1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

ANDOL 500 mg, Effervescent Tablet.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient

Paracetamol	500,00 mg

Excipients

Anhydrous citric acid	1299,00 mg
Sodium Bicarbonate	830,00 mg
Sodium carbonate anhydrous	220,00 mg
Povidone K 29-30	40,00 mg
Macrogol 6000	40,00 mg
Lemon flavor 84260-51	35,00 mg
Sodium saccharin	20,00 mg
Aspartame	15,00 mg
Magnesium Stearate	1,00 mg

For one effervescent tablet

Excipients with known effects: Sodium, aspartame

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Effervescent Tablet.

White, round, flat effervescent tablets with chamfer.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Symptomatic treatment of mild to moderate pain and/or fever.

This presentation is reserved for use only in adults and children of 27 kg and above (aged about 8 years and above).

4.2. Posology and method of administration

Posology

Pediatric Patients:

It is imperative to respect the dosages defined according to the weight of the child and thus to choose an adapted presentation. The approximate ages based on weight are given for information.

The recommended daily dose of paracetamol is approximately 60 mg/kg/day, divided into 4 or 6 doses, i.e. approximately 15 mg/kg every 6 hours or 10 mg/kg every 4 hours, ie:

- Children of 27 to 40 kg (approximately 8 to 13 years): 1 tablet of 500 mg per dose, to be renewed if necessary after 6 hours without exceeding 4 tablets per day;
- Children of 41 to 50 kg (approximately 12 to 15 years): 1 tablet of 500 mg per dose, to be renewed if necessary after 4 hours, without exceeding 6 effervescent tablets per day.

Adults and children weighing more than 50 kg (aged 16 years and older):

The usual single dose is 1 to 2 tablets at 500 mg, to be renewed if necessary after a minimum of 4 hours.
It is generally not necessary to exceed 3 g of paracetamol per day, i.e. 6 tablets per day.
However, in case of more intense pain, the maximum dosage can be increased up to 4 g per day, i.e. 8 tablets per day.
Always respect a 4 hour interval between doses.

Maximum recommended doses: (see part 4.4)

Frequency of administration:

Systematic administration enables to avoid pain or fever oscillation.

In children, they should be regularly spaced, including at night, preferably 6 hours, and at least 4 hours.

In adults, they must be spaced at least 4 hours apart.

Renal Insufficiency:

In patients with severe renal impairment (creatinine clearance less than 10 ml / min), the interval between two doses should be increased to a minimum of 8 hours. The total dose of paracetamol should not exceed 3 g per day, i.e. 6 tablets.

- The lowest possible daily effective dose should be considered, without exceeding 60 mg/kg/day (without exceeding 3g/day) in the following situations:adults weighing less than 50 kg
- mild to moderate hepatocellular insufficiency
- chronic alcoholism
- dehydration
- Glutathione deplete such as, for example, chronic malnutrition, young recent weight loss, subject aged over 75 or over 65 and polypathological, chronic viral hepatitis HIV, cystic fibrosis, familial cholemia (Gilbert's disease)

Method of administration

Oral use.

Dissolve completely the tablet in a glass of water.

The intake of tablet or capsule is contraindicated in children under 6 years of age, as it can lead to aspiration. Use a different dosage form.

4.3. Contraindications

- Hypersensitivity to the active ingredient or to any of the excipients listed in section 2,
- Severe hepatocellular insufficiency,
- Children under 6 years of age, as it can lead to aspiration,
- In case of phenylketonuria, due to the presence of aspartame,

4.4. Special warnings and precautions for use

Special warnings

To avoid the risk of overdose,

- Verify the absence of paracetamol in the composition of other medicines.
- Respect the maximum recommended doses.

Recommended maximum doses:

- *Children under 40 kg:* the total dose of paracetamol should not exceed 80 mg/kg/day (see part 4.9).
- *Children between 41 kg and 50 kg:* the total dose of paracetamol should not exceed 3g/day (see part 4.9).
- *Adults and children over 50 kg*: the total dose of paracetamol should not exceed 4g/day (see part 4.9).

Precautions for use

Administration of paracetamol may exceptionally lead to hepatic toxicity, even at therapeutic doses after short-term treatment and in patients without a history of hepatic disorders (see section 4.8).

