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Antibiotics Used to Treat *Streptococcus pyogenes* Infections

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ABSTRACT

Background: *Streptococcus pyogenes* (Group A *Streptococcus*, GAS) remains a globally significant human pathogen responsible for hundreds of millions of infections annually. Pharyngitis alone accounts for an estimated 616 million cases per year, with invasive disease causing more than 500,000 deaths worldwide, particularly in low- and middle-income countries. Antibiotic therapy remains the cornerstone of treatment, with penicillin maintaining its status as the drug of choice after more than 70 years of clinical use and with no documented resistance.

Conclusion: This mini review summarizes current antibiotic therapies for GAS, highlighting mechanisms of action, clinical applications, resistance patterns, global treatment guidelines, and recent developments between 2020 and 2025. Comparative and statistical data are provided on antibiotic efficacy, regional resistance rates, short-course versus standard regimens, and diagnostic advances. Emphasis is placed on evidence-based therapy to reduce complications such as rheumatic fever and post-streptococcal glomerulonephritis.

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Introduction

Streptococcus pyogenes is a beta-hemolytic, gram-positive bacterium belonging to Lancefield group A. Transmission occurs primarily through respiratory droplets, but direct skin contact with infected lesions also plays a role. The pathogen's major virulence factor, the M protein, facilitates immune evasion and is central to pathogenesis.

Globally, GAS causes an estimated 616 million cases of pharyngitis annually, resulting in approximately 517,000 deaths due to severe invasive infections and immune-mediated complications. Clinical presentations can be categorized into non-invasive infections (e.g., pharyngitis, impetigo), invasive infections (e.g., cellulitis, erysipelas, necrotizing fasciitis, bacteremia), and post-infectious sequelae (e.g., acute rheumatic fever, post-streptococcal glomerulonephritis). Timely and appropriate antibiotic therapy remains essential to reduce symptom duration, transmission, and long-term complications.

Antibiotic Therapy

Penicillin and Beta-Lactams

Penicillin remains the gold standard for GAS treatment. Its mechanism involves inhibiting bacterial cell wall synthesis by binding to PBPs, leading to cell lysis. No penicillin resistance has been documented globally in *S. pyogenes*, an exceptional finding among major pathogens.

Pharyngitis: Penicillin V 250-500 mg orally two to three times daily for 10 days, or a single intramuscular dose of benzathine penicillin G (1.2 million units) for adherence issues. Efficacy: Clinical cure rates exceed 95%, with bacteriologic eradication rates between 90–95%, depending on adherence.

Amoxicillin, dosed at 50 mg/kg (max 1000 mg) once daily for 10 days, is preferred in children for better palatability. For skin and soft tissue infections, both penicillin and amoxicillin demonstrate excellent outcomes with cure rates >90%.

Cephalosporins

Cephalosporins are suitable alternatives for non-anaphylactic penicillin allergies. Meta-analyses show bacteriologic eradication rates of 96–98%, slightly higher than penicillin, particularly for recurrent pharyngitis. Shorter 5-day cephalosporin regimens have demonstrated cure rates of 97%, comparable to 10-day penicillin courses, with adherence rates of 92% vs. 83% ($p < 0.05$). First-generation agents (cephalexin, cefadroxil) remain most appropriate for GAS; second-generation agents are generally unnecessary for routine pharyngitis.

Macrolides

Macrolides (erythromycin, azithromycin, clarithromycin) inhibit protein synthesis via the 50S ribosomal subunit. Efficacy: Azithromycin (5 days) and clarithromycin (10 days) have clinical success rates of 85-95%, depending on regional resistance. Resistance: Global resistance ranges 5–30%, with Northern Europe <5% and parts of Asia/Southern Europe up to 30%. Mechanisms: mef (A) efflux pumps and erm (B) methylation.

Clindamycin

Clindamycin binds the 50S ribosomal subunit and suppresses toxin production, making it essential for severe invasive disease (e.g., necrotizing fasciitis, toxic shock syndrome). Observational studies indicate reduced mortality and limb loss when added to beta-lactams in invasive infections. Resistance: Usually inducible (erm genes), 5–10% globally.

Other Antibiotics

Linezolid and vancomycin are reserved for severe allergies or empiric therapy in critically ill

patients. Their broad spectrum and adverse effects preclude routine use.

Treatment Guidelines

Major guidelines (IDSA, WHO, European Society of Clinical Microbiology) consistently recommend penicillin or amoxicillin as first-line therapy for 10 days. Cephalosporins are used for mild allergies, macrolides or clindamycin for true anaphylaxis, and urgent surgical debridement + penicillin G and clindamycin for invasive disease. Rheumatic fever rates are <0.1% with full adherence vs >2% with incomplete treatment.

Resistance Patterns

GAS remains universally susceptible to penicillin. Macrolide resistance: <5% in Northern Europe, 10–20% in North America, 20–30% in Asia/Southern Europe. Clindamycin resistance: 5–10%, mostly inducible. Cephalosporin resistance: rare. Temporal trends show macrolide resistance increasing by ~1–2% per year in high-prescribing regions (2015–2024).

Recent Developments (2020–2025)

Randomized trials (n > 15,000) confirmed non-inferiority of 5-day cephalosporin regimens compared with 10-day penicillin for pharyngitis. RADTs and molecular PCR increased diagnostic specificity to 95–98%, leading to 28% fewer unnecessary prescriptions in European primary care (2020–2023). IVIG is being explored as adjunctive treatment in streptococcal toxic shock syndrome to neutralize circulating exotoxins.

Epidemiological and Treatment Statistics

Global Burden: 616 M pharyngitis cases annually; 517,000 deaths from severe disease. Invasive GAS incidence: 3–4 cases/100,000 annually; mortality 20–50% depending on treatment speed. Penicillin success rates: >95% clinical, 90–95% bacteriologic. Cephalosporin success rates: 96–98%, particularly for recurrent infections. Macrolide resistance: <5% in Northern Europe vs 20–30% in Asia/Southern Europe. Clindamycin resistance: 5–10%, mostly inducible. Impact of diagnostics: 28% reduction in antibiotic overuse after RADT implementation.

Conclusion

Penicillin remains the cornerstone of GAS therapy, with unmatched long-term efficacy and no resistance. Cephalosporins, macrolides, and clindamycin are valuable alternatives in specific clinical settings. Comparative data support short-course cephalosporins as effective alternatives to 10-day penicillin regimens, with improved adherence. Rising macrolide resistance highlights the need for regional surveillance and stewardship. Incorporation of rapid diagnostics and adherence to international guidelines are key to reducing disease burden, preventing complications, and preserving antibiotic effectiveness.

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Ethics approval and consent to participate

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Conflict of interest

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