The Voice of the Patient

A series of reports from the U.S. Food and Drug Administration’s (FDA’s) Patient-Focused Drug Development Initiative

Non-Tuberculous Mycobacterial (NTM) Lung Infection
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Introduction

On October 15, 2015, FDA held a public meeting on non-tuberculous mycobacterial (NTM) lung infections to gain insight into the experiences of NTM patients, caregivers, and other patient representatives on the most significant symptoms of their disease, its impact on daily life, and on currently available therapies. FDA conducted the meeting as part of the agency’s Patient-Focused Drug Development (PFDD) initiative, an FDA commitment under the fifth authorization of the Prescription Drug User Fee Act (PDUFA V) to more systematically gather patients’ perspectives on their condition and available therapies to treat their condition. As part of this commitment, FDA is holding at least 20 public meetings between Fiscal Years 2013 and 2017, each focused on a specific disease area.

More information on this initiative can be found at http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm326192.htm

In the afternoon, FDA held a scientific workshop (summarized on page 15) to explore challenges related to drug development for NTM. This workshop was intended to provide a platform for patients, academic experts, healthcare providers, government officials, industry, and advocacy organizations, to share their perspectives and gather information on NTM lung infections.

Overview of non-tuberculous mycobacterial (NTM) lung infections

Non-tuberculous mycobacterial lung infection is a chronic, progressive disease that occurs as a result of inhalation of mycobacteria from exposure to environmental sources. The Mycobacterium genus represents more than 150 naturally-occurring Mycobacterium species that are ubiquitously found in the environment, especially in water and soil. The American Lung Association estimates that there are about 50,000 to 90,000 people living with NTM lung infections in the United States, with a higher frequency in older adult women than men. Most NTM infections are due to the Mycobacterium avium complex (MAC), Mycobacterium abscessus, and Mycobacterium kansasii. People with underlying lung conditions such as bronchiectasis, cystic fibrosis (CF), and chronic obstructive pulmonary disease (COPD) are more susceptible to NTM lung infections. NTM is characterized by a range of symptoms that often worsen over time, including persistent cough, shortness of breath, fatigue, sputum production, low-grade fever, night sweats, and weight loss.

There are several treatment options that aim to reduce symptoms, improve the quality of life, reduce lung damage, and slow disease progression. Typical treatments, which may be used by patients for 2-3 years, include a combination of oral, inhaled, and intravenous antibacterial drugs. Non-drug therapies, such as percussion vests, continuous positive airway pressure (CPAP), lifestyle modifications, diet, and exercise are also used to manage symptoms.

Meeting overview

The NTM PFDD meeting provided FDA with the opportunity to hear directly from patients, patient representatives, and patient advocates about their experiences and perspectives on NTM and its treatments. The discussion focused on two key topics: (1) disease symptoms and daily impacts that matter most to patients and (2) patients’ perspectives on current approaches to treating NTM. The questions for the morning discussion (Appendix 1) were published in a Federal Register notice that
announced the meeting. For each topic, a panel of patients and a caregiver (who is also a patient advocate) initiated the dialogue by sharing their experiences on symptoms and impacts of NTM on their daily life. Panel comments were followed by a facilitated discussion inviting comments from other patients and patient representatives in the audience. The discussion was led by an FDA facilitator, and a panel of FDA staff (Appendix 2) asked follow-up questions. Participants who joined the meeting via live webcast were able to submit comments throughout the discussion, and their comments are incorporated into this report. In-person and web participants were periodically invited to respond to polling questions (Appendix 3), which provided a sense of the demographic makeup of participants, as well as of how many participants shared a particular perspective on a given topic.

Approximately 50 patients with NTM or patient representatives attended the meeting in-person, and approximately 25 patients or patient representatives provided input through the live webcast. Based on their responses to the polling questions, in-person and web participants represented a range of experiences with NTM, with most reporting bronchiectasis as an underlying lung condition. The majority of in-person participants were between ages 61 and 74, and most had been diagnosed with NTM more than 5 years ago. Although participants at this meeting may not fully represent the overall population of patients with NTM, FDA believes that the input received reflects a range of experiences on NTM symptoms and treatments.

To supplement the input gathered at the meeting, the public was encouraged to submit comments on the topic to a public docket, which was open until December 14, 2015. Thirty-eight comments were submitted to the public docket.

More information, including the archived webcast and meeting transcript, is available on the meeting website: http://www.fda.gov/Drugs/NewsEvents/ucm453877.htm.

Report overview and key themes

This report summarizes the input provided by patients and patient representatives at the meeting, through the webcast, and in comments submitted to the public docket. It also includes a brief overview of the discussion by academic researchers and healthcare professionals during the afternoon’s scientific workshop session. To the extent possible, the terms used in this report to describe specific NTM symptoms, impacts, and treatment experiences reflect the words used by in-person participants, web participants, and docket commenters. The report is not meant to be representative in any way of the views and experiences of any specific group of individuals or entities. There may be symptoms, impacts, treatments, or other aspects of the disease that are not included in the report.

The input from the meeting and docket comments underscore the chronic and debilitating effect that NTM has on patients’ lives, the challenges they face in finding effective and tolerable therapies to manage their condition, and the diverse experiences of patients with NTM. Several key themes emerged from this meeting:

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2 A docket is a repository through which the public can submit electronic and written comments on specific topics to U.S. federal agencies such as FDA. More information can be found at www.regulations.gov.
• NTM infections cause chronic and devastating lung disease with debilitating symptoms, including fatigue, chronic cough, and shortness of breath. Participants described the significant detrimental impact of these and other symptoms on daily life. Participants emphasized how these symptoms worsen over time, and are exacerbated by common environmental factors that irritate the lungs.