- Paracetamol should be used with caution without exceeding 3g/day in the following situations (see section 4.2):
  - Weight <50 kg;
  - Mild to moderate hepatocellular insufficiency;
  - Severe renal insufficiency (creatinine clearance ≤ 30 ml / min): (see section 4.2);
  - Chronic alcoholism;

- Dehydration.
- Glutathione deplete such as, for example,chronic malnutrition , young recent weight loss, subject aged over 75 or over 65 and polypathological, chronic viral hepatitis and HIV, cystic fibrosis, familial cholemia (Gilbert's disease)
- Allergy to aspirin and/or non-steroidal anti-inflammatory drugs (NSAIDs)Consumption of alcoholic beverages during treatment is not recommended.

In case of recent withdrawal from chronic alcoholism, the risk of liver damage is increased.
If acute viral hepatitis is detected, treatment should be discontinued.
For children, the dosage should be adjusted according to body weight (see section 4.2).
For a child treated with 60mg/kg/day of paracetamol, the combination of another antipyretic is only justified in case of ineffectiveness.
This medicine contains sodium. To be taken into account in patients under strict low-sodium diet.

4.5. Interaction with other medicinal products and other forms of interaction

Combinations requiring precautions for use

Oral anticoagulants: warfarin and other antivitamin K (AVK)

Risk of increased effect of warfarin and other AVK and hemorrhagic risk if paracetamol is taken at maximum doses (4g/d) for at least 4 days. Biological control including more frequent control of INR. Possible dose adjustment of warfarin and other AVK during treatment with paracetamol and after its discontinuation.

+ Chelating resins

Taking chelating resin may decrease intestinal absorption, and potentially the effectiveness of paracetamol taken simultaneously. In general, the resin setting should be done at a distance from that of paracetamol, respecting an interval of more than 2 hours, if possible.

+ Flucloxacillin

Risk of metabolic acidosis in patients receiving concomitant treatment with flucloxacillin, especially in patients with a risk factor for glutathione deficiency, such as sepsis, malnutrition, chronic alcoholism.

+ Hepatotoxic drugs

The toxicity of paracetamol may be increased in patients treated with potentially hepatotoxic drugs or drugs that induce cytochrome P450 enzymes, such as anti-epileptic drugs (such as phenobarbital, phenytoin, carbamazepine, topiramate), rifampicin or in case of concomitant intake of alcohol. Induction of metabolism results in significant production of the hepatotoxic metabolite of paracetamol. Hepatotoxicity occurs if the amount of this metabolite exceeds the glutathione binding capacities.

Paraclinical examinations

Taking paracetamol can falsify the determination of blood glucose by the glucose oxidase-peroxidase method in the event of abnormally high concentrations.

Taking paracetamol can interfere with the dosage of uric acid in the blood by the phosphotungstic acid method.

4.6. Fertility, pregnancy and lactation

Pregnancy

Studies carried out in animals have shown no evidence of teratogenic or foetotoxic paracetamol effects.
Clinically, epidemiological studies on a large number of pregnancies have not revealed any malformative or fetotoxic effect relating to the use of paracetamol at the usual dosages.

Therefore, if clinically needed, paracetamol can be used during pregnancy. However, it should be used at the lowest effective dose for the shortest time and at the lowest possible frequency .

Lactation

At therapeutic doses, the administration of this drug is possible during lactation.

Fertility

Due to the potential mechanism of action on cyclooxygenase and prostaglandin synthesis, paracetamol may impair fertility in women, by reversing ovulation on discontinuation of treatment.
Effects on male fertility have been observed in an animal study. The relevance of these effects in humans is not known.

4.7. Effects on ability to drive and use machines

Not applicable.

4.8. Undesirable effects

Immune system disorders

Rare: hypersensitivity reactions such as anaphylactic shock, angioedema. Their occurrence requires the permanent discontinuation of this drug and related medicines.

Skin and subcutaneous tissue disorders

Rare: erythema, urticaria, skin rash have been reported. Their occurrence requires the permanent discontinuation of this drug and related medicines.
Very rare cases of serious skin side effects have been reported.
Not known: fixed pigmented erythema.

Blood and lymphatic system disorders

Very exceptional: thrombocytopenia, leukopenia and neutropenia.
Not known: agranulocytosis, haemolytic anemia in patients with glucose-6-phosphate-dehydrogenase deficiency.

Hepatobiliary disorders

Not known: increased transaminases, cytolytic liver damage, acute hepatitis, massive hepatitis, particularly when used in a risk situation (see section 4.4).

Cardiac disorders

Frequency not known: Kounis syndrome.

Respiratory, thoracic and mediastinal disorders

Not known: bronchospasm (see section 4.4).

Reporting of suspected adverse reactions

The reporting of suspected undesirable effects after authorization of the drug is important. It allows continuous monitoring of the benefit / risk ratio of drugs.

