A plain language summary of how lefamulin alone can be used to treat pneumonia caught outside of the hospital due to common bacterial causes, including drug-resistant bacteria

Susanne Paukner*1, Gregory J Moran2, Christian Sandrock3, Thomas M File, Jr4, Jorge E Vidal5, Ken B Waites6, Steven P Gelone7 & Kalvin Yu8
1Nabriva Therapeutics GmbH, Vienna, Austria; 2Department of Emergency Medicine & Division of Infectious Diseases, Olive View-UCLA Medical Center, Los Angeles, CA, USA; 3Department of Internal Medicine, UC Davis School of Medicine, Sacramento, CA, USA; 4Infectious Disease Division, Summa Health, Akron, OH, USA; 5Department of Microbiology and Immunology, University of Mississippi Medical Center, Jackson, MS, USA; 6Department of Pathology, University of Alabama at Birmingham, Birmingham, AL, USA; 7Nabriva Therapeutics US, Inc., Fort Washington, PA, USA; 8Becton, Dickinson and Company, Franklin Lakes, NJ, USA; *Author for correspondence: Susanne.Paukner@nabriva.com

First draft submitted: 29 October 2021; Accepted for publication: 3 February 2022; Published online: 14 March 2022

What is this summary about?
Bacterial pneumonia is an infection of the lung caused by bacteria that is potentially deadly, costly, and affects millions of people worldwide every year. Treatment is becoming more challenging—many current treatments no longer work well because some strains of bacteria that cause pneumonia have become resistant to current antibiotics. Many of the antibiotics that do still work have undesirable side effects. Therefore, new antibiotics that work differently are needed to treat bacterial pneumonia.

Lefamulin (brand name, Xenleta®) is an antibiotic that was approved to treat bacterial pneumonia caught outside a hospital (also called community-acquired bacterial pneumonia, or CABP) based on results of two clinical studies. In both studies, participants started treatment with lefamulin before the type of bacteria causing the infection was known. Lefamulin was well tolerated and worked well in 5 to 7 days to kill the bacteria causing the infection and to improve symptoms in almost all participants with CABP.

What were the results?
After the studies were completed, the researchers looked back at what kinds of bacteria were identified from the study participants. Lefamulin worked well to kill bacteria and to improve CABP symptoms for most kinds of infecting bacteria, including bacteria resistant to many current antibiotics.

What do the results mean?
These results suggest that lefamulin, by itself, provides a much-needed treatment option for CABP that covers most of the key bacteria causing this infection.
This summary may be useful for non-specialist healthcare professionals (such as doctors, nurse practitioners, physician assistants, clinical pharmacists, etc.) who treat patients with a clinical diagnosis of CABP as well as patients with CABP and their families or caregivers. This article may be of particular interest to people who have had CABP or clinicians who have treated patients for CABP with previous recent antibiotic therapy, which may indicate a case of antibiotic resistance.

Nabriva Therapeutics funded the LEAP studies and was involved in study design, study oversight, data collection, and data analysis. The studies were approved by ethics committees at each participating health site or clinic.

Who is this article for?

Who sponsored this study?

What are pneumonia and CABP?

Pneumonia is an infection of the lung that can be caused by bacteria, viruses, or fungi. In the United States, pneumonia is one of the most common causes of hospitalization and a leading cause of death from infection:

Each year in the United States, pneumonia results in:

- 1.3 million emergency department visits
- 740,000 to 1.6 million hospital stays
- 74,000 to 160,000 deaths

Community-acquired bacterial pneumonia, shortened to CABP, is a type of pneumonia caused by a bacterial infection of the lung. It is called ‘community acquired’ because it is caught from the local community, not from within a hospital.

Common symptoms of CABP include:

- cough
- the production of phlegm
- difficulty breathing
- chest pain
- tiredness
- fever
- chills

Phlegm is the thick mucus within the airways that is often produced in large quantities when a person has pneumonia.

