December 2023

SUMMARY OF PRODUCT CHARACTERISTIC (SPC)

1. NAME OF THE MEDICINAL PRODUCT

Adol Extra (Paracetamol 100 mg and Caffeine anhydrous 65 mg caplets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each caplet contains 500 mg paracetamol and 65 mg caffeine anhydrous.

For the full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Caplets
White to off-white oblong caplets
Marking: Face one: Engraved "adol"
Face Two**:** Engraved "EX"

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

A mild analgesic and antipyretic formulated to give extra pain relief. The caplets are recommended for the treatment of most painful and febrile conditions, for example, headache, including migraine, backache, toothache, rheumatic pain and dysmenorrhoea, and the relief of the symptoms of colds, influenza and sore throat.

4.2 Posology and method of administration

Oral use

Adults (including the elderly), and children aged 16 years and over:
Two caplets up to four times daily. The dose should not be repeated more frequently than every 4 hours. Do not exceed 8 caplets in 24 hours.
Children aged 12-15 years:
One caplet up to four times daily. The dose should not be repeated more frequently than every 4 hours. Do not exceed 4 caplets in 24 hours.
Not recommended for children under 12 years.

4.3 Contraindications

Hypersensitivity to paracetamol, caffeine or any of the other constituents

4.4 Special warnings and precautions for use

Do not exceed stated dose.
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 may require liver transplant or lead to death.
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.
Caution is advised if paracetamol is administered concomitantly with flucloxacillin due to increased risk of high anion gap metabolic acidosis (HAGMA), particularly in patients with severe renal impairment, sepsis, malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism), as well as those using maximum daily doses of paracetamol. Close monitoring, including measurement of urinary 5-oxoproline, is recommended.
Caution should be exercised in patients with glutathione depleted states, as the use of paracetamol may increase the risk of metabolic acidosis (see section 4.9).

Excessive intake of caffeine (e.g. coffee, tea and some canned drinks) should be avoided while taking this product.
If symptoms persist, medical advice must be sought.
Keep out of the sight and reach of children.
Patient Information Leaflet:
Talk to a doctor at once if you take too much of this medicine even if you feel well. This is because too much paracetamol can cause delayed, serious liver damage.

4.5 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.
Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis, especially in patients with risks factors (see section 4.4)
Caffeine may increase clearance of lithium. Concomitant use is therefore not recommended.

4.6 Pregnancy and Lactation

Paracetamol-caffeine is not recommended for use during pregnancy due to the possible increased risk of lower birth weight and spontaneous abortion associated with caffeine consumption.
Caffeine in breast milk may potentially have a stimulating effect on breast fed infants.
Due to the caffeine content of this product it should not be used if you are pregnant or breast feeding.

4.7 Effects on ability to drive and use machines

None.

4.8 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 MedDRA System Organ Class. Adverse reactions identified during post-marketing use are reported voluntarily from a population of uncertain size, the frequency of these reactions is unknown but likely to be very rare (<1/10,000).

Post marketing data

Paracetamol:

Body System	**Undesirable effect**
Blood and lymphatic system disorders	Thrombocytopenia Agranulocytosis
Immune system disorders	Very rare cases of serious skin reactions have been reported. Anaphylaxis Cutaneous hypersensitivity reactions including (amongst others) skin rashes and angioedema.
Respiratory, thoracic and mediastinal disorders	Bronchospasm– more likely in patients sensitive to aspirin and other NSAIDs
Hepatobiliary disorders	Hepatic dysfunction

Caffeine:

* 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.

Body System	**Undesirable effect**
Central nervous system	Dizziness Headache
Cardiac disorders	Palpitation
Psychiatric disorders	Insomnia Restlessness Anxiety and irritability
Gastrointestinal disorders	Gastrointestinal disturbances

Healthcare professionals are asked to report any suspected adverse reactions via:
Pharmacovigilance and Medical Device Section
Drug Department - U.A.E M.O.H
Hotline: 80011111
Email: pv@mohap.gov.ae
P.O. Box: 1853 Dubai U.A.E.

4.9 Overdose

Liver damage is possible in adults who have taken 10 g or more of paracetamol. Ingestion of 5 g or more of paracetamol may lead to liver damage if the patient has risk factors (see below).

Risk factors

If the patient

a) Is on long term treatment with 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. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms

Symptoms of paracetamol overdosage 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, haemorrhage, hypoglycaemia, cerebral oedema, and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis 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 (earlier concentrations are unreliable). 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. The 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 vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital. Management of patients who present

with serious hepatic dysfunction beyond 24h from ingestion should be discussed with the NPIS or a liver unit.

Caffeine

Symptoms

Overdose of caffeine may result in epigastric pain, vomitting, 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 this product, 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 the overdose, but can be considered for up to four hours after the overdose. The CNS effects of overdose may be treated with 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

ATC code: N02B E51

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

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch
Povidone
Polysorbate-80 (tween-80)
Microcrystalline cellulose (Avicel PH 102)
Sodium starch glycolate
Cross carmellose sodium (Ac-Di-Sol)
Stearic acid fine powder

Cellulose powder
Talc fine powder
Purified water *

* Evaporated during manufacturing process and not appearing in the final product

6.2 Incompatibilities

None.

6.3 Shelf life

36 months from the date of manufacturing.

6.4 Special precautions for storage

Store below 30^{o}C, in the original container

6.5 Nature and contents of container

- 12 Caplets in a blister, 2 blisters packed in a printed carton along with a leaflet.
- 12 Caplets in a blister, 4 blisters packed in a printed carton along with a leaflet.

6.6 Special precautions for disposal and other handling

None.

7. MARKETING AUTHORISATION HOLDER

Gulf Pharmaceutical Industries - Julphar
Digdaga, Airport Street.
Ras Al Khaimah - United Arab Emirates.
P.O. Box 997
Tel. No.: (9717) 2 461 461
Fax No.: (9717) 2 462 462

8. MARKETING AUTHORISATION NUMBER(S)

08519/VAR/2023

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

03. April. 2000

10. DATE OF REVISION OF THE TEXT

14. September. 2022