National Agency for Food & Drug Administration & Control

(NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC) TEMPLATE

Name of the medicinal product

Novadex Extra Caplets

2. Qualitative and quantitative composition

Each tablet contains Paracetamol 500mg and Caffeine 30mg
For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Caplets

4. Clinical particulars

4.1 Therapeutic indications
The tablets are recommended for use as an analgesic in the relief of mild to moderate pain such as is associated with rheumatism, neuralgia, musculoskeletal disorders, headache and of discomfort associated with influenza, feverishness and feverish colds, toothache and dysmenorrhea.

4.2 Posology and method of administration
Adults, including the Elderly and Children aged 12 years and over:

For oral administration. Adults (including the elderly) and children aged 12 years and over: 2 caplets three to four times daily or as directed by the physician.
DO NOT EXCEED THE STATED DOSE.
If symptoms persisit after 2 days, consult your doctor.
Do not take with other products containing paracetamol.

Children under 12 years of age

Novadex Extra Caplets are not recommended for this age group.

4.3 Contraindications

- Known hypersensitivity to paracetamol, caffeine or any of the other ingredients.

4.4 Special warnings and precautions for use
Contains paracetamol. Do not use with any other paracetamol-containing products. The concomitant use with other products containing paracetamol may lead to an overdose. Paracetamol overdose may cause liver failure which can lead to liver transplant or death.

Cases of paracetamol induced hepatotoxicity, including fatal cases, have been reported in patients taking paracetamol at doses within the therapeutic range. These cases were reported in patients with one or more risk factors for hepatotoxicity including low body weight (<50 Kg), renal and hepatic impairment, chronic alcoholism, concomitant intake of hepatotoxic drugs, sepsis and in acute and chronic malnutrition (low reserves of hepatic glutathione). Paracetamol should be administered with caution to patients with these risk factors.

Caution is also advised in patients on concomitant treatment with drugs that induce hepatic enzymes and in conditions which may predispose to glutathione deficiency. In patients with glutathione depleted states such as sepsis; the use of paracetamol may increase the risk of metabolic acidosis.
Doses of paracetamol should be reviewed at clinically appropriate intervals and patients should be monitored for emergence of new risk factors for hepatoxicity which may warrant dosage adjustment

Underlying liver disease increases the risk of paracetamol related liver damage. Patients who have been diagnosed with liver or kidney impairment must seek medical advice before taking this medication.

Excessive intake of caffeine (e.g. coffee and some canned drinks) should be avoided while taking this product.

In general, medicinal products containing paracetamol should be taken for only a few days without the advice of a doctor or dentist and not at high doses. Do not exceed the stated dose. Take only when necessary. If high fever or signs of secondary infection occur or if symptoms persist for longer than 3 days, a physician should be consulted. Keep out of the sight and reach of children

4.5 Interaction with other medicinal products and other forms of interaction

- Paracetamol: Paracetamol may increase the elimination half-life of chloramphenicol. The absorption of paracetamol may be increased by metoclopramide and decreased by colestyramine. Oral contraceptives may increase the rate of clearance of paracetamol. 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.

- Caffeine: Caffeine can increase the elimination of lithium from the body. Concomitant use is therefore not recommended.

4.6 Pregnancy and lactation

Pregnancy:

Paracetamol: A large amount of data on pregnant women indicate neither malformative, nor feto/neonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results.

Caffeine: Paracetamol-caffeine is not recommended for use during pregnancy due to the possible increased risk of spontaneous abortion associated with caffeine consumption.

Lactation:

Paracetamol and caffeine are excreted in breast milk. Not recommended for use during breastfeeding

4.7 Effects on ability to drive and use machines

None anticipated.

4.8 Undesirable effects

Undesirable effects are listed by MedDRA System Organ Classes.

Assessment of undesirable effects is based on the following frequency groupings:

Very common: ≥1/10

Common: ≥1/100 to <1/10

Uncommon: ≥1/1,000 to <1/100

Rare: ≥1/10,000 to <1/1,000

Very rare: <1/10,000

Adverse event frequencies have been estimated from spontaneous reports received through post marketing data.