CABP can be caused by any kind of bacteria that infect the lung; however, the kinds of bacteria that most often cause CABP are:

- *Streptococcus pneumoniae* (shortened to *S. pneumoniae*)
- *Haemophilus influenzae* (shortened to *H. influenzae*)
- *Staphylococcus aureus* (shortened to *S. aureus*)
- *Chlamydia pneumoniae* (shortened to *C. pneumoniae*)
- *Mycoplasma pneumoniae* (shortened to *M. pneumoniae*)
- *Legionella pneumophila* (shortened to *L. pneumophila*)

People are at higher risk of getting CABP if they are:

- 65 years or older
- smoke
- have a weak immune system
- have other health conditions such as asthma, diabetes, or heart, kidney, liver, or chronic lung disease
What are antibiotics?

An antibiotic is a type of medicine that kills bacteria or stops bacterial growth.

Antibiotics are grouped into categories according to their chemical structure or shape and how they kill bacteria or stop bacterial growth.

Antibiotic categories that are discussed in this article include:

- **Macrolides**: antibiotics with a unique chemical structure that stop bacterial growth by blocking their ability to make proteins; common examples of macrolides include azithromycin, clarithromycin, and erythromycin.

- **Penicillins**: antibiotics with a unique chemical structure that kill bacteria by blocking their ability to build a cell wall; common examples of penicillins include amoxicillin, ampicillin, and penicillin.

- **Fluoroquinolones**: antibiotics with a unique chemical structure that kill bacteria by blocking their ability to copy their genetic material; common examples of fluoroquinolones include ciprofloxacin, moxifloxacin, and levofloxacin.

- **Pleuromutilins**: antibiotics with a unique chemical structure (but different from that of macrolides) that stop bacterial growth by blocking their ability to make proteins; lefamulin, the medicine discussed in this article, is a pleuromutilin.

Why is antibiotic resistance a growing problem in CABP?

Antibiotic resistance means that:

- The bacteria are not killed and continue to grow
- The antibiotic no longer works as a medicine
- Infections caused by antibiotic-resistant bacteria are harder to treat

For a long time, antibiotics called macrolides have been a key medicine used for empiric treatment of CABP.

However, *S. pneumoniae* and other bacteria that frequently cause CABP are becoming resistant to many of the antibiotics that are used to treat it, such as macrolides.

When treating CABP, most recent guidelines that healthcare practitioners follow recommend avoiding macrolides if the local *S. pneumoniae* resistance to macrolides is 25% or greater (see text and map on next page for more details).

To understand what this means, let’s take a closer look at resistance of *S. pneumoniae* bacteria to macrolide antibiotics:

- When a person with a respiratory infection seeks medical attention, the healthcare practitioner wants to know what has caused that person’s infection. To find that out, a sample that is coughed up (sputum) will usually be tested. Sometimes, if a patient is seen in the Emergency Room, a blood sample might also be tested.
  - If bacteria are found in a patient’s sample, then additional tests are done to find out what antibiotics those bacteria are resistant to, if any.
  - Across the United States, many thousands of patient samples are tested in this way every year, and those test results can answer questions about patterns of infections and antibiotic resistance.
They took samples from 329 medical care facilities across the United States. *S. pneumoniae* was found and isolated 3626 independent times.

Of the 3626 specimens, 39.5% were resistant to the macrolide antibiotics azithromycin, clarithromycin, or erythromycin.

Looking at the 9 individual census regions within the United States, resistance rates ranged from 14% to 54%.

- This map shows that resistance rates to macrolide antibiotics are greater than 25% in many regions in the US.

- Because resistance rates vary considerably even within US states, some states with lower overall resistance rates may still have a town or county with resistance rates that are higher than 25%.

When conducting a census, the US Department of Health and Human Services divides the United States into 9 regions. *S. pneumoniae* macrolide resistance rates between October 2018 and September 2019 were measured for each census region and are shown in this map. The following 21 individual states did not have enough data to contribute to this analysis: Alaska, Arizona, Colorado, Connecticut, Delaware, Hawaii, Idaho, Kansas, Maine, Massachusetts, Montana, Nevada, New Hampshire, North Dakota, Oregon, Rhode Island, South Carolina, Tennessee, Utah, Vermont, and Wyoming.