• NTM affects all aspects of patients’ lives. Participants described the drastic change from their active and independent lives before diagnosis. Many participants noted that the significant decline in health caused them or their loved ones to limit or completely stop participating in activities that they once enjoyed or were able to do, which led to social isolation. Participants also shared that their constant coughing was often misunderstood by others as being contagious, which left them or their loved ones feeling stigmatized and embarrassed.

• Participants described using a combination of antibiotic drugs, steroids, and pain medicines in addition to non-drug therapies, all of which had varying degrees of success with managing symptoms. Participants emphasized the downsides of treatment and the life-threatening side effects they experienced. Participants shared that they valued the benefits of non-drug therapies, especially exercise and pulmonary rehabilitation.

• Nearly all participants expressed the need for treatment that was effective in slowing down disease progression in addition to stopping lung deterioration. Participants focused on the need for treatments that have minimal life threatening side effects, decreased the number of exacerbations they experienced, and on drugs with shorter, less complicated dosing schedules. Other participants expressed the need for earlier and better diagnosis, stem cell research, and personalized therapy.

The patient input generated through this Patient-Focused Drug Development meeting and public docket comments strengthens FDA’s understanding of the burden of NTM disease on patients and their experiences on treatments currently used to manage NTM disease and its symptoms. FDA will carefully consider this input as it fulfills its role in the drug development process, including when advising sponsors on their drug development programs and when assessing products under review for marketing approval. For example, Appendix 4 shows how this input may directly support our benefit-risk assessments for products under review. This input may also be of value to the drug development process more broadly. For example, the report may be useful to drug developers as they explore potential treatments that are effective in limiting disease progression and preventing lung deterioration. It could also point to the potential need for a better understanding of particular aspects of disease treatments, such as the best ways to define response to therapy, and the development and qualification of new outcome measures in clinical trials.

Topic 1: Disease Symptoms and Daily Impacts That Matter Most to Patients

The first discussion topic focused on patients’ experiences with their NTM symptoms and the resulting effects on their daily lives. FDA was particularly interested in hearing about specific activities that patients can no longer do, or as fully as they would like, because of their condition.

Four panelists (Appendix 2) provided comments to begin the dialogue. They included: a caregiver
speaking on behalf of his late wife who had died from NTM; a woman who described experiencing symptoms for several years before a formal diagnosis; a woman diagnosed 15 years ago who was off medications for over two years because her lung scans showed improvement; and a woman who was diagnosed with NTM two years ago.

All panelists reported having symptoms for several years prior to a formal diagnosis, and described the difficulty of living with an “invisible disorder” with significant physical, emotional, and social impacts. Panelists shared their feelings of stress, anxiety, and fear of recurrence or re-infection because of their condition. In the large-group facilitated discussion that followed the panel discussion, the majority of patients, caregivers, and patient representatives in the audience indicated by a show of hands that the panelists’ comments resonated with their experiences (or those of loved ones). Several participants described the unexpected and unpredictable nature of their condition.

Perspectives on most significant symptoms

In a polling question (Appendix 3, Q7), participants were asked to identify up to three symptoms that have the most significant impact on daily life. Coughing (including coughing up blood, phlegm or mucus), fatigue, shortness of breath and other breathing difficulties received the highest number of responses. Responding web participants reported similar results to those in person. The facilitated discussion provided deeper insights into how different symptoms manifest, what triggers them, and how they have changed over time. The range of symptoms discussed by in-person and web participants is described in more detail below.

Coughing

Chronic cough or coughing up blood (hemoptysis), phlegm, and sputum was mentioned by the majority of in-person participants and web participants as being the most significant symptom they experienced. Participants described their experiences with coughing up green sputum. Coughing was identified in unique ways: “hacking,” “barking,” “episodic,” “choking mucous,” “deep,” and “painful.” Some participants shared that severe bouts of coughing often left them “doubled-over” in pain. One participant compared her coughing at night to feeling like she is “drowning in mucous and can't swallow.”

The following examples provide a description of participants coughing experiences:

- “[My coughing] will go on for 5 or 10 minutes... I walk up the street and suddenly I'm seized with this huge coughing episode... It just doesn't stop.”

- “It [coughing] could go on for a good 90 minutes, and I'm just down on the floor, on my knees, grabbing my ribs, hacking.”

- “The first year I was coughing, I broke two ribs and vertebrae in my back.”

Participants identified several triggers as “lung irritants” that can result in prolonged episodes of coughing fits, including:
- Changes in weather
- Sprays and fumes
- Sleeping position (e.g., lying down flat)
- Physical exertion
- Air conditioning
- Talking
- Eating
- Laughing
- Dust
- Mold

Several participants described “a vicious cycle of symptoms,” in which one symptom led to or exacerbated other symptoms. One participant described that “cough[ing] causes so much pain [due to] pulling muscles [and] it leads right into the fatigue.” Participants commented that severe coughing often led to vomiting and a loss of appetite. Several participants also noted that their fatigue was due to a lack of sleep from trying to find a good position that prevents wheezing and coughing.

**Fatigue**

The majority of in-person and web participants identified fatigue as one of the most significant symptoms impacting their daily life. Descriptions of fatigue ranged from feeling “tired to your core,” to “walking through molasses.” One participant noted, “I've been in the grocery store with the shopping cart, but I didn't have the energy to wait in line to check out.” Participants also described sudden, unpredictable bouts of fatigue. One participant shared, “It's just hard to accept, to surrender, to give in, but that's how suddenly it [fatigue] comes upon you.”

Participants also described average and severe days of fatigue. One participant shared, “On those [severe] days, if I can, I cancel everything and try to lay low.” Another participant described an average day of fatigue as “a day where I... get a bunch of things done [by] mostly do[ing] one thing and then I have to take a nap.” Several participants noted that even after taking a long nap, they often woke up feeling unrefreshed.

