Augmentin SR
1000 mg/62.5 mg
Amoxicillin/Clavulanic Acid
Prolonged-Release Tablets

Spreading Infectious Liveliness
Increasing burden of lower respiratory tract infections\textsuperscript{1}

- *S. pneumoniae* is the most common pathogen in CAP in both outpatient (44\%) and inpatient (50\%) settings\textsuperscript{1}
- Incidence rate increases with age > 70 years, and more prevalent in males\textsuperscript{1}
- The role of atypical pathogens in CAP is controversial; it is unknown whether atypicals are copathogens or if they predispose patients to subsequent bacterial infection.\textsuperscript{2}

Recent Survey of Antibiotic Resistance (SOAR) studies reveal decreasing antibiotic susceptibility in CA-RTI *S. pneumoniae* isolates in many of the participating countries\textsuperscript{*1,4,5}

\*Susceptibility patterns may vary with time and geography

Gradual emergence of resistance to several commonly used antimicrobials is a growing healthcare concern\textsuperscript{2}

CDC: “Antibiotic Resistance has been called one of the world’s most pressing public health problems”\textsuperscript{2}
**Augmentin SR** - Designed to combat emerging resistance\(^2,6,7,8\)

- A Unique bilayer tablet, providing **sustained release** delivery of amoxicillin\(^3\)
- Bacteriological and clinical efficacy demonstrated in trials\(^7,8\)
- Effective against emerging and increasing prevalence of strains of *S. pneumoniae* with high-level penicillin and/or macrolide resistance\(^7\)

**Immediate-release layer:**
- Amoxicillin trihydrate 562.5 mg allows for peak plasma concentration
- Clavulanate 62.5 mg

**Sustained-release layer:**
- Crystalline Sodium Amoxicillin 437.5 mg maintains extended plasma concentration
  
  *Adapted from Benninger MS\(^2\)*

**Augmentin SR**  
1000 mg/62.5 mg  
**Amoxicillin/Clavulanic Acid** is indicated for the treatment of community-acquired pneumonia in adults and adolescents aged at least 16 years, caused or thought likely to be caused by penicillin-resistant *S. pneumoniae*\(^6\)

**Community Acquired Pneumonia**\(^6\)
**Augmentin SR** uses sustained-release technology to provide superior efficacy against resistant pathogens

- Maximizing bacterial eradication is a key goal in the selection of appropriate antimicrobial therapy in respiratory tract infections
- For amoxicillin, a $T > MIC$ of 30-40% of the dosing interval is required for maximal bacteriological efficacy against the key respiratory pathogens

**Bacteriological efficacy of antimicrobials is dependent on their pharmacokinetic/pharmacodynamic (PK/PD) properties**

**Mean plasma concentration-time profile for amoxicillin after oral administration of pharmacokinetically enhanced Augmentin SR (2000/125 mg) (n=55) compared with conventional release Augmentin 1g (875/125 mg) (n=14). Adapted from White AR**

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**Immediate-release of 562.5 mg amoxicillin 62.5 mg clavulanate**

**Sustained-release of 437.5 mg amoxicillin**

**Augmentin 875/125 mg**

**Augmentin SR 2000/125 mg**

Mean plasma concentration-time profile for amoxicillin after oral administration of pharmacokinetically enhanced Augmentin SR (2000/125 mg) (n=55) compared with conventional release Augmentin 1g (875/125 mg) (n=14). Adapted from White AR
**Augmentin SR** has been developed to maximise PK/PD against resistant strains\(^9\)

<table>
<thead>
<tr>
<th>Augmentin Formulations</th>
<th>Ratio</th>
<th>Dosing Regimen</th>
<th>Mean T&gt;MIC for amoxicillin (% of dosing interval) for MICs (mg/L) of:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Augmentin 625 mg (500/125 mg)</td>
<td>4:1</td>
<td>TDS</td>
<td>55</td>
</tr>
<tr>
<td>Augmentin 1 g (875/125 mg)</td>
<td>7:1</td>
<td>BD</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TDS</td>
<td>69</td>
</tr>
<tr>
<td><strong>Augmentin SR</strong> 2000/125 mg</td>
<td>16:1</td>
<td>BD</td>
<td>70</td>
</tr>
</tbody>
</table>

Adapted from White AR\(^9\)

For pathogens with MICs of 4 mg/L, **Augmentin SR** 2000/125 mg twice daily achieves a mean **T > MIC** of 49% of the dosing interval\(^9\)

“For macrolides, limitations in pharmacokinetics and safety prevent dosages being increased or modified sufficiently to overcome macrolide resistant *S. pneumoniae* or to confer *in vivo* bacteriological efficacy against *H. influenzae*\(^9\)”

“For fluoroquinolones have a relatively narrow safety window, limiting the doses that can be given, and most agents would not be able to maintain an acceptable safety/tolerability profile and overcome quinolone resistance in *S. pneumoniae*\(^9\)”
Efficacy, safety and tolerability with Augmentin SR