Follow this link to the original published article to see a detailed map of macrolide resistance rates by individual US zip codes: [https://academic.oup.com/ofid/article/8/7/ofab063/6128791](https://academic.oup.com/ofid/article/8/7/ofab063/6128791)
Why are new antibiotics needed?

- Because *S. pneumoniae* rates of resistance to macrolides are so high, alternative antibiotics to macrolides are needed for empiric treatment (i.e., treatment given before a complete diagnosis is established). However, many of the currently available alternatives kill not only the types of bacteria that often cause pneumonia, but also the types of beneficial bacteria that help the body with other necessary functions such as maintaining gut health.

- Many non-macrolide antibiotic alternatives may also have safety concerns:
  - **Penicillin antibiotics** such as amoxicillin are effective against many of the types of bacteria that cause CABP, but penicillin resistance is very common and up to 10% of the population reports some form of allergy to these drugs. Also, penicillins often require multiple pills per dose and 3 or more doses within 24 hours. These requirements might result in some patients taking only part of the prescribed treatment, which increases the risk of drug resistance because not all of the bacteria may be killed.
  - **Fluoroquinolone antibiotics** such as moxifloxacin are active against a wider range of bacteria and are often used in more serious infections, or to treat infections thought to be resistant to penicillins. However, side effects involving tendons, muscles, joints, nerves, blood vessels, blood sugar, and mental health have been seen with these antibiotics.

- The ability to take these antibiotics **orally** often allows patients to leave the hospital and complete treatment of pneumonia and other severe infections at home. As antibiotic resistance and safety concerns grow, however, some of these antibiotics will no longer be able to treat infections at home.

- Therefore, new antibiotic options are needed for the types of bacteria that often cause CABP.

What is lefamulin?

- Lefamulin is used to treat people with CABP and is the first pleuromutilin antibiotic for humans that can be taken by mouth or **IV infusion** twice a day for 5 to 7 days.

- Pleuromutilin antibiotics such as lefamulin kill bacteria by blocking bacterial protein production, which prevents bacterial growth and reproduction.

- Because lefamulin belongs to a new group of antibiotics and works in a unique way, bacteria are less likely to be resistant or to become resistant to lefamulin than to some other antibiotics.

- Lefamulin works well against bacteria that are resistant to other antibiotics often prescribed in CABP.

- Researchers have shown that lefamulin has a **narrow spectrum** of antibacterial activity, which means that it works well against the kinds of bacteria that often cause pneumonia but not against the kinds of good bacteria that help the body with necessary functions such as maintaining a healthy gut. This means that lefamulin does not kill most gut bacteria, so relevant gastrointestinal side effects may be minimized.
Function of the bacterial ribosome

1. Messenger RNA contains the instructions to build a protein, and a ribosome is the machinery that reads and carries out those instructions.

2. The ingredients needed to make a protein are called amino acids, which are carried to the ribosome by transfer RNA.

3. Transfer RNA moves through the ribosome and the new amino acid is added to build a growing protein chain.

4. Empty transfer RNA exits the ribosome.

5. Newly created proteins go on to contribute to vital functions in bacteria such as growth and replication.

Bacterial ribosome blocked by lefamulin

1. Lefamulin binds to ribosomes, blocking binding of transfer RNA.

2. Transfer RNA with amino acid is blocked and cannot bind to the ribosome.

3. No new proteins can be created, vital functions such as growth and replication stop, and bacteria die.

- When a patient has CABP, the bacteria infecting their lungs are growing and multiplying.
- Inside those bacteria, cellular machinery called ribosomes create proteins, which are vital building blocks that bacteria use to grow and multiply.

- When a patient with CABP is treated with lefamulin, lefamulin travels through the body until it finds the bacteria.
- Lefamulin binds to ribosomes inside the bacteria and blocks the ability of those ribosomes to create proteins.
- Without proteins, bacteria cannot grow or multiply and the infection is stopped.
- Once the infection has been stopped, the patient’s body can begin to recover.
What was the purpose of the LEAP 1 and LEAP 2 clinical studies?

