-life varies from about 1 – 4 hours. Plasma-protein is negligible at usual therapeutic concentrations but increases with increasing concentrations.

A minor hydroxylated metabolite which is usually produced in very small amounts by mixed-function oxidases in the liver and which is usually detoxified by conjugation with liver glutathione may accumulate following paracetamol over dosage and cause liver damage.

Caffeine

Caffeine is completely and rapidly absorbed after oral administration with peak concentrations occurring between 5 and 90 minutes after dose in fasted subjects. There is no evidence of pre-systemic metabolism. Elimination is almost entirely by hepatic metabolism in adults.

In adults, marked individual variability in the rate of elimination occurs. The mean plasma elimination half-life is 4.9 hours with a range of 1.9 – 12.2 hours. Caffeine distributes into all body fluids. The mean plasma protein binding of caffeine is 35%.

Caffeine us metabolized almost completely via oxidation, demethylation, and acetylation, and is excreted in the urine. The major metabolites are 1-methylxanthine, 7-methylxanthine, 1,7-dimethylxanthine (paraxanthine). Minor metabolites include 1-methyluric acid and 5-acetylamino-6 formylamino-3-methyluracil (AMFU).

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber in addition to that included in other sections of the summary of product characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Maize Starch, Povidone K25, Sepistab ST-200 (Pregelatinised Starch), Purified Talc, Stearic Acid and Potassium Sorbate

6.2 Incompatibilities

None known

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store in a dry place below 30^0C

Protect from light

6.5 Nature and contents of container

Hedex Caplets are packed in PVC-Aluminium blister packs and contained in a dispenser cartons made of chipboard.

6.6 Special precautions for disposal and other handling

No special requirements

7. Marketing Authorisation Holder & Manufacturing Site Addresses

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8. Marketing Authorisation Number

14

9. Date of First Registration/Renewal of the Registration

This is a new application

10. Date of revision of the text

November 2019