- Comparable clinical and bacteriological efficacy vs. Augmentin 1g TDS\textsuperscript{10,11}
- Comparable safety and tolerability when compared to other conventional Augmentin formulations\textsuperscript{9,10,11}

A randomized, double-blind, double-dummy, multicentre study compared the efficacy and safety of Augmentin SR (2000/125 mg) BD versus Augmentin 1g (875/125 mg) TDS, for 7 or 10 days, in the treatment of community-acquired pneumonia (CAP). The per-protocol (PP) population at follow-up (Days 18-39) comprised 114 patients receiving Augmentin SR (2000/125 mg) and 116 receiving Augmentin 1g (875/125 mg). Adapted from Garau J\textsuperscript{11}

Undesirable effects, Contraindications, Precautions\textsuperscript{6}:

- The most common adverse effects are diarrhoea, nausea, vomiting and mucocutaneous candidiasis
- Nausea is more often associated with higher oral dosages. If gastrointestinal reactions are evident, they may be reduced by taking Augmentin at the start of a meal
- Augmentin SR is indicated for use in adults and adolescents aged \geq 16 years
- Careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens, before initiating therapy with Augmentin
- Should be used with caution in patients with evidence of hepatic dysfunction
- Treatment should not be extended beyond 14 days without review.
AUGMENTIN SR Abridged Prescribing Information: Please refer to the full Summary of Product Characteristics (SPC) before prescribing. TRADE NAME: Augmentin SR. ACTIVE INGREDIENTS: Amoxicillin (as trihydrate), potassium clavulanate. PHARMACEUTICAL FORM: 1000 mg/62.5 mg prolonged-release tablets. INDICATIONS: Treatment of community acquired pneumonia in adults and adolescents aged at least 16 years, caused or thought likely to be caused by penicillin-resistant Streptococcus pneumoniae. POSOLOGY: Adults and adolescents ≥16 years: Oral use. 2 tablets, twice daily for seven to ten days. Administer with a meal. CONTRAINDICATIONS: Hypersensitivity to active substances/penicillins/cephalosporins. History of: severe immediate hypersensitivity reaction to another beta-lactam agent, jaundice/hepatic impairment due to amoxicillin/clavulanic acid. PRECAUTIONS: Enquiry of previous hypersensitivity reactions to beta-lactams. Switch to an amoxicillin-only preparation (to be considered for infections proven due to amoxicillin susceptible organism). Convulsions may occur in patients receiving high doses or impaired renal function. Concomitant use of allopurinol increase likelihood of allergic skin reactions. Overgrowth of non-susceptible organisms with prolonged use. Occurrence of a feverish generalised erythema associated with pustula at treatment initiation may be symptom of AGEP (reaction requires discontinuation and contra-indicates subsequent administration of amoxicillin). Caution in patients with hepatic impairment. Hepatic events may be associated with prolonged treatment. Antibiotic-associated colitis. Periodic assessment of organ system functions, including renal, hepatic and haematopoietic function is advisable during prolonged therapy. Appropriate monitoring when anticoagulants are prescribed concomitantly. Creatinine clearance less than 30 ml/min (not recommended). Possibility of amoxicillin crystalluria. Potential of incorrect diagnostic test results during treatment (refer to full SPC for details). Contains 29.3 mg (1.3 mmol) of sodium per tablet. Refer to the SPC for full details of precautions. pregnancy/Fertility/LACTATION: Pregnancy: Use should be avoided unless considered essential by the physician. Lactation: benefit/risk assessment to be considered. UNDESIRABLE EFFECTS: Very common (>1/10): diarrhoea. Common (≥1/100 to <1/10): mucocutaneous candidosis, nausea, abdominal pain. Refer to full SPC for the full list of adverse reactions. LOCAL PRESENTATION: 28 tablets/pack. MARKETING AUTHORISATION NUMBER: AA1051/00102. MARKETING AUTHORISATION HOLDER: GlaxoSmithKline Bulgaria EOOD. LEGAL CATEGORY: POM. DATE OF PREPARATION: November 2017.

In order to ensure that this product information reflects the most up-to-date clinical and post-marketing surveillance data, please always refer to the latest Summary of Product Characteristics (SPC) which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21238131)

REPORTING ADVERSE EVENTS (AEs):
If you become aware of any AEs, medication errors and/or use during pregnancy in association with GSK products, please report the event promptly to: GSK (Malta) Ltd, 1, De la Cruz Avenue, Qormi QRM 2458, Malta (Tel: +356 21238131).

Alternatively, any suspected AEs and medication errors can be reported via the Medicines Authority Adverse Drug Reactions reporting website: www.medicinesauthority.gov.mt/adrportal

References
Co-amoxiclav Sustained Release - Recommended by Leading Guidelines in the treatment of CAP\textsuperscript{12,13}

- The Unique bilayer tablet provides sustained release delivery of amoxicillin\textsuperscript{2}
- Sustained-release technology provides superior efficacy against resistant pathogens\textsuperscript{9}
- Effective against emerging and increasing prevalence of strains of *S. pneumoniae* with high-level penicillin and/or macrolide resistance\textsuperscript{7}

Two tablets BD for 7-10 days