DUOCLAV®

THE MOST COMMONLY USED ANTIBIOTIC IN EMPIRICAL TREATMENT

Packaging:
DUOCLAV®
film-coated tablets (500+125) mg x 15
(authorization no.: XX-XXX-XXXX/XX)
film-coated tablets (875+125) mg x 10
(authorization no.: XX-XXX-XXXX/XX)
oral suspension (400+57) mg/5 ml x 70 ml
(authorization no.: XX-XXX-X-XXXX/XX)

Prescription Only Medicine
Bosnalijek d.d., Jukićeva 53, Sarajevo, B&H

APPROVED INDICATIONS: Treatment of the following infections in adults and children: acute bacterial sinusitis (adequately diagnosed), acute otitis media, acute exacerbations of chronic bronchitis (adequately diagnosed), community-acquired pneumonia, cystitis, pyelonephritis, infections of the skin and subcutaneous tissue particularly cellulitis, animal bites, severe dental abscesses with accompanying cellulitis and bone and joint infections, particularly osteomyelitis. **CONTRAINDICATIONS:** Hypersensitivity to active substances, any of the penicillins or any of the drug excipients. A history of severe hypersensitivity reaction (e.g. anaphylaxis) caused by the use of beta-lactam antibiotics (e.g. cephalosporin, carbapenem or monobactam). Jaundice or other hepatic impairments caused by the use of amoxicillin and clavulanic acid combination. **SPECIAL WARNINGS AND PRECAUTIONS FOR USE:** Special caution is necessary in patients allergic to penicillins, cephalosporins or other beta-lactam antibiotics. Convulsions can occur in patients with impaired renal function or in those receiving high doses. During prolonged treatment periodical evaluation of the renal, hepatic and hematopoietic function is recommended. The drug should be avoided if infectious mononucleosis is suspected. The use of allopurinol increases the incidence of allergic reactions on the skin. A long-term use may result in development of superinfections caused by resitant microorganisms. If at the beginning of treatment symptoms of acute generalized exanthematous pustulosis occur, the therapy should be discontinued, and any next administration of amoxicillin is contraindicated. The use of the drug during pregnancy should be avoided if not strictly recommended by a doctor and during lactation the drug is used only if the doctor determines that the potential benefit for the mother exceeds the potential risk for the fetus. **ADVERSE EFFECTS:** Mucocutaneous candidiasis, diarrhea, nausea and vomiting. **DOSAGE AND METHOD OF ADMINISTRATION:** When determining the dose, take into consideration the expected causative agents, their sensitivity to antibacterial drugs, infection site, age, patient's weight and renal function. The recommended dosage in adults and children with weight ≥40 kg is (for all indications): 1 film-coated tablet (500 mg/125 mg) 3 times a day or 1 film-coated tablet (875 mg/125 mg) twice a day. For severe infections (especially for infections such as otitis media, sinusitis, lower respiratory system infections and urinary system infections) higher doses are recommended: 875 mg/125 mg three times a day. Film-coated tablets or suspension can be used in children. In children with body weight < 40 kg, 20 mg/5mg/kg/day up to 60mg/15mg/kg/day is administered divided in three doses. The recommended doses: 25mg/3.6mg/kg a day up to 45 mg/6.4 mg/kg a day administered in two divided doses and up to 70 mg/10mg/kg a day administered in two divided doses can be recommended for the treatment of some infections (such as otitis media, sinusitis and infections of the lower respiratory system). If it is determined that a higher amoxicillin dose is necessary, the administration of another form of the drug is necessary in order to avoid the use of unnecessary high daily doses of clavulanic acid. The length of the treatment depends on the patient's reaction to the drug, and the treatment should not last longer than 14 days without medical reexamination. It is recommended to take the film-coated tablet immediately before the meal. For any detailed information about the drug dosage use the approved Summary of Main Product Characteristics.

