

1.3 Product Information

1.3.1 Summary of Product Characteristics (SmPC) - Enclosed

Summary of Product Characteristics (SPC)

1. NAME OF THE MEDICINAL PRODUCT

ZANITIN DUO 1000 (Co-Amoxiclav Tablets BP)

1.1 (INVENTED) NAME OF THE MEDICINAL PRODUCT

ZANITIN DUO 1000 (Co-Amoxiclav Tablets BP)

1.2 STRENGTH

Strength per tablet:

Each film coated tablet contains:

Amoxicillin Trihydrate BP

Equivalent to Amoxicillin 875 mg

Diluted Potassium Clavulanate BP

Equivalent to Clavulanic Acid125 mg

1.3 PHARMACEUTICAL FORM

Tablets (Oral)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Chemical Name	Approved Name (if any)	Quantity per tab in mg	Active / Non- active
Part (A) Granulation:			
(2S,5R,6R)-6-[[[(2R)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid	* Amoxicillin Trihydrate (Compacted) BP	875 (1014.37)	Active
4-oxa-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 3-(2-hydroxyethylidene)-7-oxo-, monopotassium salt, [2R-(2 α , 3Z, 5 α)]Potassium(2R,3Z,5R)-3-(2-hydroxyethylidene)-7-oxo-4-oxa-1-azabicyclo[3.2.0]heptane-2-carboxylate.	*Potassium Clavulanate Diluted (Syloid 1:1) BP	125 (300.730)	Active
1-Ethenyl-2-pyrrolidinone homopolymer	Crospovidone BP	40.000	Non- Active Ingredient
Cellulose	Microcrystalline Cellulose PH-112 BP	34.000	Non- Active Ingredient
Silica	Silicon Dioxide BP	10.000	Non- Active Ingredient
Part (B) Lubrication:			
Silica	Colloidal Silicon Dioxide BP	5.000	Non- Active Ingredient
Octadecanoic acid magnesium salt	Magnesium stearate BP	6.9022	Non- Active Ingredient
Part (B) Blending:			
Silica	Colloidal Silicon Dioxide BP	15.000	Non- Active Ingredient
Octadecanoic acid magnesium salt	Magnesium stearate BP	5.000	Non- Active Ingredient
Cellulose	Microcrystalline Cellulose BP	17.302	Non- Active Ingredient
Cellulose	**Microcrystalline Cellulose PH-112 BP	15.000	Non- Active Ingredient
Part (B) Lubricants:			
Talc	Purified Talc BP	1.000	Non- Active Ingredient

Silica	Colloidal silicon dioxide BP	5.000	Non- Active Ingredient
Octadecanoic acid magnesium salt	Magnesium Stearate BP	10.7022	Non- Active Ingredient
Total		1465.00 mg	
Cellulose	Hydroxy Propyl Methyl Cellulose (Any coat-C AN-6) BP	2.000	Non- Active Ingredient
Cellulose	Hydroxy Propyl Methyl Cellulose (Any coat-C AN-15) BP	15.000	Non- Active Ingredient
Cellulose	Ethyl cellulose N-20 BP	1.000	Non- Active Ingredient
Talc	Purified talc BP	1.000	Non- Active Ingredient
---	Titanium dioxide BP	9.000	Non- Active Ingredient
benzenedicarboxylic acid	Dibutyl Phthalate BP	2.000	Non- Active Ingredient
---	Methylene Dichloride BP	460.000	Non- Active Ingredient
---	Iso Propyl Alcohol BP	140.000	Non- Active Ingredient
---	#Purified talc BP	1.000	Non- Active Ingredient
Total		1495.00 mg	

* 1 % Overages added for Amoxicillin Trihydrate and Potassium Clavulanate.

**Quantity of Amoxicillin Trihydrate and Potassium Clavulanate will be compensated with Microcrystalline Cellulose PH-112.

Does not appear in final product

Definition:

BP = British Pharmacopoeia

3. PHARMACEUTICAL FORM

Tablets (Oral)

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Lower Respiratory Tract Infections: Caused by beta lactamase-producing isolates of Haemophilus influenzae and Moraxella catarrhalis.

Acute Bacterial Otitis Media: Caused by beta lactamase-producing isolates of H. influenzae and M. catarrhalis.

Sinusitis: Caused by beta lactamase-producing isolates of H. influenzae and M. catarrhalis.

Skin and Skin Structure Infections: Caused by beta lactamase-producing isolates of Staphylococcus aureus, Escherichia coli, and Klebsiella species.

