1. NAME OF THE MEDICINAL PRODUCT

ANDOL 1000 mg, Effervescent tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient

PARACETAMOL ..... 1000,00 mg

Excipients

Anhydrous citric acid .....1210 mg
Sodium Bicarbonate .....830 mg
Sorbitol .....334 mg
Sodium carbonate anhydrous.....260 mg
Povidone K29-32.....80 mg
Macrogol 6000.....65 mg
Orange Flavour 74016-71 .....50 mg
Apricot Flavour 75731-31 .....20 mg
Sodium Saccharin .....20 mg
Aspartam.....15 mg
Beta-carotene 1%.....15 mg
Magnesium Stearate .....1 mg

For one effervescent table

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Effervescent Tablet.

Yellowish, speckled with orange, round, flat, effervescent tablets with chamfer.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

This presentation is reserved for adults and children from 50 kg (about 15 years).

4.2 Posology and method of administration

Posology

Caution: This presentation contains 1000 mg of paracetamol per unit; do not take 2 units at a time.

The usual unit dosage is half to one tablet at 1000 mg per dose, to be renewed after 6 to 8 hours. If necessary, the intake can be repeated after a minimum of 4 hours.

It is generally not necessary to exceed 3 g of paracetamol per day, i.e. 3 tablets.

However, in case of intense pain, the maximum posology can be increased up to 4 g, i.e. 4 tablets per day.

Always respect a 4 hour interval between doses.

Maximum recommended doses:

(See part Special warnings and precautions for use)

Frequency of administration:

Systematic intakes avoid pain or fever oscillations:

- For children and adolescents, they must be regularly spaced, including at night, preferably 6 hours, and at least 4 hours;
- For adults, they must be spaced at least 4 hours apart.

Renal failure:

In case of severe renal insufficiency (creatinine clearance less than 10 ml/min): the interval between two doses should be at least 8 hours.

Do not exceed 3 g of paracetamol per day, i.e. 3 effervescent tablets.

Other clinical situations:

The lowest effective daily dose should be considered, without exceeding 60 mg/kg/day (i.e.3g/day) in the following situations:

- Weight < 50 kg
- mild to moderate hepatocellular insufficiency
- chronic alcoholism
- dehydration
- low glutathione reserves such as, for example, chronic malnutrition, fasting, recent weight loss, subject aged over 75 or over 65 and polypathological, chronic viral hepatitis and HIV, cystic fibrosis, familial cholemia (Gilbert's disease).

Method of administration

Oral use.

Completely dissolve the tablet in a glass of water. Drink immediately.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section "Composition".
- Severe hepatocellular insufficiency.
- Child under 6 years old due to the risk of going the wrong way.
- Due to the presence of aspartame, this drug is contraindicated in case of phenylketonuria.

4.4 Special warnings and precautions for use

Special warnings

Due to the unit dose per effervescent tablet (1000 mg), this presentation is not suitable for children under 15 years of age.

To avoid the risk of overdose,

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

Maximum recommended dose

For information:

For children under 40 kg, the total dose of paracetamol should not exceed 80 mg/kg/day (see Overdose).

For children weighing 41 to 50 kg, the total dose of paracetamol should not exceed 3 g per day (see Overdose).

For adults and children over 50 kg, THE TOTAL DOSE OF PARACETAMOL MUST NOT EXCEED 4 GRAMS PER DAY (see Overdose).

Precautions for use

The administration of paracetamol can exceptionally lead to liver toxicity, even at therapeutic doses, after short-term treatment and in patients with no history of liver problems (see Undesirable effects).

Paracetamol should be used with caution without exceeding 3 g/day in the following situations (see Dosage and method of administration):

- Weight <50 kg;
- Mild to moderate hepatocellular insufficiency;
- Severe renal insufficiency (creatinine clearance ≤ 30 ml / min): (see part Pharmacokinetic properties);
- Chronic alcoholism;
- Dehydration;
- low glutathione reserves such as, for example, chronic malnutrition, fasting, 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 weight (see Dosage and method of administration).

For a child treated with 60 mg/kg/day of paracetamol, the combination of another antipyretic is only justified in the event of ineffectiveness.

This medicine contains sodium. To be taken into account in patients under strict low-sodium diet.

This medicine contains sorbitol. Its use is not recommended in patients with fructose intolerance (rare hereditary disease).

4.5 Interaction with other medicinal products and other forms of interaction

Combinations subject to 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/day) for at least 4 days. Biological control including more frequent control of the INR. Possible adjustment of the dosage 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.

Interaction with 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 Pregnancy, Breastfeeding and Fertility

Pregnancy

Studies in animals have shown no evidence of teratogenic or foetotoxic paracetamol effects.

Clinically, the results of epidemiological studies seem to exclude a particular malformative or fetotoxic effect of paracetamol at the usual dosages.

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

Breastfeeding

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 like anaphylactic shock, angioedema. Their occurrence requires the permanent discontinuation of this drug and related drugs.

Skin and subcutaneous tissue disorders

Rare: erythema, urticaria, skin rash have been reported. Their occurrence requires the permanent discontinuation of this drug and related drugs.

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 Special warnings and precautions for use).

Cardiac disorders

Frequency not known: Kounis syndrome.

Respiratory, thoracic and mediastinal disorders

Not known: bronchospasm (see section Special warnings and precautions for use).

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 Posology and method of administration), fasting, recent weight loss, aging, chronic viral hepatitis and HIV viruses, 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.

Overdose of paracetamol may cause hepatic cytolysis which may lead to hepatocellular failure, gastrointestinal bleeding, metabolic acidosis, encephalopathy, coma and death.

In the event of acute overdose, an increase in hepatic transaminases, lactic dehydrogenase, bilirubin and a decrease in prothrombin levels may be observed within 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 taking and the time of sampling.
- Quick evacuation of the ingested product by gastric lavage.
- Treatment of overdose typically involves administration as early as possible of the N-acetylcysteine antidote intravenously 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 10 ml/min) the elimination of paracetamol and its metabolites is delayed.
- Elderly Subjects: 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
Sorbitol	Anhydrous sodium carbonate
Povidone K 29-32	Macrogol 6000
Lemon flavor 74016-71	Apricot flavour 75731-31
Sodium Saccharin	Aspartam
Beta-carotene 1%	Magnesium stearate

Excipients with notorious effect: Sodium, Sorbitol, Aspartam.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Keep tightly closed away from humidity and heat.

6.5 Nature and contents of container

ANDOL1000mg Effervescent tablets are packaged in a polypropylene tube, box of 8.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADRESS

- Marketing Authorization holder:

COOPER PHARMA
41, Rue Mohamed DIOURI, 20110 Casablanca
Morocco

- Manufacturing, Control & Packaging site:

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

- Batch Release site:

COOPER PHARMA
Route 107, Km 2.5 Douar Oulad Sidi Abbou
Tit Mellil Casablanca
Morocco

8. MARKETING AUTHORISATION NUMBER

20/4362/DGC&PHS/2018.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 06 June 2018.

10. DATE OF REVISION OF THE TEXT

October 2020.

PRESCRIPTION AND DELIVERY CONDITIONS

Medicinal product not subject to medical prescription.