4.9. Overdose

The risk of severe intoxication may be particularly high in elderly patients, in young children (therapeutic overdose or frequent accidental poisoning), in patients with hepatic impairment, in case of chronic alcoholism, in patients with low glutathione reserves such as chronic malnutrition (see section 4.2), fasting, recent weight loss, aging, chronic viral hepatitis and HIV, cholemia familial (Gilbert's disease). In these cases, intoxication can be fatal.

Symptoms

Nausea, vomiting, anorexia, pallor and abdominal pain usually appear within the first 24 hours.
Overdosage of paracetamol may cause hepatic cytolysis which may lead to hepatocellular insufficiency, gastrointestinal bleeding, metabolic acidosis, encephalopathy, coma and death.
In the event of acute overdose, an increase in hepatic transaminases, lactic dehydrogenase, bilirubin, and decreased prothrombin levels may occur 12 to 48 hours.

Overdose can also lead to pancreatitis, hyperamylasemia, acute renal failure and pancytopenia.

Emergency management

- Immediate transfer to hospital.
- Take a tube of blood to make the initial plasma dosage of paracetamol. This dosage will be interpreted according to the deadline between the supposed time of the intake and the time of sampling.

- Quick evacuation of the ingested product by gastric lavage. In case of oral use.
- Treatment of overdose typically involves administration as early as possible of the intravenous N-acetylcysteine antidote or orally, if possible before the tenth hour.
- Symptomatic treatment.

5. Pharmacological properties

5.1. Pharmacodynamic properties

***Pharmacotherapeutic group: Other analgesics and antipyretics-anilides*: ATC code: N02BE01 (N: central nervous system).**

Mechanism of action

Paracetamol has a central and peripheral mechanism of action.

5.2. Pharmacokinetic properties

Absorption

The absorption of paracetamol by the oral route is rapid and complete. Maximum plasma concentrations are reached 30 to 60 minutes following ingestion.

Distribution

Paracetamol is distributed rapidly throughout all tissues. Concentrations are comparable in blood, saliva and plasma. Protein binding is low.

Metabolism

Paracetamol is metabolized mainly in the liver following two major metabolic pathways: glucuronic acid and sulphuric acid conjugates. The latter route is rapidly saturated at doses higher than the therapeutic dose. A minor route, catalyzed by the cytochrome P450, results in the formation of an intermediate reagent (N-acetyl-p-benzoquinoneimine) which under normal conditions of use is rapidly detoxified by reduced glutathione and eliminated in the urine, after conjugation with cystein and mercaptopuric acid. Conversely, when massive intoxication occurs, the quantity of this toxic metabolite is increased.

Elimination

Elimination is essentially through the urine. 90% of the ingested dose is eliminated via the kidneys within 24 hours, principally as glucuronide (60 to 80%) and sulphate conjugates (20 to 30%). Less than 5% is eliminated in unchanged form.
Elimination half-life is about 2 hours.

Physiopathological variations

Renal insufficiency: In cases of severe renal insufficiency (creatinine clearance lower than 30 ml/min) the elimination of paracetamol and its metabolites is delayed.
Elderly: The capacity for conjugation is not modified.

5.3. Preclinical safety data

Not applicable.

6. Pharmaceutical particulars

6.1. List of excipients

Anhydrous citric acid
Sodium bicarbonate
Anhydrous sodium carbonate
Povidone K 29-32
Macrogol 6000
Lemon flavor 84260-51
Saccharin sodium
Aspartam
Magnesium stearate

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

36 months.

6.4. Special precautions for storage

Keep away from moisture and heat.

6.5. Nature and contents of container

ANDOL 500mg effervescent tablets is packaged in a polypropylene tube, box of 8.

6.6. Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with current requirements..

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES

- **Marketing Authorization Holder:**

COOPER PHARMA
41, Rue Mohamed DIOURI, 20110
Casablanca - Morocco

- **Manufacturing, control, packaging & batches release sites:**
  - Manufacturing, Control & Packaging site:

MC PHARMA
Z.I. Oulad Salah – préfecture de Nouaceur
Casablanca – Morocco

  - Batches Release site:

COOPER PHARMA
Route 107, Km 2,5 Douar Oulad Sidi Abbou, Tit Melil
Casablanca - Morocco

8. MARKETING AUTHORISATION NUMBER(S)

20/4361/DGC&PHS/2018.

9. DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION

Date of first authorization: 06 June 2018.
Date of last renewal: Not applicable

10. DATE OF REVISION OF THE TEXT

Octobre 2020.

PRESCRIPTION AND DELIVERY CONDITIONS

Medicinal product not subject to medical prescription