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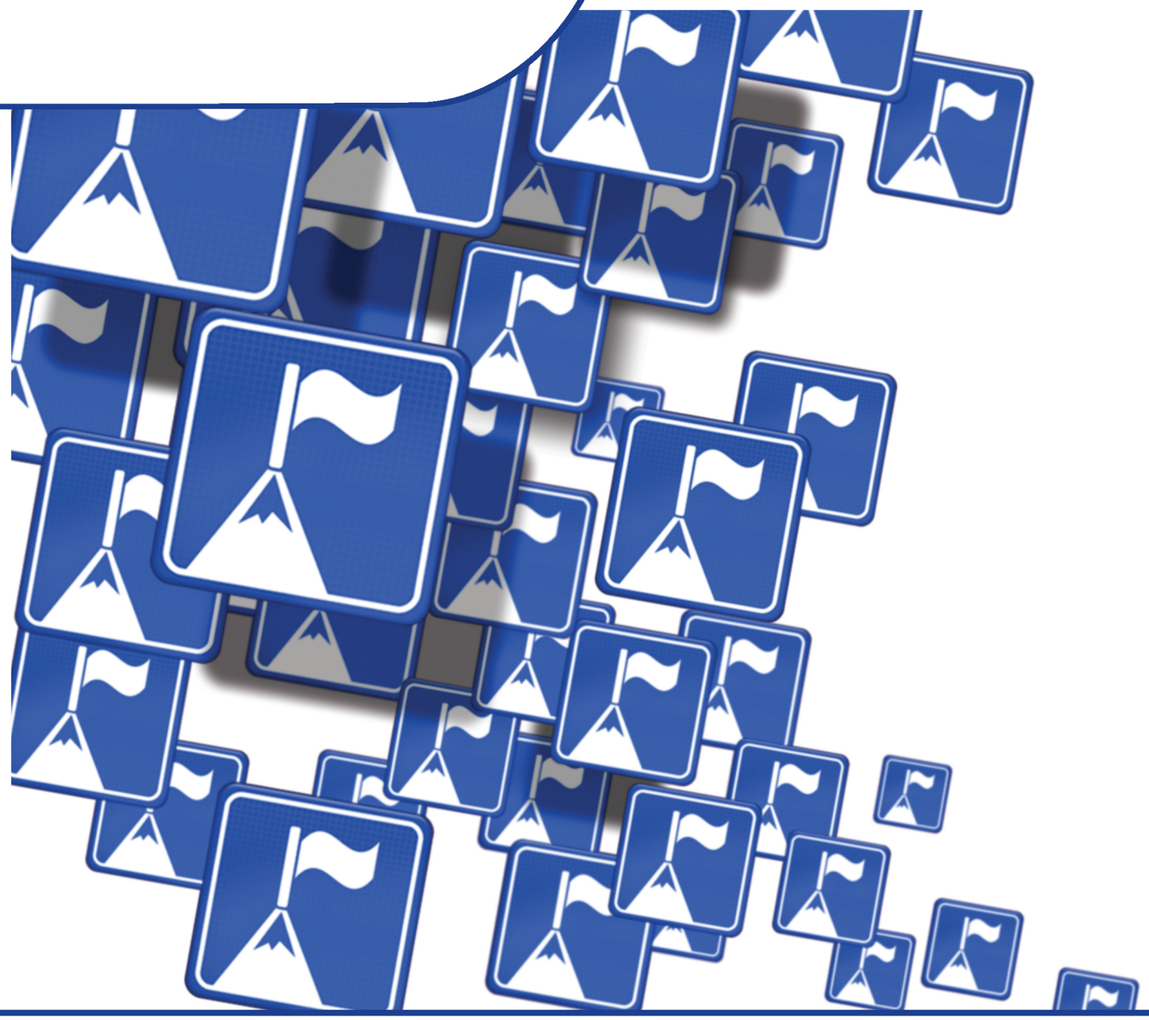
DUOCLAV®

amoxicillin/
clavulanic acid

STILL GOING STRONG AT 35

The most commonly used
antibiotic in empirical treatment



For any detailed information about the drug use the latest approved Summary of Main Product Characteristics and Patient Leaflet should be used.

BOSNALIJEK

DUOCLAV®

amoxicilli/ clavulanic acid

THE MOST COMMONLY USED ANTIBIOTIC IN EMPIRICAL TREATMENT

- ***ANTIMICROBIAL SPECTRUM COVERS CAUSATIVE AGENTS OF MOST COMMON INFECTIONS CAUSED BY G+, G- AND ANAEROBIC BACTERIA, INCLUDING A GREAT NUMBER OF BACTERIA PRODUCED BY BETA-LACTAMASES [1]***
- ***DRUG OF CHOICE IN THE TREATMENT OF COMMUNITY-ACQUIRED INFECTION OF THE UPPER AND LOWER RESPIRATORY TRACT***
- ***DRUG OF CHOICE IN THE TREATMENT OF URINARY TRACT INFECTIONS, INFECTIONS OF THE SKIN AND SOFT TISSUES (INLCUDING ANAEAROBIC BITE-CAUSED INFECTIONS), AS WELL AS DENTAL INFECTIONS***
- ***PALETTE OF FORMS ADAPTED FOR USE IN ALL AGE GROUPS***