Other participants commented on how they often had to “allocate” their energy to manage their fatigue. One participant shared, “My day is based on personal energy. I plan out what I am going to do based on how I feel.”

**Shortness of breath**

Nearly half of in-person and web participants identified shortness of breath as one of their most significant symptoms. For most participants, the severity of their shortness of breath had a major impact on daily life and their overall health. Participants noted how shortness of breath impacts almost every activity, and often requires that they pace themselves to avoid feeling winded. Participants described episodes of breathing difficulty, including one grandmother who shared that her breathing difficulty impacts her interaction with her grandchildren, because she has to walk at her own pace and finds it impossible to talk and walk at the same time.

Participants identified several triggers that can result in breathing difficulties, including scents, walking, talking, and any physical activity that causes exertion.

A web participant described having an “asthmatic component to the illness.” One participant with a history of bronchitis and pneumonia due to having asthma and allergies noted that it was difficult to
differentiate whether her shortness of breath resulted from asthma or the underlying NTM lung infection.

Other symptoms

Several participants described a variety of gastrointestinal (GI) issues, including increased acid reflux, belching, and gastroesophageal reflux disease (GERD). One participant described her acid reflux as “trapped air in parts of the body.”

Other symptoms mentioned included, depression, anxiety, hemorrhoids, urinary incontinence, loss of appetite, weight loss, night sweats, and fever. Participants also mentioned a range of comorbid conditions such as osteoporosis and Sjogren's Syndrome.

Overall impact of NTM on daily life

Both in-person and web participants described in great detail the impact that their condition has on their daily life, including:

- **The ability to perform activities.** The majority of participants shared that the “lack of stamina” and “decreased energy” from fatigue, chronic coughing, and shortness of breath made them unable to participate in activities that they previously enjoyed. Participants described being unable to run, hike, “go walking through the woods,” exercise, sing, perform on stage, and paint. Many participants also shared that they were unable to perform household chores such as cooking, cleaning, and gardening. Although participants stated that shortness of breath limited their ability to perform activities, they stressed the importance of staying physically active.

- **The impact on work and career.** Participants stated that the impact of fatigue and chronic coughing made it difficult or impossible to perform their job duties or continue in their careers. One participant described stopping her career as an interior designer due to increased coughing caused by “being on a construction site with a lot of dust.” Another participant shared, “I retired early from teaching and no longer can participate in my theater or music activities because the constant coughing from bringing up the sputum has affected my vocal chords.”

- **Stigma and embarrassment.** Many participants described the reactions and embarrassment they experienced from constantly coughing, as others often assume they are contagious. One participant shared that when she was newly diagnosed with NTM, she would excuse herself to go to the restroom to cough, but now “because the bronchiectasis has gotten worse, you just cough up in tissues, and it’s repulsive to some.” Others felt embarrassed by the reaction their coughing provokes when they are out in public from people who think they are “dying” or that “something awful” is happening to them. One participant commented, “I was sitting on the front stoop, cough-spit, cough-spit. My neighbor came rushing over... It’s just an embarrassment…”

- **The impact on relationships.** Participants described the significant impact NTM lung infections had on their relationships with their family and friends. As one participant explained, “I don't go out. Most people go to barbecues and outdoor events. I stay in a lot because I don't want to
take the risk of getting sick.” Another participant explained how they “can barely hold conversations” with their children, friends and grandchildren. Several participants shared that their constant coughing made it difficult to participate in social situations. Some participants also shared how they often had to delay or cancel their plans due to the severity of their cough.

- **Fear of the future.** Several participants noted their fear of the future. As one participant shared, “I could take good care of myself [before], but I've declined a lot in the last couple of years.” Another participant worried about “being a pulmonary cripple.” Some participants stated that worry for the future was constantly on their mind.

**Topic 2: Patient Perspectives on Treatments for Non-tuberculous Mycobacterial Lung Infections**

The second discussion topic focused on patients’ experiences with therapies used to treat their NTM infection. Five panelists provided comments to start the dialogue, including: a woman who was diagnosed with both *M. abscessus* and *M. avium* and was not using any therapies to currently manage her NTM lung infection, a woman with bronchiectasis and *M. abscessus* who had been on treatment for 20 years, a woman who shared her experience with misdiagnosis, a thirty-five-year-old woman who described how NTM had impacted her ability to have children, and a woman with a lung infection caused by *M. abscessus* in the last five years.

In the large group facilitated discussion that followed, participants indicated by a show of hands that their experiences (or those of loved ones) were reflected in the panelists’ comments. Following the panel comments, there was a facilitated discussion on participants' perspectives on treatment approaches. Participants described their experiences switching between various medications to find an effective treatment regimen (including drug and non-drug therapies). Participants also discussed what they would look for in an ideal treatment, including considerations on clinical trial design. Their perspectives are summarized below.

**Prescription and over-the-counter drugs**

According to a polling question (*Appendix 3, Q8*), the majority of in-person and web participants reported taking or having taken drug therapies to treat their NTM symptoms. The most commonly mentioned drug therapies used were antibiotics, administered orally, intravenously, or inhaled. Prescription drug therapies were described as having widely varying degrees of effectiveness, and many participants noted decreased benefits over time.

