

FROM THE ANALYST'S COUCH

The antibacterial drugs market

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The pharmaceutical industry owes a great deal of its early prosperity to the development of antibacterial drugs, and as a consequence the market encompasses several of the oldest drug classes. The market is highly saturated and has significant generic penetration, yet still experiences continuous growth due to increasing sales volume, as well as the rise of premium-priced novel treatments for resistant bacteria (for example, Pfizer's Zynox (linezolid)). Key drivers for this market include the growing number of people with weakened immune systems, such as the elderly and immunosuppressed patients (HIV patients and organ recipients, for example).

However, the development of antibacterials has become increasingly unattractive to big pharma for a number of reasons: short antibacterial drug lifecycles; the fact that antibacterial therapy is acute, not chronic; the mature nature of the market, which is characterized by low growth and high generic penetration; and the raising of the bar for the statistical standards needed to show the efficacy of experimental drugs in clinical trials. A key factor contributing to shorter drug lifecycles is bacterial resistance. Shorter lifecycles increases the risk to drug developers (as they have less time to recoup their R&D investments); restricts sales growth (as many governments have introduced schemes to limit antibiotic use to combat resistance issues such as methicillin-resistant *Staphylococcus aureus* (MRSA)); and prioritizes the need for intensive lifecycle-management strategies (for example, developing an extended-release formulation).

All of these factors have led to the overriding view that big companies can spend their research dollars in more productive ways. Although the market size is significant, with an estimated total sales of US\$25.5 billion in 2005¹, 10 out of the 15 largest companies have fully abandoned, or cut down significantly, their discovery efforts in this field since 1999². Smaller firms (such as Basilea, Theravance and Cubist) have been taking over the drug development role, both by identifying innovative drugs or formulations, and/or by picking up

clinical programmes aborted by the larger companies. However, big pharma often becomes involved later through in-licensing later-stage pipeline drugs, as a strong salesforce is key to success in the community antibacterials market.

The net result of this is that the overall growth rate in the seven major pharma markets (which has been primarily driven by price increases) has slowed to a compound annual growth rate (CAGR) of just 5% from 2001–2005.

Antibacterial drug market drivers

The antibacterials market is highly fragmented and can be split into two major groups: the larger community market (estimated at 62% of total antibacterial sales), with a lower average drug price and growth prospects; and the smaller but more attractive hospital market, with a higher average drug price and growth prospects.

There is no single market-leading drug or class of antibacterials. Penicillins (for Gram-positive pathogens) and cephalosporins (for Gram-positive and Gram-negative pathogens) are the most widely used antibacterials, followed by fluoroquinolones for Gram-negative pathogens. Macrolides are popular for respiratory- and urinary-tract infections — the two commonest indications for antibacterials. The market share of the various drug classes are shown in FIG. 1, while sales generated by each of these classes are shown in FIG. 2.

Although there are good treatment options available for most common infections, several opportunities exist in niche indications with high unmet needs. The most significant are oral drugs to treat MRSA, the prevalence of which has dramatically increased in both hospital and community settings since 2001. The second exists in resistant Gram-negative bacterial infections, in particular *Pseudomonas* and *Acinetobacter*. Unfortunately, there are few drugs in development addressing these needs. Instead, drug developers have focused on injectable MRSA drugs, such as Pfizer's Zeven (dalbavancin) and Theravance's Arbelic (telavancin). As many of these pipeline drugs are structurally related to existing drugs, they are likely to

face resistance issues within a few years. However, they do drive the increased usage of injectable antibacterials, as treatment strategies for moderate to severe infections are moving towards using more potent therapies for a shorter period of time.

