the phase III Lefamulin Evaluation Against Pneumonia (LEAP 1) trial [published February 4, 2019]. *Clin Infect Dis*. doi:10.1093/cid/ciz090

16. Mandell LA, Wunderink RG, Anzueto A, et al; Infectious Diseases Society of America; American Thoracic Society. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis*. 2007;44(suppl 2):S27-S72. doi:10.1086/511159

17. US Food and Drug Administration. Avelox (moxifloxacin hydrochloride): full prescribing information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/021085s063lbl.pdf. Accessed August 26, 2019.

18. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310(20):2191-2194. doi:10.1001/jama.2013.281053

19. US Food and Drug Administration. Guidance for industry and Food and Drug Administration staff: collection of race and ethnicity data in clinical trials. https://www.fda.gov/media/75453/download. Accessed August 26, 2019.

20. US Food and Drug Administration. Guidance for industry: community-acquired bacterial pneumonia: developing drugs for treatment. https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM123686.pdf. Accessed August 26, 2019.

21. European Medicines Agency Committee for Human Medicinal Products. Addendum to the guideline on the evaluation of medicinal products indicated for treatment of bacterial infections. https://www.ema.europa.eu/documents/scientific-guideline/addendum-guideline-evaluation-medicinal-products-indicated-treatment-bacterial-infections_en.pdf. Accessed August 26, 2019.

22. European Medicines Agency Committee for Human Medicinal Products. Guideline on the evaluation of medicinal products indicated for treatment of bacterial infections. https://www.ema.europa.eu/en/documents/scientific-guideline/draft-guideline-evaluation-medicinal-products-indicated-treatment-bacterial-infections-revision-2_en.pdf. Accessed September 3, 2019.

23. Talbot GH, Powers JH, Fleming TR, Siuciak JA, Bradley J, Boucher H; CABP-ABSSSI Project Team. Progress on developing endpoints for registrational clinical trials of community-acquired bacterial pneumonia and acute bacterial skin and skin structure infections: update from the Biomarkers Consortium of the Foundation for the National Institutes of Health. *Clin Infect Dis*. 2012;55(8):1114-1121. doi:10.1093/cid/cis566

24. Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med*. 1997;336(4):243-250. doi:10.1056/NEJM199701233360402

25. US Food and Drug Administration. Guidance for industry drug-induced liver injury: premarketing clinical evaluation. https://www.fda.gov/downloads/guidances/UCM174090.pdf. Accessed August 26, 2019.

26. US Food and Drug Administration Antimicrobial Drugs Advisory Committee. Solithromycin for the treatment of community acquired bacterial pneumonia. https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Anti-InfectiveDrugsAdvisoryCommittee/UCM527691.pdf. Accessed August 26, 2019.

27. US Food and Drug Administration. Nuzyra (omadacycline): full prescribing information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/209816_209817lbl.pdf. Accessed August 26, 2019.

Editor's Note

Lefamulin—A New Antibiotic for Community-Acquired Pneumonia

Preeti N. Malani, MD, MSJ

A robust antibiotic pipeline is essential for patient care and public health. Yet compared with other classes of drugs, the development of antibiotics presents unique scientific, regulatory, and economic challenges. Most notably, antibiotics provide less financial reward for pharmaceutical companies because these medications are used for a short duration and newer agents are often restricted for use only in the setting of antimicrobial resistance. In fact, most large pharmaceutical companies have reduced or stopped antibiotic research altogether, leaving the critical task of discovering new antibiotics to small companies with limited budgets and research capacity. For these and other reasons, the development and approval of a new antibiotic is a rare occurrence and a reason to celebrate.

Related article page 1661

In this issue of *JAMA*, Alexander et al[1] report the findings of the Lefamulin Evaluation Against Pneumonia 2 (LEAP 2) trial, a phase 3, randomized, noninferiority trial that compared 5-day oral lefamulin with 7-day oral moxifloxacin in the management of community-acquired bacterial pneumonia (CABP). In this trial of 738 patients, the primary outcome of early clinical response at 96 hours (within a 24-hour window) after the first dose of study drug was 90.8% in the lefamulin group and 90.8% in the moxifloxacin group, a difference that met the noninferiority margin of 10%. Patients in the lefamulin group reported a higher incidence of gastrointestinal-related treatment-emergent adverse effects (17.9% vs 7.6% in the moxifloxacin group), primarily diarrhea.

Lefamulin (both intravenous and oral formulation) was approved in August 2019 by the US Food and Drug Administration (FDA) to treat CABP. This approval was based on data in the current LEAP 2 study as well as the previously published LEAP 1 study.[2] Although lefamulin will offer another oral option to treat CABP, the spectrum of activity is similar to fluoroquinolones. In recent years, more attention has been given to uncommon but serious adverse effects associated with fluoroquinolone use including Q-T prolongation, hypoglycemia, and tendinitis and tendon rupture.

Cost will likely be a barrier to lefamulin use. A press release from the manufacturer stated that the wholesale acquisition cost of lefamulin will be $205 per day for intravenous treatment and $275 per day for oral treatment.[3] This is

several-fold more than moxifloxacin or levofloxacin, which are the most commonly prescribed fluoroquinolones for CABP. Tolerability (especially diarrhea and vomiting) may be another issue, and deserves close postmarketing monitoring.

Despite these concerns, lefamulin is an important addition to the current antibiotic armamentarium, especially because bacterial pneumonia remains one of the most common indications for antibiotic use.[4,5]

Author Affiliations: Division of Infectious Diseases, Department of Internal Medicine, University of Michigan, Ann Arbor; Associate Editor, *JAMA*.

Corresponding Author: Preeti N. Malani, MD, MSJ, 4135F University Hospital South, 1500 East Medical Center Dr, Ann Arbor, MI 48109 (pmalani@umich.edu).

Published Online: September 27, 2019. doi:10.1001/jama.2019.16215

Conflict of Interest Disclosures: None reported.

1. Alexander E, Goldberg L, Das A, et al. Oral lefamulin vs moxifloxacin for early clinical response among adults with community-acquired bacterial pneumonia: the LEAP 2 randomized clinical trial [published September 27, 2019]. *JAMA*. doi:10.1001/jama.2019.15468

2. File TM, Goldberg L, Das A, et al. Efficacy and safety of intravenous-to-oral lefamulin, a pleuromutilin antibiotic, for the treatment of community-acquired bacterial pneumonia: the phase III Lefamulin Evaluation Against Pneumonia (LEAP 1) trial [published February 4, 2019]. *Clin Infect Dis*. doi:10.1093/cid/ciz090

3. Nabriva. Press release. https://investors.nabriva.com/news-releases/news-release-details/nabriva-therapeutics-receives-us-fda-approval-xenleta. Accessed September 15, 2019.

4. Magill SS, Edwards JR, Beldavs ZG, et al; Emerging Infections Program Healthcare-Associated Infections and Antimicrobial Use Prevalence Survey Team. Prevalence of antimicrobial use in US acute care hospitals, May-September 2011. *JAMA*. 2014;312(14):1438-1446. doi:10.1001/jama.2014.12923

5. Fleming-Dutra KE, Hersh AL, Shapiro DJ, et al. Prevalence of inappropriate antibiotic prescriptions among US ambulatory care visits, 2010-2011. *JAMA*. 2016;315(17):1864-1873. doi:10.1001/jama.2016.4151