*Prescription Drug Therapies*

Antibiotics were the most common treatments mentioned by participants for treating their conditions, such as bronchiectasis, bronchitis, pneumonia, *Staphylococcus, Serratia* and *Pseudomonas* infections. The majority of the participants stated that they began treatment with a three drug cocktail consisting of Biaxin (clarithromycin), Myambutol (ethambutol), and Rifadin (rifampin). Participants noted that more medications were often added as the disease progressed.
Participants shared that they took multiple antibiotics on and off for a very long time, with the exception of when they were given “drug holidays,” described by participants as a period of time during which their physician took them off a specific drug(s) due to a variety of reasons, including: intolerable side effects, potential drug resistance, the drug becoming ineffective, and lung scans showing improvements. Common antibiotics mentioned by participants included Amikin (amikacin), Mefoxin (cefoxitin), Biaxin (clarithromycin), Bactrim (trimethoprim), Cayston (aztreonam), , Augmentin (amoxicillin- clavulanate), Zithromax (azithromycin), Merrem (meropenem), and fluoroquinolones such as Cipro (ciprofloxacin), Levaquin (levofloxacin), and Avelox (moxifloxacin).

In addition to the antibiotics, participants identified several other prescription therapies. Therapies mentioned included Atrovent (ipratropium bromide) and AccuNeb (albuterol) to bring up more mucous and sputum, and decongestants to dry up excess mucous, Prozac (fluoxetine) for depression and anxiety, anti-fungal medicines such as Noxafil (posaconazole) and Diflucan (fluconazole), Prilosec (omeprazole) for acid reflux, Pyridoxine (vitamin B6) for neuropathy, and Lyrica (pregabalin) for pain.

Participants described the range of effectiveness for prescription therapies. Several participants shared that they could tell if a medication was effective when they experienced alleviation of symptoms, including increased energy and appetite, and decreased coughing and mucous production. Other participants shared that they were aware of improvements in their condition only through laboratory and imaging results. Some participants noted variability in antibiotic effectiveness due to drug resistance over the course of treatment, while others commented that they never experienced any treatment benefits.

Although participants acknowledged the benefits of these therapies, they also commented on the downsides. Participants mentioned a range of side effects of the antibiotics. These included: neuropathy, numb toes, severe vertigo, hearing loss, optic nerve damage, vision loss, sensitivity to stimuli, nausea, acid reflux, kidney and liver damage, and tinnitus. In addition, a thirty-five-year-old participant expressed concerns on the effect of prolonged use of antibiotics on fertility.

The majority of participants commented on the burdensome nature of prescription drug therapies, highlighting complicated dosing schedules and the complexity of taking multiple therapies. One participant mentioned that, “some medications have to be taken with food, while others have to be taken on an empty stomach.” Another participant commented on the timing of the different medications stating, “three times a week, I need an hour or two to take my inhaled amikacin [and] when intravenous antibiotics enter the regimen, they are usually [taken] 2 to 3 times a day.” Participants described the inconvenience this presents during travel and most stated that they had to limit travel during treatment. As one participant described, “inhaled therapy ... was a little tedious, because there was a nebulizer you had to keep clean. I had to take it with me on an airplane and a hotel room, and then sterilize the equipment.”

Devices and Medical Procedures

Several participants commented on the use of airway clearance devices, airway oscillating devices (such as Acapella or Aerobika), percussion vest therapy (such as the ABI vest), and using a continuous positive airway pressure (CPAP) machine. One participant mentioned pain and fatigue as downsides of having to wear the ABI vest for three to five hours a day to clear her lungs.
Some participants also mentioned undergoing medical procedures on their lungs, such as a lung resection in the upper and middle lobes (lobectomy). One participant stated that the procedure was very effective that, they had a “negative [sputum] for about three and a half years.” Another participant noted that their surgery was so successful that it “greatly improved [their] condition and reduced the sensitivity [to scents].”

Non-drug therapies

Several participants mentioned the importance of non-drug therapies as part of their treatment regimen. The most commonly mentioned non-drug therapies noted by webcast and meeting participants were exercise, pulmonary rehabilitation, breathing and relaxation techniques. Other non-drug therapies mentioned included hypertonic saline solution rinse, dietary supplements, and diet modifications such as probiotics from yogurt to “balance the negative effects of the medications on [the] digestive system and [to deal with] yeast infections.” Some participants described alternative approaches to therapies including acupuncture, massage, meditation, and prayer.

Participants stated that these treatments helped to increase their ability to function and quality of life, despite diminished lung capacity. Several participants shared the importance of exercise, noting that it was a “lifesaver” and “the key to staying well.” Specifically, one participant with bronchiectasis noted that in addition to the drugs, exercise helped boost her energy, mental acuity, and oxygen saturation levels, which led to improved lung functioning, such that she “no longer [has to] take the portable oxygen concentrator to the gym. Despite the fatigue, shortness of breath, and concerns about frail bones, participants commented that they still pushed themselves to exercise because of its benefits.

Perspectives on an ideal treatment for Non-tuberculous Mycobacterial Lung Infections

Participants also provided their perspectives on what they would look for in an ideal treatment for NTM. Participants commented that outside of a cure, they hoped for treatments that are less burdensome, addresses the underlying cause of illness, improves symptoms, slow down the disease progression, and also stop lung deterioration. In addition, participants stressed the need for targeted treatments based on their genetic profile, and they discussed their general preference for inhaled drug therapies over other routes of administration.

They followed up with descriptions of what they would like to see in an ideal treatment. A summary of these is listed below.

- “An ideal treatment for me would be one that does little harm... [and takes into account] the long-term effects of the use of these toxic antibiotics on our overall health.”
- “The goals are... improve quality of life, reduce the amount of fatigue, increase stamina, and decrease the number of exacerbations.”
- Several participants noted that their ideal treatment would “slow the growth of the bacteria,” or “put the infection into remission for more than a few months while decreasing further damage of [the] lungs.”
• Several participants also shared that they would like to have drugs they can take for a shorter duration, with a less complicated dosing schedule.

• Participants shared that the ideal drug would “combat resistant species,” and address “common NTM infections like Klebsiella.”