- LEAP is an abbreviation of the study name Lefamulin Evaluation Against Pneumonia. There were two studies, LEAP 1 and LEAP 2, that were standard clinical studies to investigate lefamulin as a treatment for patients with CABP.

- The main aim of the studies was to see if lefamulin was at least as good as moxifloxacin (a fluoroquinolone antibiotic) in treating patients with CABP.

  - In both studies, moxifloxacin was the positive control, which means that the researchers already knew before starting the study that it would likely work as a treatment for CABP.

Who took part in the clinical studies?

- The LEAP 1 and LEAP 2 studies included 1289 participants (56% men, 44% women) who ranged in age from 19 to 97 years old.

  - The trials included participants from 23 countries:

    - Argentina
    - Brazil
    - Bulgaria
    - Chile
    - Colombia
    - England
    - France
    - Georgia
    - Greece
    - Hungary
    - India
    - Indonesia
    - Italy
    - Japan
    - Korea (Republic of)
    - Mexico
    - Nigeria
    - Pakistan
    - Poland
    - Russia
    - Spain
    - Taiwan
    - The Netherlands
    - United States

- LEAP is an abbreviation of the study name Lefamulin Evaluation Against Pneumonia. There were two studies, LEAP 1 and LEAP 2, that were standard clinical studies to investigate lefamulin as a treatment for patients with CABP.

- The main aim of the studies was to see if lefamulin was at least as good as moxifloxacin (a fluoroquinolone antibiotic) in treating patients with CABP.

- In both studies, moxifloxacin was the positive control, which means that the researchers already knew before starting the study that it would likely work as a treatment for CABP.

- A positive control group in a study does not receive the experimental treatment but instead receives a treatment that is known to produce a positive result; the positive control group provides the basis for comparison to the experimental group.

- All participants had CABP, with the diagnosis confirmed by x-ray, and some or all of the following symptoms:

  - Fever
  - Low blood oxygen
  - Levels of white blood cells that indicate the body is fighting an infection
  - Difficulty breathing
  - New or increased cough
  - Chest pain
  - Production of phlegm

- Some key reasons why people were not allowed to participate in the studies were:

  - Had already received antibiotics for their current illness
  - Had already been hospitalized for their current illness
  - Had, or were at risk for developing, significant liver or heart disease
What happened during the clinical studies?

- These studies looked at how many participants responded to each treatment.

- Researchers considered CABP to be resolved (i.e., successfully treated) if patients were alive and met 3 conditions:
  - At least 2 of 4 CABP symptoms (difficulty breathing, cough, chest pain, production of phlegm) improved, and
  - No CABP symptoms worsened, and
  - No extra antibiotics were needed to treat the infection.

What were the overall study results?

After 3 to 5 days of treatment with lefamulin, symptoms were improved or CABP was resolved in most patients:

- **Lefamulin**
  - Twice daily for 5 – 7 days
  - Symptom improvement
  - 89% resolved
  - Of 646 participants who received lefamulin

- **Moxifloxacin**
  - Once daily for 7 days
  - Symptom improvement
  - 85% resolved
  - Of 641 participants who received moxifloxacin

At 5 to 10 days after the last day of treatment, symptoms remained improved or CABP remained resolved in most patients:

- **Lefamulin**
  - Twice daily for remaining days
  - Symptom improvement
  - 91% resolved
  - Of 643 participants who received moxifloxacin

- **Moxifloxacin**
  - Once daily for remaining days
  - Symptom improvement
  - 87% resolved
  - Of 641 participants who received moxifloxacin
Lefamulin improved symptoms and resolved CABP in most participants regardless of medical history or pre-existing conditions, including:

- Advanced age
- Diabetes
- Heart disease
- Smoking history
- Lung disease
- Kidney disease
- Liver disease

Lefamulin and moxifloxacin improved symptoms and resolved CABP in most participants regardless of whether given by IV infusion or by mouth.

