SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ACAMOL® TEVA Tablets
ACAMOL® TEVA Caplets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet/caplet contains paracetamol 500 mg.

There are no excipients with known effect. For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets, Caplets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Acamol tablet or caplet is a mild analgesic and antipyretic and is recommended for relief of pain and fever of different etiologies such as headache, toothache, colds, influenza, rheumatic pain and dysmenorrhea.

4.2 Posology and method of administration

Posology

Adults and children aged 12 years and over:

1-2 tablets/caplets every 4-6 hours, as needed. Do not exceed a dosage of 8 tablets/ caplets per day. (4 grams a day)

Children aged 9-12 years:

½ -1 tablet/caplet every 4-6 hours, as needed. Do not exceed a dosage of 4 tablets/caplets in a day (2 grams a day).

Children aged 6-9 years:

½ tablet/caplet every 4-6 hours, as needed. Do not exceed a dosage of 3 tablets/ caplets in a day (1.5 grams a day).

Do not give a tablet/caplet to children under 6 years of age.

Do not exceed the recommended dose. Patient should refer to a doctor if the fever persists for more than 3 days or if the symptoms do not pass within 5 days, despite use of the medicine.

Method of Administration

For oral use only.

Intake of paracetamol with food and drink does not affect the efficacy of the medicinal product.

The tablets/caplets can be halved on the score line.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the other excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Prolonged or frequent use is discouraged. Patients should be advised not to take other Paracetamol containing products , including cold and cough medicines concurrently. Taking multiple daily doses in one administration can severely damage the liver; in such case unconsciousness does not occur. However, medical assistance should be sought immediately. Caution is advised if skin side effects have been developed in the past as a result of taking products containing paracetamol, products containing paracetamol should not be used, so that severe skin effects will not recur.

Prolonged use except under medical supervision may be harmful.

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment and sepsis, or in patients with malnutrition or other sources of glutathione deficiency (e.g. chronic alcoholism) who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If HAGMA due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.

Caution is advised in the administration of Paracetamol to patients with moderate and severe renal insufficiency, mild to moderate hepatic insufficiency (including Gilbert's syndrome), severe hepatic insufficiency (child-pugh>9), acute hepatitis, concomitant treatment with medicinal products affecting hepatic functions, glucose-6 phosphatedehydrogenase deficiency, hemolytic anemia, alcohol abuse dehydration and chronic malnutrition (see section 4.2).

The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease. Caution should be exercised in cases of chronic alcoholism. The daily dose should not exceed 2 grams in such case. Alcohol should not be used during the treatment with Paracetamol.
Caution is advised in asthmatic patients sensitive to aspirin because light reaction bronchospasm with paracetamol (cross-reaction) has been reported in less than 5% of the patients tested.
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.
Do not exceed the stated dose.
Patients should be advised to consult their doctor if their headaches become persistent.
Caution should be exercised in patients with glutathione depleted states, as the use of paracetamol may increase the risk of metabolic acidosis (refer also to section 4.9).
In the case of high fever, or signs of secondary infection or persistence of symptoms a doctor should be consulted. Immediate medical advice should be sought in the event of overdosage even if the patient feels well because of the risk of irreversible liver damage (see section 4.9).
If symptoms persist consult your doctor.
Keep out of the sight and reach of children.

This medicine contains less than 23 mg sodium in a tablet/caplet and is therefore considered “sodium-free

The leaflet contains the following wordings:

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

Hepatotoxic substances may increase the possibility of Paracetamol accumulation and overdose. The risk of hepatotoxicity of paracetamol may be increased by drugs which induce liver microsomal enzymes such as **barbiturates, tricyclic antidepressants**, and **alcohol.**

Probenecid causes an almost 2-fold reduction in clearance of Paracetamol by inhibiting its conjugation with glucuronic acid. A reduction of the Paracetamol dose should be considered for concomitant treatment with probenecid.

Salicylamide may prolong the elimination $t_{1/2}$ of 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 may be increased by metoclopramide and domperidone. However, concurrent use need not be avoided.

Concomitant use of Paracetamol (4 g per day for at least 4 days) with **oral anticoagulants** may lead to slight variations of INR values. In this case, increased monitoring of INR values should be done during the duration of the combination and after its discontinuation.

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.

Isoniazid: Reduction of paracetamol clearance, with possible potentiation of its action and/or toxicity, by inhibiting its metabolism in the liver.

Lamotrigine: Decrease in the bioavailability of lamotrigine, with possible reduction of its effect, due to possible induction of its metabolism in the liver.

Interference with laboratory tests: Paracetamol may affect uric acid tests by wolframatop phosphoric acid, and blood sugar tests by glucose-oxydaseperoxydase.

Flucloxacillin: Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis, due to pyroglutamic acidosis especially in patients with risks factors (see section 4.4)

4.6 Fertility, pregnancy and lactation

Pregnancy

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. If clinically needed, paracetamol can be used during pregnancy however, as with any medicine it should be used at the lowest effective dose for the shortest possible time.

Breast-feeding

Following oral administration, Paracetamol is excreted into breast milk in small quantities. To date, no adverse reactions or undesirable effects are known in association with lactation. Therapeutic doses of Paracetamol can be administered during breast-feeding.