Body System	Undesirable Effects	Frequency
Paracetamol		
Blood and lymphatic system disorders	Thrombocytopaenia	Very rare

Immune System disorders	Anaphylaxis, Cutaneous hypersensitivity reactions, Angiodema, Stevens Johnson Syndrome and toxic epidermal necrolysis	Very rare
	Very rare cases of serious skin reactions have been reported	
Respiratory, thoracic and mediastinal disorders	Bronchospasm in patients sensitive to aspirin and other NSAIDs	Very rare
Hepatobiliary disorders	Hepatic dysfunction	Very rare
Caffeine		
Central Nervous System	Nervousness, Dizziness	Unknown
Cardiac disorders	Palpitation	Not known
Psychiatric disorders	Insomnia, restlessness, anxiety and irritability	Not known
Gastrointestinal disorders	Gastrointestinal disturbances	Not known

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. Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

4.9 Overdose

Paracetamol

Paracetamol overdose may cause liver failure which can lead to liver transplant or death. Acute pancreatitis has been observed, usually with hepatic dysfunction and liver toxicity. There is a risk of poisoning with paracetamol particularly in elderly subjects, young children, patients with liver disease, cases of chronic alcoholism and in patients with chronic malnutrition. Overdosing may be fatal in these cases. Symptoms generally appear within the first 24 hours and may comprise: nausea, vomiting, anorexia, pallor, and abdominal pain, or patients may be asymptomatic. Overdose of paracetamol in a single administration in adults or in children can cause liver cell necrosis likely to induce complete and irreversible necrosis, resulting in hepatocellular insufficiency, metabolic acidosis and encephalopathy which may lead to coma and death. Simultaneously, increased levels of hepatic transaminases (AST, ALT), lactate dehydrogenase and bilirubin are observed together with increased prothrombin levels that may appear 12 to 48 hours after administration. Liver damage is likely in adults who have taken more than the recommended amounts of paracetamol. It is considered that excess quantities of toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested), become irreversibly bound to liver tissue.

Some patients may be at increased risk of liver damage from paracetamol toxicity.Risk Factors include: If the patient;

- Is on long-term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.
- Regularly consumes ethanol in excess of recommended amounts.

• Is likely to be glutathione depleted e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia

Emergency Procedure:
Immediate transfer to hospital. Blood sampling to determine initial paracetamol plasma concentration. In the case of a single acute overdose, paracetamol plasma concentration should be measured 4 hours post ingestion.
Administration of activated charcoal should be considered if >150mg/kg paracetamol has been taken within 1 hour.
The antidote N-acetylcysteine, should be administered as soon as possible in accordance with National treatment guidelines. Symptomatic treatment should be implemented.

Caffeine
Overdose of caffeine may result in epigastric pain, vomiting, diuresis, tachycardia or cardiac 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 this product, the amount ingested would be associated with serious paracetamol-related liver toxicity.
No specific antidote is available, but supportive measures such as beta adrenceptor antagonists to reverse the cardiotoxic effects may be used.

5. Pharmacological properties

5.1 Pharmacodynamic properties
The combination of paracetamol and caffeine is a well-established analgesic combination

5.2 Pharmacokinetic properties
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 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 the urine as 1- methyluric acid and 1-methylxanthine.

5.3 Preclinical safety data
Preclinical safety data on paracetamol in the literature have not revealed any pertinent and conclusive findings which are of relevance to the recommended dosage and use of the product and which have not been mentioned elsewhere in this Summary.

6. Pharmaceutical particulars

6.1 List of excipients
Sodium Starch Glycolate
Povidone
Methyl hydroxybenzoate
Talc Powder
Magnesium Stearate

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
24 months.

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and contents of container
The product is presented in blister strip is composed of PVC with a printed aluminium foil.

The product is available in packs of 10x10 caplets.

6.6 Special precautions for disposal and other handling
Not applicable.

7. Applicant/Manufacturer
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