**What bacteria were found in participants?**

- In patients with pneumonia, identification of the underlying bacterial cause is difficult because of problems in obtaining a reliable sample to test. However, in the LEAP studies, bacteria were identified in 709 of 1289 (55%) participants. In these participants, the bacteria that were found included:

| Bacteria                        | Percentage | Participants Infected with |
|---------------------------------|------------|-----------------------------|
| *Streptococcus pneumoniae*     | 62%        |                             |
| *Haemophilus influenzae*       | 30%        |                             |
| *Staphylococcus aureus*        | 5%         |                             |
| *Mycoplasma pneumoniae*        | 10%        |                             |
| *Legionella pneumophila*       | 9%         |                             |
| *Chlamydia pneumoniae*         | 8%         |                             |
Did lefamulin work against each of these different kinds of bacteria?

Yes, both in the laboratory setting (where lefamulin was tested directly on the bacteria) and in study participants (who were treated with oral or IV lefamulin)

- Although participants were treated with lefamulin or moxifloxacin for 5 to 7 days, symptoms were improved or CABP was resolved within 3 to 5 days of treatment in 85% to 100% of participants, regardless of the bacterial cause
- For all bacterial types, symptoms were improved or CABP was resolved in similar percentages of patients, regardless of whether they were treated with lefamulin or moxifloxacin:

### Percentages of patients with improved symptoms or resolved CABP by bacterial cause of infection

| Bacterial Cause                  | Participants Receiving Lefamulin | Participants Receiving Moxifloxacin |
|----------------------------------|----------------------------------|-------------------------------------|
| *Streptococcus pneumoniae*       | 89% (192 of 216)                 | 92% (206 of 223)                    |
| *Staphylococcus aureus*          | 100% (23 of 23)                  | 100% (10 of 10)                     |
| *Haemophilus influenzae*         | 91% (97 of 107)                  | 93% (98 of 105)                     |
| *Mycoplasma pneumoniae*          | 92% (36 of 39)                   | 94% (32 of 34)                      |
| *Legionella pneumophila*         | 85% (29 of 34)                   | 90% (28 of 31)                      |
| *Chlamydia pneumoniae*           | 93% (25 of 27)                   | 97% (30 of 31)                      |

*Antibiotics that do not work might include: oral penicillin, moxifloxacin, ceftriaxone, clindamycin, azithromycin or erythromycin, doxycycline, or trimethoprim/sulfamethoxazole*

Were antibiotic-resistant bacteria found in the study participants?

Yes – among the 439 participants who were infected with *S. pneumoniae*, 3 categories of antibiotic resistance were found:

- **Penicillin resistant**
  - In 14 participants, isolates were **PENICILLIN RESISTANT**, which means that the antibiotic penicillin **DOES NOT WORK** against these isolates

- **Macrolide resistant**
  - In 31 participants, isolates were **MACROLIDE RESISTANT**, which means that antibiotics such as azithromycin or erythromycin **DO NOT WORK** against these isolates

- **Multidrug resistant**
  - In 32 participants, isolates were **MULTIDRUG RESISTANT**, which means that at least 1 antibiotic in at least 3 antimicrobial categories **DO NOT WORK** against these isolates
Did lefamulin work against these antibiotic-resistant bacteria?

Yes, both in the laboratory setting (where lefamulin was tested directly on the bacteria) and in study participants (who were treated with oral or IV lefamulin):

- In the laboratory setting, the antibiotic resistance of these bacteria had no effect on how well lefamulin and moxifloxacin worked
- In the study participants who were infected with drug-resistant *S. pneumoniae*, symptoms were improved or CABP was resolved in 93% to 100% of those who received lefamulin and in 82% to 86% of those who received moxifloxacin, regardless of the type of antibiotic resistance of these bacteria:

| Antibiotic resistance | Participants receiving lefamulin | Participants receiving moxifloxacin |
|-----------------------|----------------------------------|-----------------------------------|
| S. pneumoniae         | 100% (7 of 7)                    | 86% (6 of 7)                      |
| Penicillin-resistant  |                                  |                                   |
| Macrolide-resistant   | 93% (13 of 14)                   | 82% (14 of 17)                    |
| S. pneumoniae         |                                  |                                   |
| Multidrug-resistant   | 100% (14 of 14)                  | 83% (15 of 18)                    |

These results were observed after 3 to 5 days of treatment, and, in all but 2 patients, symptoms did not return and CABP remained resolved in most patients after completing the full 5 to 7 days of treatment.