Future focus

Two trends are shaping the antibacterial market. First, following the patent expiries of Pfizer's Zithromax (azithromycin) and Abbott's Biaxin/Klacid (clarithromycin) in late 2005, the previously slow growth-rate of community antibiotics turned negative in the first half of 2006. Only two major brands, J&J/Sanofi-Aventis's Levaquin (levofloxacin) and Bayer's Avelox (moxifloxacin) remain; newer drugs in this field have been dogged by clinical and regulatory setbacks. Rising cost pressures add to the gloomy outlook. The market's high degree of maturity and generic penetration requires competitors to be well differentiated (for example, by showing superior efficacy and/or safety in certain populations) in order to gain market share, as well as to secure stronger pricing and reimbursement levels.

Second, the smaller hospital market continues to expand rapidly, driven by rising resistance rates, a more severely ill patient population and newer, premium-priced injectable antibiotics. Interestingly, several big pharma companies have recently made strategic decisions to expand their presence in this sector by either acquiring companies (such as Pfizer's acquisition of Vicuron and Novartis's acquisition of Neutec) or in-licensing compounds (such as J&J's licensing of Basilea's ceftobiprole and Astellas's licensing of Theravance's telavancin; TABLE 1). Although aiming at niche patient populations limits the sales potential and requires greater innovation, it should also decrease the intensity of both competition and pricing pressures — two key factors that increase the attractiveness of this strategy, proven by the rising number of smaller drug developers in this field. There is scope for greater innovation, powering the transition towards a more diversified antibacterial pipeline. There is also a commercial need for products, proven by a number of lucrative licensing deals. ▶

THE ANTIBACTERIAL DRUGS MARKET | MARKET INDICATORS

► Of the 21 different classes of antibacterial drugs, the dominant antibacterial drug classes (in 2005 market share order) are cephalosporins, macrolides, fluoroquinolones and penicillins, which together generated around 80% of total sales and total prescription volume in 2005 (FIG. 1). Sales of these antibacterial classes in 2001 and 2005, together with CAGRs and leading examples of each drug class are provided in FIG 2.

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FURTHER READING Christoffersen, R. E. Antibiotics — an investment worth making? *Nature Biotechnol.* **24**, 1512–1514 (2006) | Payne, D. J. et al. Drugs for bad bugs: confronting the challenges of antibacterial discovery. *Nature Rev. Drug Discov.* **1**, 29–40 (2007) | Pink, R. et al. Opportunities and challenges in antiparasitic drug discovery. *Nature Rev. Drug Discov.* **4**, 727–740 (2005) | Silver, L. L. Multi-targeting by monotherapeutic antibacterials. *Nature Rev. Drug Discov.* **1**, 41–55 (2007).

Table 1 | Key late-stage (Phase III) antibacterial drugs in development

Compound	Class	Company	Indication
Doripenem	Carbapenem	Peninsula/Johnson&Johnson	HAP/VAP, cUTIs, cIAIs
Dalbavancin	Glycopeptide	Vicuron/Pfizer	cSSSIs
Ceftobiprole (BAL5788)	Cephalosporin	Basilea/Johnson&Johnson	cSSSIs/HAP
Cethromycin	Ketolide	Advanced Life Sciences	CAP, other RTIs
Telavancin	Glycopeptide	Theravance/Astellas	cSSSIs/HAP
Iclaprim	DHFR inhibitor	Arpida	cSSSIs

CAP, community-acquired pneumonia; cIAIs, complicated intra-abdominal infections; cSSSIs, complicated skin and skin structure infections; cUTI, complicated urinary-tract infections; DHFR, dihydrofolate reductase; HAP, hospital-acquired pneumonia; RTIs, respiratory-tract infections; VAP, ventilator-associated pneumonia.