Significantly wider antibiotic spectrum compared to other most commonly used antibiotics [2]

BACTERIA	Aminopenicillins		Pencillins		Cephalosporins				Macrolides			Aminoglycosides	Ketolides	Tetracyclines		Uroantiseptics	Karbapenems	
	Amox/clav	**Amp/Amox**	**Amp-Sulb**	**Penicillin G**	**Penicillin V**	**Cephalexin**	**Cephaclor/ Loracarbef**	**Cefuroxime axetil**	**Cefixime**	**Erythromycin**	**Azithromycin**	**Clarithromycin**	**Amikacin**	**Clindamicyn**	**Telithromycin**	**Doxycycline**	**Trimethoprim**	**Nitrofurantoin**	**Ertapenem**	**Meropenem**
GRAM-POSITIVE:																				
Strep. grupe A,B,C,G	**+**	+	+	+	+	+	+	+	+	±	±	±	0	+	+	+	+	+	+	+
Strep. pneumoniae	**+**	+	+	+	+	+	+	+	+	+	+	+	0	+	+	+	±	+	+	+
Strep. viridans	**±**	±	±	±	±	+	+	+	+	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	+	+
Enterococcus faecalis	**+**	+	+	+	+	0	0	0	0	0	0	0	±	0	0	0	+	+	0	±
Staph. aureus (MSSA)	**+**	0	+	0	0	+	+	+	0	±	+	+	+	+	+	±	±	+	+	+
Staph. aureus (MRSA)	**0**	0	0	0	0	0	0	0	0	0	0	0	0	0	0	±	±	+	0	0
Staph. epidermidis	**0**	0	0	0	0	±	±	±	0	±	0	0	±	0	0	0	+	n/a	+	+
GRAM-NEGATIVE:																				
N. gonorrhoeae	**+**	0	+	0	0	0	±	±	+	±	±	±	0	0	+	±	0	+	+	+
N. meningitidis	**+**	+	+	+	0	0	±	±	±	+	+	n/a	0	0	+	+	±	n/a	+	+
M. catarrhalis	**+**	0	+	0	0	0	±	+	+	+	+	+	+	0	+	+	n/a	n/a	+	+
H. influenzae	**+**	±	+	0	0	0	+	+	+	±	+	+	+	0	+	+	±	n/a	+	+
E. coli	**+**	±	+	0	0	+	+	+	+	0	0	0	+	0	0	+	+	+	+	+
Klebsiella sp.	**+**	0	+	0	0	+	+	+	+	0	0	0	+	0	0	±	±	±	+	+
Enterobacter sp.	**0**	0	0	0	0	0	0	0	0	0	0	0	+	0	0	0	±	±	+	+
Salmonella sp.	**+**	±	+	0	0	0	n/a	n/a	+	0	±	0	n/a	0	0	±	±	+	+	+
Shigella sp.	**+**	±	+	0	0	0	n/a	n/a	+	0	±	0	+	0	0	±	±	+	+	+
Proteus mirabilis	**+**	+	+	0	0	+	+	+	+	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	+	+
Proteus vulgaris	**+**	0	+	0	0	0	0	0	+	0	0	0	+	0	0	0	0	0	+	+
Acinetobacter sp.	**0**	0	+	0	0	0	0	0	0	0	0	0	±	0	0	0	0	n/a	0	±
Ps. aeruginosa	**0**	0	0	0	0	0	0	0	0	0	0	0	+	0	0	0	0	0	0	+
Y. enterocolitica	**±**	0	±	0	0	n/a	n/a	n/a	+	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Legionella sp.	**0**	0	0	0	0	0	0	0	0	+	+	+	n/a	n/a	+	+	+	n/a	0	0
MISCELLANEOUS:																				
M. pneumoniae	**0**	0	0	0	0	n/a	n/a	n/a	n/a	+	+	+	0	0	+	+	n/a	n/a	0	0
ANAEROBIC:																				
Actinomyces	**+**	+	+	+	±	n/a	n/a	n/a	n/a	+	+	+	0	+	n/a	+	n/a	n/a	+	n/a
Bacteroides fragilis	**+**	0	+	0	±	0	0	0	0	0	0	0	±	n/a	±	+	n/a	+	+	
P. melaninogenica	**+**	+	+	+	0	n/a	+	+	+	n/a	+	+	0	+	n/a	+	n/a	n/a	+	+
Clostridium difficile	**n/a**	n/a	+[2]	+[2]	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0	n/a	n/a	n/a	n/a	n/a	+	+
Clostridium (not difficile)	**+**	+	+	+	+	n/a	n/a	+	0	±	+	+	n/a	n/a	n/a	+	n/a	n/a	+	+
Peptostreptococcus sp.	**+**	+	+	+	+	+	+	+	+	±	+	±	0	+	+	+	n/a	n/a	+	+

