1. NAME OF THE MEDICINAL PRODUCT:

Action Tablets

2. QUALITATIVE AND QUANTITAVE COMPOSITION

Each tablet contains: Aspirin 600mg, Paracetamol 300mg and Caffeine 50mg.

3. PHARMACEUTICAL FORM

Tablets.

4.0 CLINICAL PARTICULARS

4.1 Therapeutic Indications

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 and Method of Administration

For oral administration only

Adults and young persons over 16 years:-

1 or 2 tablets every 4 hours as required. Dose not to be taken more frequently than every 4 hours, with a maximum of 6 tablets in 24 hours.

Do not give to children under 16 years, unless specifically indicated (e.g. for Kawasaki's disease).

Adult dosage is suitable for the elderly.

4.3 Contraindications

In patients with haemophilia or those with intolerance to Aspirin, Paracetamol or Caffeine.

4.4 Special Warnings and Precautions for Use

Warning: Do not exceed the stated doses.

Precautions: Not to be taken when on anticoagulant drugs. Children under 12 years should not use this medicine as Raye syndrome, which is associated with the use of aspirin in children, may occur. Not to be taken by those allergic to aspirin or have asthma, or recurrent ulcers. Should be given with care to patients with impaired kidney or liver function.

4.5 Interaction with other medicinal products and other forms of interaction

Aspirin

Antacids and Absorbents: Increase excretion of aspirin in alkaline urine.

Mifepristone: Increased risk of bleeding – avoid use of aspirin for 8-12 days after administration of mifepristone.

Spironolactone: Antagonism of diuretic effect.

Heparin: Increased risk of bleeding.

Phenindione: Increased risk of bleeding.

Warfarin & other coumarins: Increased risk of bleeding.

Domperidone & Metoclopramide: Enhance the effect of aspirin.

Phenytoin & valproate: Enhance the effect of phenytoin and valproate.

Methotrexate: Delayed excretion and increased toxicity of methotrexate.

Uricosurics: Inhibition of uricosurics.

Paracetamol

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone. Colestyramine may reduce the absorption of paracetamol.

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.

Caffeine

- **Ephedrine interacts with Caffeine**

Stimulant drugs speed up the nervous system. Caffeine and ephedrine are both stimulant drugs. Taking caffeine along with ephedrine might cause too much stimulation and sometimes serious side effects and heart problems. Do not take caffeine-containing products and ephedrine at the same time.

4.6 Adverse Reactions

Action Tablet is generally well tolerated when used in the recommended dosage.

4.7 Overdose

Over dosages may cause dizziness, tinnitus, sweating, nausea, mental confusion, hyperventilation, ketosis or coma.

Treatment of over dosage:

For mild intoxication emptying the stomach by emesis or aspiration or gastric lavage. Prompt administration of 50g activated charcoal and ½ liter of iced mannitol reduces absorption. In severe intoxication the risk of severe liver damage can be significantly reduced by the administration of methionine 2.5g by mouth every four hours until 10g has been given or IV 20% N-acetyl cysteine should be administered.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacological Properties

ATC Code: N02BA51

Aspirin

White powder or crystals soluble in alcohol and slightly soluble in water.

Mechanism of action/effect:

Salicylate inhibit 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

Stearic Acid, Sepistab ST-200 (Pregelatinised starch), Avicel PH-200 (Microcrystalline Cellulose), Acdisol NF 18 (Crosscarmellose Sodium) and Aerosil 130V.

6.2 Incompatibilities

None known

6.3 Shelf life

60 months

6.4 Special precautions for storage

Store in a cool dry place below 30^0C. Keep out of reach of children

6.5 Nature and contents of container

Action Tablets are packed in strips of two tablets each made of polypaper; which are then packed in dispensers made of cardboard.

Pack sizes: 100’s and 20’s

6.6 Special precautions for disposal and other handling

No special requirements

7.0 Name & Address of Manufacturer

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8.0 Date of revision of the text

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