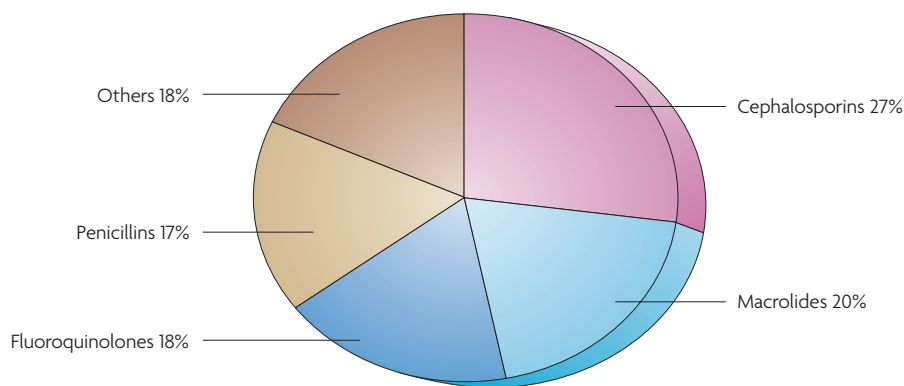


Figure 1 | Market shares (by sales) of the leading antibacterial drug classes. Source: Datamonitor, MIDAS Sales Data, IMS Health, September 2006.

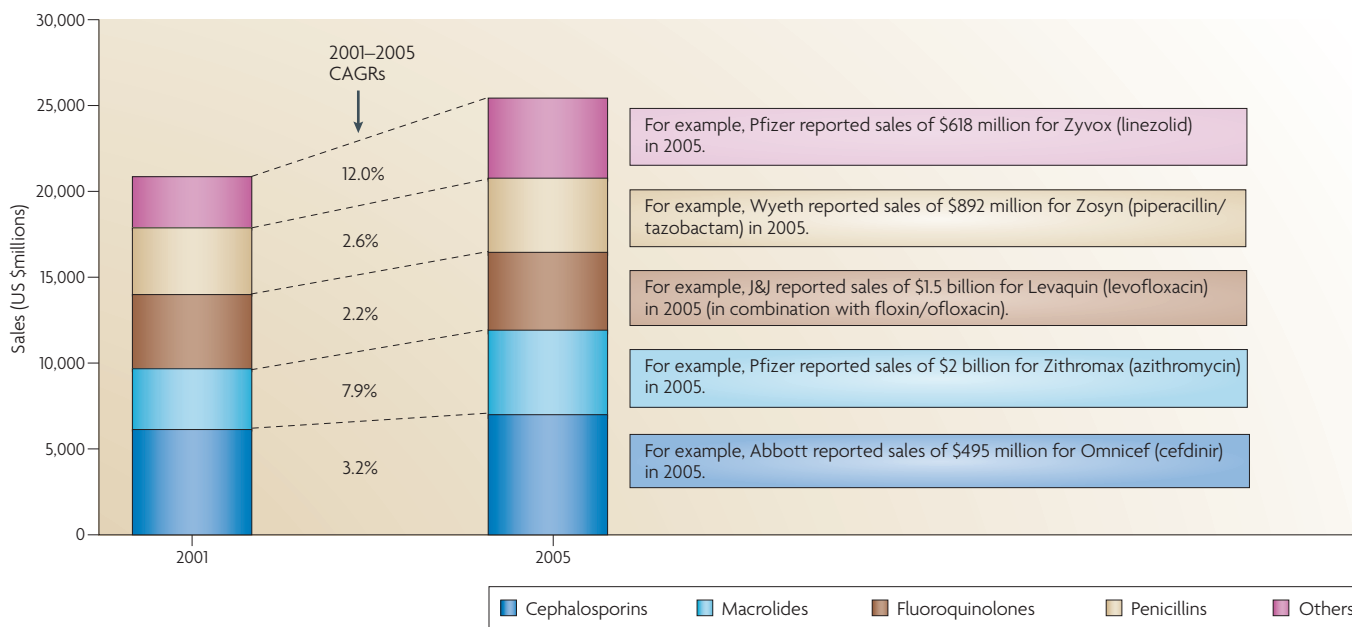


Figure 2 | Growth rates of major antibacterial classes in 2001–2005. Individual sales generated by the lead marketer of the drug are based on company reported data; total classes are based on MIDAS Sales Data, IMS Health, September 2006. CAGR, compound annual growth rate.