A full report of the combined LEAP 1 and LEAP 2 study results can be found on the websites listed at the end of this summary.

What were the most common side effects?

- For both lefamulin and moxifloxacin, the most common side effects during the clinical studies were diarrhea, nausea, and vomiting; this is similar to many other antibiotic treatments
- In more than 95% of patients, side effects were mild to moderate in severity and did not lead to stopping the medication
- These side effects happened more often when medications were given by mouth than by IV infusion
Percentages of patients with the most common side effects

- Lefamulin and moxifloxacin both have the potential to cause a disturbance in the normal rhythm of the heart. Treatment should therefore be avoided in patients taking medications known to have similar effects on the heart and in patients with certain heart conditions.
- Findings from studies in animals suggest that lefamulin may cause fetal harm if given to pregnant women. Women of reproductive potential should be made aware of this possible risk.

What do the results of these studies mean?

- The results from these studies showed that:
  - In almost all participants, 5 to 7 days of treatment with lefamulin was sufficient to improve symptoms and resolve CABP.
  - Lefamulin worked well against the most common causes of CABP, including several types of infections that cannot be treated with other antibiotics due to resistance.
  - Lefamulin worked at least as well as moxifloxacin to improve symptoms and resolve CABP and could be considered an alternative to fluoroquinolones.
  - The total duration of treatment with lefamulin, 5 to 7 days, was the same as or shorter than treatment with moxifloxacin (7 days).
  - Lefamulin was well tolerated, and side effects were similar between treatment groups.
  - Lefamulin can be taken as either an IV infusion or oral tablet and can be used in patients being treated either in or out of the hospital.

- Because of growing concerns regarding the safety and tolerability of commonly used antibiotics, these results suggest that lefamulin, by itself, provides a much-needed treatment option for CABP without needing to identify the bacteria causing the infection.

Based on the results of these studies, lefamulin was the first pleuromutilin antibiotic approved in the United States, Europe, and Canada as an empiric IV infusion and/or oral single-drug treatment for people with CABP.
How lefamulin alone can be used to treat pneumonia

Plain Language Summary of Publication

Where can readers find more information?

• Lefamulin prescribing information can be accessed here: https://www.xenleta.com

• The information summarized in this article about lefamulin for treatment of CABP is from the article “Pooled Microbiological Findings and Efficacy Outcomes by Pathogen in Adults With Community-Acquired Bacterial Pneumonia from the Lefamulin Evaluation Against Pneumonia (LEAP) 1 and LEAP 2 Phase 3 Trials of Lefamulin Versus Moxifloxacin,” which was published in the Journal of Global Antimicrobial Resistance in 2021. The original article is free to access and can be found at: https://www.sciencedirect.com/science/article/pii/S2213716521002459

• The information summarized in this article about bacterial resistance to macrolide antibiotics in the United States is from the article “A Multicenter Evaluation of the US Prevalence and Regional Variation in Macrolide-Resistant S. pneumoniae in Ambulatory and Hospitalized Adult Patients in the United States,” which was published in Open Forum Infectious Diseases in 2021. The original article is free to access and can be found at: https://academic.oup.com/ofid/article/8/7/ofab063/6128791