Several participants also mentioned other considerations to ideal treatments for NTM, including: earlier and better diagnosis, stem cell research, personalized therapy, genetic research, biologics, and cellular mechanisms. Another participant stressed the need for more coordinated care between their treating physicians (such as the primary care and infectious disease physicians).

**Perspectives on Clinical Trials**

To further understand patient perspectives on treatments, participants were asked to consider a hypothetical scenario (see full text in Appendix 4) regarding a clinical trial on a treatment for NTM. With only minimal information provided on what the trial entails, participants were asked to share what thoughts or considerations come to mind as they decide whether they would be interested in enrolling in the study. Some participants stated that they would be willing to participate in the trial, regardless of the side effects mentioned. Other considerations raised included the burden of travel to the clinical trial site, the invasiveness of the procedures, side effects, toxicity of the drug, and how participation would impact a patient’s lifestyle.

**Comments on six-minute walk test**

Several participants shared their experience with lung function testing for monitoring their NTM symptoms, using the six-minute walk test. FDA asked participants whether they routinely undergo the six-minute walk test to track their progress; about one-half of the participants responded by a show of hands that they do. FDA asked participants about which symptoms prevented them from being able to complete their six-minute walk test. One participant commented on fatigue and not having the stamina, another commented on having cold hands, and so “the finger measure of blood oxygen doesn’t work.” One participant suggested that the six-minute walk test does not truly reflect the impact of the weather on their NTM symptoms and their ability to walk.

**Summary of Comments Submitted to the Public Docket**

FDA received 38 comment submissions to the public docket that supplemented the Patient-Focused Drug Development meeting on non-tuberculous mycobacterial (NTM) lung infections. The majority of comments were submitted by patients, or their loved ones and caregivers. Most comments reflected experiences of patients who had been newly diagnosed to those diagnosed more than 18 years ago. FDA also received two comments from advocacy organizations: NTM Info and Research (which submitted comments on behalf of its patient population) and the Cystic Fibrosis Foundation.

Overall, the submitted comments reflected the perspectives shared by participants at the meeting. They also provided additional context to supplement the meeting input. The following is a summary of comments provided through the docket on the symptoms associated with NTM, current treatment options, and what participants look for in an ideal treatment.
Submitted comments on symptoms of NTM

Similar to the public meeting, docket commenters reemphasized that coughing, fatigue, and shortness of breath had a significant impact on the daily lives of patients with NTM. Despite treatment, some commenters shared that they experienced worsening of symptoms over time, while others noted that their symptoms remained steady or improved.

A brief summary of the input on symptoms is described below:

- Most commenters described severe, deep cough that involved bringing up sputum and coughing up blood (hemoptysis). For example, one commenter described: “Initially, I had violent coughing spasms to dry cough to... productive cough.” Several commenters shared that their cough worsened at night, especially when they lay down.

- Many commenters described sudden and debilitating fatigue, and commented that it “robbed” them of their energy and stamina. In one example, one commenter shared that she was unable to bathe herself due to severe lack of energy.

- Many commenters discussed shortness of breath, most often attributing the symptom to physical exertion. Many described shortness of breath as limiting the types of activities they were able to do, including walking, shopping, or travelling.

- Other symptoms included “stabbing” chest pain, night sweat, fever, weight loss and a loss of appetite.

Submitted comments on the overall impact of NTM on daily life

The comments submitted to the docket reflected the input received during the meeting regarding the impact that NTM has on patients’ daily lives.

Most commenters reiterated the impacts on the ability to perform activities including difficulties taking care of themselves or their families, performing their job, or managing their household. Many described that physical activity, such as walking or playing with their children led to severe exhaustion such that they have to “sit down and be still until it [exhaustion] stops.” One commenter noted that severe lack of energy limited her ability to work full time. Some commenters shared that they felt “guilty” for becoming increasingly dependent on caregivers.

Many commenters noted that specific NTM symptoms, such as “relentless, time-consuming” cough and fatigue, resulted in significant social impacts. Commenters noted that being unable to plan or participate in social engagements led to social isolation and depression. This was further emphasized by one participant who shared that she often felt that the public viewed her as contagious, because the “coughing always involved bringing up sputum and... blood.”
Submitted comments on current treatments for NTM

Similar to the public meeting, the submitted comments reflected the challenges of controlling NTM symptoms and managing treatment burdens. Antibiotics were the most frequently mentioned prescription drug therapies. Most commenters stated using a combination of different antibiotics, including Zithromax (azithromycin), Myambutol (ethambutol), Rifadin (rifampin), Biaxin (clarithromycin), Mefoxin (cefoxitin), and Lamprene (clofazamine). One commenter noted the benefits of inhaled liposomal amikacin, sharing that, “my deep coughing lessened considerably and the secondary Pseudomonas lung infection I had dealt with for several years disappeared on sputum culture.”

Some commenters also indicated that they used asthma medications including Advair (fluticasone propionate), Singular (montelukast sodium), and AccuNeb (albuterol). One commenter also shared that Symbicort (budesonide and formoterol fumarate dihydrate) was effective in controlling his cough. Some commenters noted having lung resection surgeries.

Other non-drug therapies mentioned included Aerobika, CPAP, oxygen concentrators, and alternative therapies such as acupuncture, physiotherapy to help clear sputum, yoga, pulmonary rehabilitation, breathing exercises, homeopathic and other herbal respiratory therapy.

Downsides of Drug Therapies

Similar to what was shared at the meeting, the majority of commenters noted that they had to stop treatment due to the intolerable side effects, potential drug resistance, or when the drug became ineffective. Many of them described side effects such as loss of vision and hearing, tinnitus, gastrointestinal problems (including GERD), leukopenia, peripheral neuropathy, vertigo, diarrhea, and nausea.