+ = usual clinical efficacy or >60% of susceptible; ± = clinical trial lacking or 30-60% of the susceptible; 0 = not clinically efficient or <30% of susceptible; n/a = data not available; [2] no clinical evidence of action against C. difficile (but in case of mixed intra-abdominal and pelvic infections it can show action)

According to the current world and European guidelines first-choice antimicrobial in the empirical treatment of the respiratory infections: [3-9]

- *acute otitis media*
- *sinusitis*
- *acute exacerbation of chronic bronchitis*
- *community-acquired pneumonia*

Indication	Guideline/guide	Recommendation
Acute otitis media	*US Centers for Disease Control and Prevention* *American Academy of Pediatritian*	Amoxicillin/clavulanic acid the first-choice antibiotic. Amoxicillin/clavulanic acid the first-choice antibiotic.
Acute sinusitis	*American Academy of Otolaryngology – Head and Neck Surgery Foundation* *American College of Physician*	Amoxicillin/clavulanic acid the first-choice antibiotic. Amoxicillin/clavulanic acid the first-choice antibiotic.
Acute exacerbation of chronic bronchitis	*NHS Primary Care Antibiotic Guideline 2015* *British Thoracic Society* *European Society of Clinical Microbiology and Infection Disease*	Amoxicillin/clavulanic acid the first-choice antibiotic. Amoxicillin/clavulanic acid the first-choice antibiotic. Amoxicillin/clavulanic acid the first-choice antibiotic.
Community-acquired pneumonia	*British Thoracic Society* *European Society of Clinical Microbiology and Infection Disease*	A combination of amoxicillin/clavulanic acid and macrolide antibiotic is recommended in the empirical treatment of medium severe and severe community-acquired pneumonias. A combination of amoxicillin/clavulanic acid and macrolide antibiotic is recommended in the initial empirical treatment, if an antibiotic has already been used in the last three months or if comorbidity is present.

Efficient against all causative agents of odontogenic infections [10]

	Act. actinomycetemcomitans	Peptostreptococ. spp	Prevotella spp	Porhyromonas spp	Fusobacterium spp	Oral streptococci
Penicillin G	±	+	±	±	+	+
Amoxicillin	+	+	±	±	+	+
Amoxicillin/davulanate	**+**	**+**	**+**	**+**	**+**	**+**
Doxycycline	+	±	±	±	+	±
Clindamicyn	0	+	+	+	+	+
Metronidazole	0	+	+	+	+	0
Macrolides	±	±	±	±	±	±

+ over 80% of the sensitive strains; ± between 30-80% of the sensitive strains; 0 less than 30% of the sensitive strains

1. K. Fong, R. McMullan, Antimicrobial Therapeutics in Critical Care, Critical Care Horizons 2015
2. Gilbet D.N. et al, The Sanford Guide to Antimicrobial Therapy 2010. 40th edition
3. NHS Primary Care Antibiotic Guideline 2015
4. British Thoracic Society, Guidelines for the management of community acquired pneumonia in adults, 2009
5. European Society of Clinical Microbiology and Infectious Diseases: Guidelines for the management of adult lower respiratory tract infections – Summary, Clinical Microbiology and Infection, Volume 17 Supplement 6, November 2011
6. Rosenfeld et al, American Academy of Otolaryngology—Head and Neck Surgery Foundation 2015, Clinical Practice Guideline (Update): Adult Sinusitis, Otolaryngology–Head and Neck Surgery 2015, Vol. 152(2S) S1–S39,
7. Lieberthal AS, et al, Clinical practice guideline, The Diagnosis and Management of Acute Otitis Media American academy of pediatritian, Pediatrics, Volume 133, Number 2, 2014
8. Harris AM et al, American College of Physician, Appropriate antibiotic use for acute respiratory tract infection in adults: advice for high value care from the American Collage of Physicion and the centers for disease control and prevention, Annals of Internal Medicine, Vol. 164 No. 6, 2016
9. USA Centers for disease control and prevention
10. Bascones MA et al, Consensus statement on antimicrobial treatment of odontogenic bacterial infections, Avances en odontoestomatologia, Vol. 21, Núm. 6, 2005