Urinary Tract Infections: Caused by beta lactamase-producing isolates of E. coli, Klebsiella species, and Enterobacter species.

4.2 Posology and method of administration

Adults: The usual adult dose is one ZANITIN DUO 562.5 tablet every 12 hours.

For more severe infections, the dose should be one ZANITIN DUO 1000 tablet every 12 hours. Treatment should usually be continued for 48 to 72 hours beyond the time that the patient becomes asymptomatic or evidence of bacterial eradication has been obtained. Treatment should not exceed 14 days without review by medical practitioner. Adults with Impaired Renal Function:

ZANITIN DUO 1000 tablets should not be used in patients with moderate to severe renal impairment (creatinine clearance 30mL/min). Both amoxicillin and clavulanic acid are excreted by the kidneys and the serum half life of each increases in patients with renal failure. *No adjustment to the initial ZANITIN DUO dose is necessary, but the dosing interval should be extended according to the degree of renal impairment. The following schedule is proposed for ZANITIN DUO 562.5:

Mild Impairment: No change in dosage. (Creatinine clearance > 30ml/min).

Moderate Impairment: One ZANITIN DUO 562.5 tablet 12 hourly (Creatinine clearance 10 - 30mL/min).

Severe Impairment: One ZANITIN DUO 562.5 tablet every 24 hours (Creatinine clearance < 10mL/min).

Haemodialysis decreases serum concentrations of both amoxicillin and clavulanic acid and an additional dose should be administered at the end of dialysis.

Adults with Impaired Hepatic Function: Data is currently insufficient for a dosage recommendation. Dose with caution, and monitor hepatic function at regular intervals.

Children: Children weighing 40Kg and more should be dosed according to the adult recommendations.

Method of administration: Oral use.

4.3 Contraindications

ZANITIN DUO is contraindicated in patients with a history of allergic reactions to any penicillin. It is also contraindicated in patients with a previous history of cholestatic jaundice/hepatic dysfunction associated with ZANITIN DUO.

4.4 Special warnings and precautions for use

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe reactions when treated with cephalosporins. Before initiating therapy with ZANITIN DUO, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens. If an allergic reaction occurs, ZANITIN DUO should be discontinued and the appropriate therapy instituted.

General: History of allergy especially to penicillin's & cephalosporins. Infectious mononucleosis. Severe renal impairment.

Pregnancy & Nursing mothers: This drug should be used during pregnancy only if clearly needed under the supervision of a medical practitioner. Ampicillin-class antibiotics are excreted in the milk; therefore, caution should be exercised when ZANITIN DUO is administered to a nursing woman.

4.5 Interaction with other medicinal products and other forms of interaction

Allopurinol may reduce renal tubular secretion of amoxicillin thus increasing the serum levels of amoxicillin. Concurrent use may reduce the efficacy of oral contraceptives.

4.6 Pregnancy and lactation

Use in Pregnancy: (Category B1). Animal studies with orally and parenterally administered ZANITIN DUO have shown no teratogenic effects. There is limited experience of the use of ZANITIN DUO in human pregnancy. In women with preterm, premature rupture of the foetal membrane (pPROM), prophylactic treatment with ZANITIN DUO may be associated with an increased risk of necrotising enterocolitis in neonates. As with all medicines, use should be avoided in pregnancy, especially during the first trimester, unless considered essential by the physician. **Use in Labor and Delivery:** Oral ampicillin class antibiotics are generally poorly absorbed during labour. Studies in guinea pigs have shown that intravenous administration of ampicillin decreased the uterine tone, frequency of contractions, height of contractions and duration of contractions. However, it is not known whether the use of ZANITIN DUO in humans during labour or delivery has immediate or delayed adverse effects on the foetus, prolongs the duration of labour or increases the likelihood that forceps delivery or other obstetrical intervention or resuscitation of the newborn will be necessary.

Use in Lactation: Amoxycillin is excreted in the milk; there are no data on the excretion of clavulanic acid in human milk. Therefore, caution should be exercised when ZANITIN DUO are administered to a nursing woman.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions), which may influence the ability to drive and use machines.

4.8 Undesirable effects

The most frequently reported adverse effects were diarrhea/loose stools, nausea, skin rashes and urticaria, vomiting and vaginitis. Other less frequently reported reactions include: Abdominal discomfort, flatulence, and headache.