Several commenters described the downsides of inconvenient dosing schedules of the multiple medications, routes of administration, and the time and effort required to administer treatment. Others commented that it was often burdensome and inconvenient to travel with the nebulizer apparatus. Several commenters mentioned that they were no longer able to consume alcohol due to their treatment regimen; however one commenter noted that “giving up alcohol was one of the least objectionable requirements [of treatment].”

Submitted comments on ideal treatments for NTM

Several perspectives were provided on ideal treatments for NTM. The majority of commenters shared the need for medications that were safe and effective to control their NTM symptoms. Several commenters stressed the need for medications with minimal side effects on their lungs or other organs. One commenter noted that an ideal treatment “would be a drug to kill the bacteria without killing the patient in the process.” Commenters noted their desire for drugs that were faster and easier to administer and had more convenient dosing schedules. Some commenters noted their preference for more oral or inhaled medications rather than intravenous medications.

A few commenters identified the need for faster and improved diagnostic procedures other than the six-minute walk test. One commenter shared that her ability to walk for six minutes depends on how she
feels at that time. Another commenter shared her perspective on the six minute walk test saying, “I have cold hands, and ... finger oximeters do not record accurately when I am active.”

Other commenters also identified the need to develop and improve upon modern technology, including stem cell therapy, for faster diagnosis and treatments. One commenter noted that diagnoses should come “much faster than the 6-8 weeks the culture now takes to grow.”

Highlights of Scientific Workshop

FDA held a scientific workshop in the afternoon following the morning meeting to further explore several issues related to drug development for NTM, such as clinical trial designs and endpoints. This workshop enabled patients, advocacy organizations, academic experts, healthcare providers, government officials, and industry to share their perspectives on these aspects as it relates to NTM lung infection. The workshop was split into presentation and discussion segments.

Dr. Kenneth Olivier, MD from the National Heart, Lung and Blood Institute (NHLBI) began the presentations with an overview of the epidemiology and natural history of NTM disease. Dr. Olivier also examined the prevalence of NTM in the U.S.; geographic variability and associated risk factors due to environmental influences; the burden of having NTM disease in terms of the cost of treatment and overall impact of disease; and mortality risk factors. He concluded by pointing out that the prevalence of NTM in the U.S. is difficult to assess partly due to diagnostic and screening practices.

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The second presentation by Dr. David Griffith, MD from the University of Texas Health Science Center addressed NTM treatment guidelines, the current standard of care and how it differs from those of tuberculosis. Dr. Griffith also discussed the limitations of using only the guideline for identifying and diagnosing the 160 different Mycobacterium (MAC) species. He then showed normal and abnormal computerized axial tomography (CAT) scans of different patients to highlight cases where they were positive for MAC, but were not on medications or instances where they were successfully treated with medicines. Next, he focused on issues related to drug resistance, in particular acquired mutational resistance in patients being treated. He concluded by discussing the need for more physician education on the NTM guidelines for diagnosing and treating patients.

Following the two presentations, participants were given the opportunity to ask the presenters questions. Based on the epidemiological graphs Dr. Olivier showed of NTM prevalence, one participant inquired as to the reason for the low prevalence of NTM lung infection in the U.S. compared to other parts of the world. Dr. Olivier responded by suggesting that one would have to consider the genetic risk factors in the population which would vary by ethnicity and geographic background. In addition, he suggested that more awareness of NTM means that physicians are more likely to diagnose.

Another participant wanted to know if an underlying lung condition such as bronchiectasis served as a risk factor that predisposes an individual to NTM or vice versa. Drs. Olivier and Wallace suggested that the answer would lie in identifying the different genes and risk factors that likely result in different strains of mycobacteria causing NTM infection.

Following the brief question and answer session, the workshop resumed with the third presentation by Dr. Hala Shamsuddin, MD from the FDA, who examined review considerations for new drugs in the U.S.
Dr. Shamsuddin first provided a general overview of adequate and well-controlled clinical trials, including the need to demonstrate safety and efficacy, the statutory standards for efficacy trials, and the types of trials specifically outlined in FDA’s regulations (placebo concurrent control, dose comparison concurrent control, active treatment concurrent control, no treatment concurrent control, and historical control). Dr. Shamsuddin then discussed NTM trials, and concluded by exploring three examples of endpoints under consideration in NTM trials such as: clinician-reported outcomes (CROs), patient-reported outcomes (PROs), and surrogate biomarkers (such as sputum culture conversion to negative).

The fourth presentation by Dr. Selena Daniels, PharmD from the FDA focused on how information obtained from patients during the PFDD meetings is utilized in developing patient-focused outcome measures and clinical study endpoints. Dr. Daniels highlighted how information from patients supports FDA’s drug reviews of the benefits and risks of drugs, and guides FDA’s review of patient questionnaires. She also provided a brief overview of the regulatory standards for the assessment of patient questionnaires, while also noting that the FDA is not aware of any patient questionnaire that is ready for use in clinical studies for NTM. She concluded by commenting on the two pathways for FDA to provide advice to those interested in developing patient questionnaires, including: within an active investigational new drug (IND) application; and within the Drug Development Tool qualification program.

The fifth presentation by Dr. Alexandra Quittner, MD from the University of Miami focused on the development of a patient-reported outcome (PRO) instrument for NTM symptoms, which she suggested could be used with already validated PROs for cystic fibrosis (CFQ-R) and bronchiectasis (QOL-B). Dr. Quittner described the initial steps leading to the development of a PRO for NTM, from focus group discussions with adult NTM and bronchiectasis patients to open-ended interviews with pulmonology NTM experts and patients, and cognitive testing of the draft instrument with patients. She concluded with a discussion of the recently completed psychometric validation of the PRO instrument that was conducted with NTM patients.