• Additional findings from the LEAP 1 and LEAP 2 studies of lefamulin for CABP can be found in the following articles:
  • The main results from the LEAP 1 study, entitled “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,” were published in Clinical Infectious Diseases in 2019. The original article is free to access and can be found at: https://academic.oup.com/cid/article/69/11/1856/5306243
  • The main results from the LEAP 2 study, entitled “Oral Lefamulin vs Moxifloxacin for Early Clinical Response Among Adults With Community-Acquired Bacterial Pneumonia: the LEAP 2 Randomized Clinical Trial,” were published in JAMA in 2019. The original article is free to access and can be found at: https://jamanetwork.com/journals/jama/fullarticle/2752331
  • The results from the subgroup analysis of outpatients from the LEAP 2 study, entitled “Oral 5-Day Lefamulin for Outpatient Management of Community-Acquired Bacterial Pneumonia: Post-hoc Analysis of the Lefamulin Evaluation Against Pneumonia (LEAP) 2 Trial,” were published in the Journal of Emergency Medicine in 2021. The original article is free to access and can be found at: https://www.sciencedirect.com/science/article/pii/S0736467921001025?via%3Dihub
  • The results from the LEAP 1 and LEAP 2 studies in subgroups of participants with CABP simultaneously with other common medical conditions such as advanced age, diabetes, chronic lung disease, heart disease, kidney disease, or liver disease, entitled “Lefamulin Efficacy and Safety in a Pooled Phase 3 Clinical Trial Population With Community-Acquired Bacterial Pneumonia and Common Clinical Comorbidities,” were published in BMC Pulmonary Medicine in 2021. The original article is free to access and can be found at: https://bmcpulmmed.biomedcentral.com/articles/10.1186/s12890-021-01472-z

What other resources are available?

• Lefamulin: treatment of CABP and its place in therapy: https://www.youtube.com/channel/UCcXLVC0xsFEw16KA2s8NdVQ/videos
• Bacterial pneumonia: https://www.webmd.com/lung/bacterial-pneumonia
• Management of CABP: https://www.uptodate.com/contents/treatment-of-community-acquired-pneumonia-in-adults-in-the-outpatient-setting?topicRef=70278&source=see%20link
• CABP Treatment Guidelines: https://www.atsjournals.org/doi/10.1164/rccm.201908-1581ST
• Antibiotic resistance: https://www.cdc.gov/drugresistance/index.html
• Drug-resistant Streptococcus pneumoniae: https://www.cdc.gov/Pneumococcal/Drug-Resistance.html
• Interactive dashboard for surveillance of bacterial infections in the United States: https://www.cdc.gov/abcs/bact-facts-interactive-dashboard.html
• Penicillin allergies: https://www.cdc.gov/antibiotic-use/clinicians/penicillin-allergy.html
• Risks associated with fluoroquinolone antibiotics: https://www.fda.gov/news-events/press-announcements/fda-updates-warnings-fluoroquinolone-antibiotics-risks-mental-health-and-low-blood-sugar-adverse
Acknowledgements
The authors and sponsor would like to thank the patients, their families and caregivers, the investigators, and the investigational site staff from the LEAP 1 and LEAP 2 studies.

Financial & competing interests disclosure
Drs Paukner and Gelone are employees of stockholders in Nabriva Therapeutics plc. Dr Moran has received grants from ContraFect and Nabriva Therapeutics. Dr Sandrock has served as a consultant for Allergan and Nabriva Therapeutics, received grants from the National Institutes of Health and the Health Resources Services Administration, and received nonfinancial support from the State of California. Dr File was an investigator for the LEAP 1 trial, for which his institution received a research grant, and has served as a consultant for Nabriva Therapeutics. Dr Vidal has received grants or research contracts from the Bill and Melinda Gates Foundation, Melinta Therapeutics, MSD, Nabriva Therapeutics, the National Institutes of Health, and Pfizer. Dr Waites has received research grants and/or contracts from Akonni Biosystems, Covance, Inc., Everest Pharmaceuticals, mFluiDx, Roche Molecular Systems, SpeeDx, Ltd., US Centers for Disease Control and Prevention, National Institutes of Health, and Wockhardt Ltd. Dr Yu is an employee of Becton, Dickinson & Company, which was contracted to perform microbiological analyses for Nabriva Therapeutics, and owns stock in Becton, Dickinson & Company. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Editorial assistance and medical writing support for development of this publication were provided by Morgan C. Hill, PhD, ISMPP CMPP™, an employee of ICON (Blue Bell, PA, USA) and were funded by Nabriva Therapeutics.