4.9 Symptoms of Overdosage & Treatment

Following overdosage, patients have experienced primarily gastrointestinal symptoms including stomach and abdominal pain, vomiting, and diarrhea. Rash, hyperactivity or drowsiness have also been observed in a small number of patients. Treatment is supportive and symptomatic and as directed by the physician.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: ZANITIN DUO is an oral anti-bacterial combination consisting of the semisynthetic antibiotic amoxicillin and β -lactamase inhibitor clavulanate potassium (the potassium salt of clavulanic acid) which is a β -lactam structurally related to the penicillins.

ATC code: J01CR02.

Mechanism of action

Amoxicillin is a semi-synthetic antibiotic with a broad spectrum of bactericidal activity against many gram-positive and gram-negative microorganisms. Amoxicillin inhibits cell wall synthesis leading to lysis of the bacterial cell.

Amoxicillin is, however, susceptible to degradation by β -lactamases, and therefore, the spectrum of activity does not include organisms which produce these enzymes. Clavulanic acid is a β -lactamase inhibitor which possesses the ability to inactivate a wide range of β -lactamase enzymes commonly found in microorganisms resistant to penicillin and cephalosporins. In particular, it has good activity against clinically important plasmid-mediated β -lactamases frequently responsible for drug resistance. The formulation of Amoxicillin and Clavulanic acid in ZANITIN DUO effectively extends the antibiotic spectrum of amoxicillin to include many bacteria normally resistant to Amoxicillin and other β -lactam antibiotics.

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5.2 Pharmacokinetic properties

Absorption: ZANITIN DUO 562.5 tablets are stable in the presence of gastric acid. Their two components are rapidly absorbed if administered before or with a meal, but if given after meals, the serum levels of Clavulanic acid are significantly reduced. To optimise absorption of Clavulanic acid, ZANITIN DUO 562.5 tablets should be administered at the start of a meal. The pharmacokinetics of amoxicillin is not affected by food. The following mean pharmacokinetic parameters were observed for amoxicillin for ZANITIN DUO 562.5 taken every 12 hours: peak plasma concentration (C_{max}) of 11.64 $\mu\text{g/mL}$, area under the plasma concentration-time curve between 0 and 24 hours after the first dose (AUC 0-24 hours) of 53.52 $\mu\text{g.h/mL}$, half life ($t_{1/2}$) of 1.19 hours, time to peak plasma concentration (T_{max}) of 1.50 hours and the time above the minimum inhibitory concentration (TMIC 24 hours) of 10.46 hours. The following pharmacokinetic parameters were observed for Clavulanic acid for ZANITIN DUO 1000 tablets taken every 12 hours: C_{max} of 2.18 $\mu\text{g/mL}$, AUC (0-24 hours) of 10.16 $\mu\text{g.h/mL}$, $t_{1/2}$ of 0.96 hours and T_{max} of 1.25 hours, and (TMIC 24 hours) of 6.08 hours.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of safety pharmacology, genotoxicity and toxicity to reproduction.

Repeat dose toxicity studies performed in dogs with amoxicillin/clavulanic acid demonstrate gastric irritancy and vomiting, and discoloured tongue.

Carcinogenicity studies have not been conducted with amoxicillin/clavulanic acid.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Crospovidone	BP
Microcrystalline Cellulose PH-112	BP
Silicon Dioxide	BP
Colloidal Silicon Dioxide	BP
Magnesium stearate	BP
Microcrystalline Cellulose	BP
Purified Talc	BP
Hydroxy Propyl Methyl Cellulose (Any coat-C AN-6)	BP
Hydroxy Propyl Methyl Cellulose (Any coat-C AN-15)	BP
Ethyl cellulose N-20	BP
Titanium dioxide	BP
Dibutyl Phthalate	BP
Methylene Dichloride	BP
Iso Propyl Alcohol	BP

6.2 Incompatibilities

None

6.3 Shelf life

24 months (2 Years)

6.4 Special precautions for storage

Keep below 25°C. Protect from sunlight and moisture. Keep out of reach of children.

6.5 Nature and contents of container

10 Tablets Alu-Alu blister. 1 such blister is packed in Printed carton with pack insert.

6.6 Special precautions for disposal and other handling

No special requirement

7. MARKETING AUTHORISATION HOLDER

Shalina Healthcare DMCC

30th Floor, Almas Towers,

Jumeirah Lakes Towers Dubai-UAE.

Telephone: +971 4 4309111

Telefax: +971 4 4309112

Website: www.shalina.com

8. MANUFACTURER

Manufacturing Site Address:

M/s Medicef Pharma, Plot No. 28, 29 & 48, Phase-I, EPIP, Jharmajri, Baddi, Distt. Solan (H.P.)

9. DATE OF REVISION OF TEXT

Every two years.

10. LEGAL CATERGORY

Prescription Only