For PPB use only	
1.17	**Summary Product Characteristics (SPC)**

1. NAME OF THE MEDICINAL PRODUCT:

Action Advance Tablet

2. QUALITATIVE AND QUANTITAVE COMPOSITION

Each tablet contains: Paracetamol 500mg

Caffeine 65mg

Excipients see section 6.1

3. PHARMACEUTICAL FORM

Tablet

4.0 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Action Advance is a mild analgesic and antipyretic formulated to give extra relief from pain. Its recommended for treatment of most painful and febrile conditions like headaches including migraine, backache, toothache, rheumatic pain and dysmenorrhea and the relief of the symptoms of colds, flu and sore throat.

4.2 Posology and Method of Administration

For oral administration

- Adults (including elderly) and children aged 16 years and over: two tablets up to4 times daily. The dose should not be repeated more frequently than every 4 hours. Do not exceed 8 tablets in 24 hours.
- Children aged 12 – 15 years: One tablet up to4 times daily. The dose should not be repeated more frequently than every 4 hours. Do not exceed 4 tablets in 24 hours.

4.3 Contraindications

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

4.4 Special Warnings and Precautions for Use

- Care is advised in the administration of paracetamol to patients with renal or hepatic impairment. The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease. Excess intake of caffeine (coffee, tea and canned drinks) should be avoided while taking this product. Do not exceed the stated doses.
- Patients are advised not to take other paracetamol containing products concurrently.
- If symptoms persist consult your doctor. Keep out of reach of children.

4.5 Interaction with other medicinal products and other forms of interaction

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.

Caffeine

Ephedrine: 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.

Adenosine (Adenocard) and Dipyridamole (Persantine): Caffeine might block the effects of adenosine (Adenocard) and dipyridamole (Persantine). Adenosine (Adenocard) and Dipyridamole (Persantine) are often used by doctors to do a test on the heart. This test is called a cardiac stress test. Stop consuming caffeine-containing products at least 24 hours before a cardiac stress test.

Antibiotics (Quinolone antibiotics): The body breaks down caffeine to get rid of it. Some antibiotics might decrease how quickly the body breaks down caffeine. Taking these antibiotics along with caffeine can increase the risk of side effects including jitteriness, headache, increased heart rate, and other side effects.

Some antibiotics that decrease how quickly the body breaks down caffeine include ciprofloxacin (Cipro), enoxacin (Penetrex), norfloxacin (Chibroxin, Noroxin), sparfloxacin (Zagam), trovafloxacin (Trovan), and grepafloxacin (Raxar).

Cimetidine (Tagamet): The body breaks down caffeine to get rid of it. Cimetidine (Tagamet) can decrease how quickly your body breaks down caffeine. Taking cimetidine (Tagamet) along with caffeine might increase the chance of caffeine side effects including jitteriness, headache, fast heartbeat, and others.

Estrogens: The body breaks down caffeine to get rid of it. Estrogens can decrease how quickly the body breaks down caffeine. Taking caffeine along with estrogens might cause jitteriness, headache, fast heartbeat, and other side effects. Some estrogen pills include conjugated equine estrogens (Premarin), ethinyl estradiol, estradiol, and others.

Lithium: The body naturally gets rid of lithium. Caffeine can increase how quickly your body gets rid of lithium. If you take products that contain caffeine and you take lithium, stop taking caffeine products slowly. Stopping caffeine too quickly can increase the side effects of lithium.

Medications for depression (MAOIs): Caffeine can stimulate the body. Some medications used for depression can also stimulate the body. Taking caffeine along with some medications for depression might cause serious side effects including fast heartbeat, high blood pressure, nervousness, and others.Some of these medications used for depression include phenelzine (Nardil), tranylcypromine (Parnate), and others.

Anticoagulant / Antiplatelet drugs: Caffeine might slow blood clotting. Taking caffeine along with medications that also slow clotting might increase the chances of bruising and bleeding.Some medications that slow blood clotting include aspirin, clopidogrel (Plavix), diclofenac (Voltaren, Cataflam, others), ibuprofen (Advil, Motrin, others), naproxen (Anaprox, Naprosyn, others), dalteparin (Fragmin), enoxaparin (Lovenox), heparin, warfarin (Coumadin), and others.

Alcohol: The body breaks down caffeine to get rid of it. Alcohol can decrease how quickly the body breaks down caffeine. Taking caffeine along with alcohol might cause too much caffeine in the bloodstream and caffeine side effects including jitteriness, headache, and fast heartbeat.

Birth control pills (Contraceptive drugs): The body breaks down caffeine to get rid of it. Birth control pills can decrease how quickly the body breaks down caffeine. Taking caffeine along with birth control pills can cause jitteriness, headache, fast heartbeat, and other side effects. Some birth control pills include ethinyl estradiol and levonorgestrel (Triphasil), ethinyl estradiol and norethindrone.