4.7 Effects on ability to drive and use machines

Paracetamol has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Events reported from extensive post-marketing experience at therapeutic/labelled dose and considered attributable are tabulated below by system class and frequency.

The frequency using the following convention: very common (> 1/10); common (>1/100 to < 1/10); uncommon (>1/1000 to < 1/100); rare (>1/10000 to < 1/1000); very rare (< 1/10000), including isolated reports; not known: frequency cannot be estimated from the available data. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Frequency	System	Symptoms
Rare >1/10000 - < 1/1000	Blood and lymphatic system disorders	Platelet disorders, stem cell disorders.
	Immune system disorders	Allergies (excluding angioedema).
	Psychiatric disorders	Depression NOS, confusion, hallucinations.
	Nervous system disorders	Tremor NOS, headache NOS.
	Eye disorders	Abnormal vision.
	Cardiac disorders	Oedema.
	Gastrointestinal disorders	Haemorrhage NOS, abdominal pain NOS, diarrhea NOS, nausea, vomiting.
	Hepatobiliary disorders	Hepatic function abnormal, hepatic failure, hepatic necrosis, jaundice.
	Skin and subcutaneous tissue disorders	Pruritus, rash, sweating, purpura, angioedema, urticaria. Very rare cases of serious skin reactions have been reported.

	General disorders and administration site conditions	Dizziness (excluding vertigo), malaise, pyrexia, sedation, drug interaction NOS.
	Injury, poisoning and procedural complications	Overdose and poisoning
Very Rare (< 10 000)	Hepatobiliary disorders	hepatotoxicity
	General disorders and administration site conditions	hypersensitivity reaction (requiring discontinuation of treatment)
	Blood and lymphatic system disorders	Thrombocytopenia, leukopenia, neutropenia hemolytic anemia, agranulocytosis
	Immune system disorders	Anaphylaxis, Cutaneous hypersensitivity reactions including, among others, skin rashes and angioedema. Very rare cases of serious skin reactions have been reported.
	Respiratory, thoracic and Mediastinal disorders	Bronchospasm*
	Metabolism and nutrition disorders	Hypoglycemia
	Renal and urinary disorders	Sterile pyuria (cloudy urine) and renal side effects
Not Known	Metabolism and nutrition disorders	High anion gap metabolic acidosis (HAGMA)

Not known: Some cases of edema of the larynx, anaphylactic shock, anaemia, bronchospasm*, liver alteration and hepatitis, renal alteration (severe renal impairment, nephrite interstitial, haematuria, anuresis), gastrointestinal effects and vertigo have been reported.

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

Description of selected adverse reactions

High anion gap metabolic acidosis

Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4).

Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.

Reporting of Suspected Adverse Reactions

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

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: https://sideeffects.health.gov.il

4.9 Overdose

Paracetamol overdose may cause liver failure which may require liver transplant or lead to death. There is a risk of poisoning, particularly in elderly subjects, in young adolescents, in patients with liver disease, in cases of chronic alcoholism, in patients with chronic malnutrition. Overdosing may be fatal.

Liver damage is possible in adults who have taken 10g or more of paracetamol.

Ingestion of 5g 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 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 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.

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-acetyl cysteine 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-acetyl cysteine, 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 24 h from ingestion should be discussed with the Poison Information Center or a liver unit.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other analgesics and antipyretics.

ATC code: N02B E01

<u>Mechanism of Action</u>

Analgesic – the mechanism of analgesic action has been fully determined. Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the central nervous system (CNS) and to a lesser extent, through a peripheral action by blocking pain-impulse generation.

Antipyretic – paracetamol probably produces antipyresis by acting centrally on the hypothalamic heat-regulation center to produce peripheral vasodilation resulting in

increased blood flow through the skin, sweating and heat loss. The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus.

5.2 Pharmacokinetic properties

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

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

5.3 Preclinical safety data

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acamol Teva Tablet contains: Microcrystalline cellulose, Maize starch, Povidone, Croscarmellose sodium, Talc, Silica colloidal anhydrouse, Magnesium stearate.

Acamol caplet contains: Microcrystalline cellulose, Maize starch, Povidone, Croscarmellose sodium, Talc, Silica colloidal anhydrouse, Magnesium stearate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Store in a dry place, below 25ºC.

6.5 Nature and contents of container

blister foil packs or a plastic bottle.

Acamol Teva Tablet: A round white tablet with a score line on one side.

Available in a blister (tray) pack of 10, 20, 30, 60 tablets.

Not all package sizes may be marketed.

Acamol Teva Caplet: An oblong white tablet (caplet) with a score line on both sides.

Available in a blister pack of 10, 20, 30, 40, 50, 60, 70 caplets

Or in a plastic bottle pack of 50, 16 caplets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Teva Israel Ltd.,
124 Dvora Hanevi'a St. Tel-Aviv, Israel

8. MARKETING AUTHORISATION NUMBER(S)

Tablets: **176-60-36645-99**
Caplets: **176-61-37219-99**

9. DATE OF REVISION OF THE TEXT

September 2025