The final presentation by Dr. Anne O’Donnell, MD from Georgetown University focused on the challenges in the design of clinical trials for NTM lung infection. Dr. O’Donnell identified several difficulties regarding how best to define response to therapy, including: microbiologic results (negative cultures), radiologic improvement, improvement in patient symptoms (PROs), and improvement in lung function. Another difficulty mentioned was addressing the heterogeneity of the disease, and challenges such as: deciding whether to include all NTM species in a clinical trial or separate them; deciding whether or not to stratify patients with nodular bronchiectasis or cavitary; and deciding whether to include patients co-infected with other bacteria or patients with only NTM infection. She then showed CAT scan images to highlight the variations in disease manifestation among patients with MAC, *M. abscessus*, or patients with MAC and a co-infection. She concluded by suggesting an exploration of serologic monitoring of NTM patients.

A panel discussion followed these six presentations, addressing topics related to clinical trial design. Topics discussed included: eligibility for patient enrollment, active treatment control versus placebo control, trial endpoints for NTM, and trial feasibility. Panelists were generally in favor of not excluding any patient population from the trial, but to include all (such as cystic fibrosis/ non-cystic fibrosis patients, MAC/ non-MAC patients, and treatment-experienced/ treatment-naïve patients). Two panelists suggested that using an active or placebo control would depend on whether the trial is
focusing on safety or efficacy, since not every NTM patient needs to be treated immediately upon diagnosis. In conclusion, it was suggested that narrowing the population of participants to be recruited into a clinical trial would not provide evidence on how different sub-populations respond to treatment.

**Conclusion**

The Patient-Focused Drug Development meeting on non-tuberculous mycobacterial (NTM) lung infections provided the FDA an opportunity to hear from patients’ and caregivers on the devastating effect NTM has on their daily life and their experience with available treatment options.

FDA recognizes that patients have a very unique ability to contribute to our understanding of the broader context of this disease, which is important to our role, and that of others, to meet the many challenges of the drug development process. As Dr. John Farley, Deputy Director from CDER’S Office of Antimicrobial Products noted, “This is a very important meeting for us. We fully understand that NTM lung infections are a serious condition and that there is unmet need for patients... having this kind of dialogue is extremely valuable for us.” FDA is grateful to all of the participants who so generously shared such personal stories, experiences, and perspectives of what it is like to live with NTM, and we admire the strength these patients have demonstrated in managing their debilitating condition. FDA shares the patient community’s commitment to furthering the development of safe and effective drug therapies for NTM.
Appendix 1: Meeting Agenda and Discussion Questions

Public Meeting on Non-Tuberculous Mycobacterial (NTM) Lung Infections
Patient-Focused Drug Development
October 15, 2015

8:00 – 9:00 am   Registration

9:00 – 9:05 am   Welcome
Soujanya Giambone, MBA
Office of Strategic Programs (OSP), Center for Drug Evaluation and Research (CDER), FDA

9:05 – 9:10 am   Opening Remarks
John Farley, MD MPH
Deputy Director, Office of Antimicrobial Products (OAP), CDER, FDA

9:10 – 9:20 am   Overview of FDA’s Patient-Focused Drug Development Initiative
Theresa Mullin, PhD
Director, OSP, CDER, FDA

9:20 – 9:30 am   An Overview of NTM Infections and Available Treatment
Hala Shamsuddin, MD
Medical officer, Division of Anti-infective Products (DAIP), CDER, FDA

9:30 – 9:35 am   Overview of Discussion Format
Soujanya Giambone
OSP, CDER, FDA

9:35 – 10:05 am   Panel #1 Comments on Topic 1
Topic 1: Disease symptoms and daily impacts that matter most to patients. A panel of patients and patient advocates will provide comments to start the discussion.

10:05 – 10:45 am   Large-Group Facilitated Discussion on Topic 1
Patients and patient representatives in the audience are invited to add to the dialogue.

10:45 – 11:00 am   Break

11:00 – 11:30 am   Panel #2 Comments on Topic 2
Topic 2: Patient perspectives on current approaches to treating NTM infections. A panel of patients and patient advocates will provide comments to start the discussion.

11:30 – 12:15 pm   Large-Group Facilitated Discussion on Topic 2
Patients and patient representatives in the audience are invited to add to the dialogue.
Lunch

Session 2: Scientific Discussion

Current Treatment of NTM Lung Infections

1:00-1:20 pm  The Epidemiology and Natural History of NTM Lung Infections
Kenneth Olivier, MD

1:20 – 1:40 pm  Treatment Guidelines for NTM Lung Infections
David Griffith, MD

Designing Clinical Trials for New Drugs to Treat NTM Lung Infections

1:40 – 1:55 pm  Review Considerations for New Drugs in the United States
Hala Shamsuddin, MD

1:55 – 2:15 pm  The Road from Patient Focused Drug Development Meetings to Clinical Trial Endpoints
Selena Daniels, PharmD and Alexandra Quittner, Ph.D.

2:15 – 2:35 pm  Challenges in the Design of Clinical Trials for NTM Lung Infections
Anne O'Donnell, MD

2:35 – 2:45 pm  Questions

2:45 – 3:00 pm  Break

3:00 – 4:30 pm  Panel Discussion
Moderator: Sumathi Nambiar, MD MPH
CDER/FDA

Clinical Trial Considerations
1. Eligible population: CF vs. non-CF, Rx naïve vs. Rx experienced, MAC vs. other NTM (especially M. abscessus)
2. Use of Control: active or placebo: Add-on therapy vs. new regimen, how to choose optimized background regimen if there is no correlation between the results of susceptibility testing and clinical activity
3. Trial endpoints
   a. Microbiologic endpoint:
      i. Effect of inhaled therapies?
      ii. Sputum Conversion and Clearance: definitions, timing and durability — how many consecutive cultures define sputum conversion to negative? Sputum clearance?
      iii. How many months after sputum clearance is a “cure” declared?
      iv. Correlation of microbiologic endpoints with clinical outcomes
   b. Patient Reported Outcome endpoint: which PRO, when to assess, effect of other concomitant interventions for underlying lung disease
   c. Assessments of exercise tolerance: 6MWT: what change is clinically meaningful, effect of other interventions for underlying lung disease
   d. Other endpoints
4. Trial feasibility: frequency of visits, frequency of labs, available treatment centers, length of study, possible need for equipment (IV or inhaled therapies)
Discussion Questions (Morning Session):