Antidiabetes drugs: Caffeine might increase blood sugar. Diabetes medications are used to lower blood sugar. Taking some medications for diabetes along with caffeine might decrease the effectiveness of diabetes medications. Some medications used for diabetes include glimepiride (Amaryl), glyburide (DiaBeta, Glynase PresTab, Micronase), insulin, pioglitazone (Actos), rosiglitazone (Avandia), chlorpropamide (Diabinese), glipizide (Glucotrol), tolbutamide (Orinase), and others.

4.6 Fertility, Pregnancy and Lactation

Paracetamol-caffeine is not recommended for use during pregnancy due to the possible increased risk of low birth weight and spontaneous abortion associated with the caffeine consumption.

Caffeine in breast may potentially have a stimulating effect on breast fed infants. Due to caffeine content of this product it should not be used if you are pregnant or breastfeeding.

4.7 Effects on Ability to Drive and use Machines

None

4.8 Adverse Effects

Body System

Blood and lymphatic system disorders: thrombocytopenia and agranulocytosis.

Immune system disorders: Anaphylaxis, cutaneous hypersentivity reaction including skin rashes, angioedema and Steven Johnson syndrome/toxic epidermal necrosis.

Respiratory, thoracic and mediastinal disorders: Bronchospasm (there has been cases of bronchospasm with paracetamol but these are more likely in asthmatic sensitive to apsirin or other NSAIDS.

Hepatobilaiary disorders: Hepatic dysfunction

Caffeine:

Central nervous system, nervousness and dizziness

When the recommended paracetamol-caffeien dosing regimen is combined with dietary caffeine intake, the resulting higher dose of caffeine may increase the potential for caffeine related adverse effects as insomnia, restlessness, anxiety, irritabilty, headaches, gastrointestinal disturbances and palpitations.

4.9 Overdose

Paracetamol

Liver damage is possible in adults who have taken 10g or more of paracetamol. Ingestion of g or more of paracetamol may lead to liver damage if the patient has the below noted risk factors:

Risk Factors:

a) If the patient is on long-term treatment 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. disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms: Symptoms of Paracetamol over dosage 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 acidosis may occur.

In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycemia, cerebral oedema and death.

Acute renal failure with tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop even in the absence of severe liver damage.

Cardiac arrhythmias and pancreatic have been reported.

Management: 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. See BNF overdose section. 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.

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.

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 the vomiting is not a problem, oral methionine may be suitable alternative for remote areas, outside hospital. Management of patients who present with serious hepatic dysfunction beyond 24 hour from ingestion should be discussed with NIPS or liver unit.

Caffeine

Symptoms: Overdose of caffeine may result in epigastric pain, vomiting, diuresis, tachycardia or cardia 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 ACTION Advance the amount ingested would be associated with serious paracetamol related toxicity.

Management:

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 overdose but can be considered for up to four hours after the overdose. The CNS effects of overdose may be treated intravenous sedatives.

Summary: Treatment of overdose requires assessment of plasma paracetamol levels for antidote treatment with signs and symptoms of caffeine toxicity being managed symptomatically.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: **Paracetamol combinations**

ATC code: **N02B E51**

Paracetamol

Paracetamol is a p-aminophenol derivative that exhibits analgesic and antipyretic activity. It does not possess anti-inflammatory activity. Paracetamol is thought to produce analgesic through a central inhibition of prostaglandin synthesis.

Caffeine

Caffeine stimulates the central nervous system (CNS), heightening alertness and sometimes causing restlessness and agitation. It relaxes smooth muscle, stimulates the contraction of cardiac muscle and enhances athletic performance.

Caffeine promotes gastric acid secretion and increases gastrointestinal motility. It is often combined in products with analgesics and ergot alkaloids, relieving the symptoms of migraine and other types of headaches. Caffeine acts as a mild diuretic.

5.2 Pharmacokinetic Properties

Paracetamol

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

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 urine as 1-methyuric and 1-methlxamine.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to prescriber which are additional to that already included in other sections of the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline Cellulose, Maize Starch, Povidone, Purified Talc, Magnesium Stearate, Colloidal Anhydrous Silica, Croscarmellose Sodium

6.2 Incompatibilities

None

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in a cool dry place below 30^0C. Protect from light.

6.5 Nature and contents of container

Action Advance Tablets are blister packed in 10 x 10 tablets or 2 x 10 tablets along with a leaflet.

6.6 Special precautions for disposal and other handling

Do not throw away any medicines you no longer use.

Ask your pharmacist or medical facility how to properly dispose of any medicine you no longer use. These measures will help protect the environment.

7.0 Name & Address of Manufacturer

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8.0 Date of revision of the text

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