Second MRSA antibiotic reaches the market

The US Food and Drug Administration (FDA) officials in August approved Orbactiv (oritavancin), a new drug to treat Gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA), developed by the Medicines Company of Parsippany, New Jersey. Orbactiv is the latest in a wave of much-needed, next-generation antibacterial agents to reach the market. But optimism surrounding the recent approvals was tempered by two near simultaneous events: the US Centers for Medicare & Medicaid Services (CMS) stripped away a federal incentive for one novel antibiotic, Dalvance (dalbavancin), and denied reimbursement in certain situations for another, Difidol (fidaxomicin). Some see these actions as disincentives, although the affected companies play down that interpretation.

Orbactiv, which is administered intravenously, is a semisynthetic lipoglycopeptide antibiotic that the Medicines Company inherited from the 2009 acquisition of Targanta Therapeutics. The drug is under review by the European Medicines Agency (EMA) for similar indications approved by the FDA, and EMA is expected to decide on Orbactiv during the first half of 2015, according to the company.

Amid the good news, the CMS took aim at two recently approved novel antibiotics: Dalvance, made by Durata Therapeutics of Chicago and approved by FDA last May (*Nat. Biotechnol.* **32**, 603, 2014), and Difidol, made by Cubist Pharmaceuticals of Lexington, Massachusetts, approved several years ago. Dalvance is approved for treating patients with acute bacterial skin infections caused by Gram-positive bacterial pathogens, including MRSA. Cubist's Difidol is used specifically to treat adults with *Clostridium difficile*-associated diarrhea.

CMS' role, since its inception a decade ago, has been to enable hospitalized patients insured under Medicare to benefit from breakthrough medical developments. Through its New Technology Add-on Payment (NTAP) program, CMS has also helped to underwrite several drugs. "Developers of new antibiotics are counting on ways such as NTAP to allow new therapies to be used in clinical practice," says Karen Bush of Indiana University in Bloomington. "However, the criteria for qualifying as an NTAP apparently are not straightforward."

Good news on the drug-resistance front. FDA adds another weapon to the anti-MRSA arsenal.

Some may interpret CMS' recent decision as discouraging, she adds.

For Cubist, the recent phasing out of its drug from the CMS program was "expected," says Elizabeth Dunavant, director of product communications at Cubist. Difidol was accepted into the CMS incentive program for a one-year stint, and later given a second-year extension. As for Durata, applying for NTAP status "was not routine or even on our radar screen when we were developing Dalvance," says Michael Dunne, chief medical officer of Durata. The company only applied when they figured Dalvance—mainly used for outpatients—seemed to meet NTAP requirements for hospitalized patients.

Failure to gain NTAP incentives for Dalvance "didn't change our forecast or commercial reality, it is an overall disappointment from a society standpoint,"

Durata's Dunne adds. The intravenous antibiotic was approved for acute bacterial skin and skin structure infections caused by Gram-positive bacteria, including MRSA. It appears to be curative with a two-dose regimen followed one week later by another, each administered over 30 minutes. The biotech's high hopes for Dalvance depend on its being used more broadly, particularly for antibiotic-resistant infections.

Orbactiv could have an advantage here because it is effective following once-only treatment of patients, albeit by a single infusion lasting three hours. This feature helped the drug to attain status as a qualified infectious disease product (QIDP) under the Generating Antibiotic Incentives Now (GAIN) Act of 2012—another federal program, but not under CMS. QIDP status qualifies Orbactiv for various incentives, including a five-year extension of any non-patent exclusivity period awarded to the drug.

Meanwhile, pressure is building from several directions to extend incentives for novel antibiotics that could help combat the problem of drug resistance. For example, a bill, the Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms (DISARM) Act of 2014, introduced earlier this year aims to broaden NTAP criteria to include virtually any new antibiotic. Despite broad support, however, there seems little practical chance for the bill to move forward anytime soon because members of

Congress are preoccupied with other matters, including November elections.

And the Infectious Diseases Society of America, headquartered in a suburb of Washington, DC, in September established a coalition,

the US Stakeholder Forum on Antimicrobial Resistance (S-FAR). Part of its mission is to seek additional federal incentives for antibiotics, including an accelerated approval pathway for such drugs. S-FAR includes several biotech companies developing antimicrobial products as well as the Washington, DC-based Biotechnology Industry Organization.

Jeffrey L. Fox, Washington, DC

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