Topic 1: Disease symptoms and daily impacts that matter most to patients

1. Of all the symptoms that you experience because of your condition, which 1-3 symptoms have the most significant impact on your life? (Examples may include cough, increased sputum production, shortness of breath, difficulty breathing, chest pain)
2. Are there specific activities that are important to you but that you cannot do at all or as fully as you would like because of your condition? (Examples of activities may include sleeping through the night, daily hygiene, driving, walking/running, exercising, etc.)
   a. How do your symptoms and their negative impacts affect your daily life on the best days? On the worst days? (Examples may include limitations on the ability to undertake physically strenuous activities, restrictions on the ability to travel, inability to sleep, lack of appetite, fatigue, etc.)
3. How has your condition and its symptoms changed over time?
   a. Do your symptoms come and go? If so, do you know of anything that makes your symptoms better? Worse?
4. What worries you most about your condition?

Topic 2: Patients’ perspectives on current approaches to treating NTM lung infections

1. What are you currently doing to help treat your condition or its symptoms? (Examples may include prescription medicines, over-the-counter products, nebulizers, and other therapies including non-drug therapies)
   a. What specific symptoms do your treatments address?
   b. How has your treatment regimen changed over time, and why?
2. How well does your current treatment regimen treat the most significant symptoms of your disease?
   a. How well do these treatments stop or slow the progression of your disease?
   b. How well do these therapies improve your ability to do specific activities that are important to you in your daily life?
   c. How well have these treatments worked for you as your condition has changed over time?
3. What are the most significant downsides to your current treatments, and how do they affect your daily life? (Examples of downsides may include bothersome side effects, need for multiple medications, need for injections, going to the hospital for treatment, etc.)
4. Assuming there is no complete cure for your condition, what specific things would you look for in an ideal treatment for your condition?
Appendix 2: FDA and Patient Panel Participants

Patient Panel, Topic 1
- Marilynn Lundy – Patient
- Philip Leitman – Caregiver/ Patient Advocate
- Barbara Hudson – Patient
- Kathleen Keating – Patient

Patient Panel, Topic 2
- Jennifer Bogenrief – Patient
- Betsy Glaeser – Patient
- Gaby Chien – Patient
- Mary Fisher – Patient
- Patricia Yost – Patient

FDA Panel
- John Farley (Office of Antimicrobial Products (OAP), Center for Drug Evaluation and Research (CDER))
- Sumathi Nambiar (Division of Anti-infective Products (DAIP), CDER)
- Theresa Mullin (Office of Strategic Programs, CDER)
- Joseph Toerner (DAIP, CDER)
- Hala Shamsuddin (DAIP, CDER)
- Karen Higgins (DAIP, CDER)
- Selena Daniels (Clinical Outcomes Assessment (COA) Staff, Office of New Drugs (OND), CDER)
- Jonathan Goldsmith (Rare Disease Program, OND, CDER)
- James Bona (Office of Orphan Product Development, CDER)

External Panelists (Afternoon)
- Kenneth Olivier (National Heart, Lung, and Blood Institute, Bethesda MD)
- Kevin Winthrop (Oregon Health Science University, Portland OR)
- David Griffith (University of Texas Health Center, Tyler TX)
- Richard Wallace (University of Texas Health Center, Tyler TX)
- David Hughes (Novartis Pharma)
- Alexandra Quitter (University of Miami, Coral Gables FL)
- Anne O’Donnell (Georgetown University, Washington DC)
- Gina Eagle (Insmed, Incorporated)
- Charles Daley (National Jewish Hospital, Denver CO)
Appendix 3: Meeting Polling Questions

The following questions were posed to in-person and web meeting participants at various points throughout the October 15, 2015, Non-tuberculous mycobacterial Patient-Focused Drug Development meeting. Participation in the polling questions was voluntary. The results were used as a discussion aid only and should not be considered scientific data.

Demographic Questions

1. Where do you live?
   a. Within Washington, D.C. metropolitan area (including the Virginia and Maryland suburbs)
   b. Outside of the Washington, D.C. metropolitan area

2. Have you ever been diagnosed as having an NTM lung infection?
   a. Yes
   b. No

We will ask that the remainder of the questions be answered by people who responded “yes” to Question 2.

3. What is your age?
   a. Younger than 18
   b. 18 – 30
   c. 31 – 50
   d. 51 – 65
   e. 66 – 75
   f. 75 or greater

4. Are you:
   a. Male
   b. Female

5. What is the length of time since your NTM diagnosis?
   a. Less than 1 year ago
   b. 1 years ago to 2 years ago
   c. 2 years ago to 5 years ago
   d. More than 5 years ago
   e. I’m not sure

6. What is your underlying lung condition?
a. Cystic fibrosis  
b. Bronchiectasis  
c. COPD/Emphysema  
d. Other lung disease  
e. Other condition not mentioned  
f. I don’t know

**Question for Topic 1**

7. Of all the **symptoms** you have experienced because of your NTM lung infection, which do you consider to have the **most significant impact on your daily life**? **Please choose up to three symptoms.**

   a. Chronic cough  
   b. Coughing up blood, phlegm, and mucus  
   c. Shortness of breath, wheezing or other breathing difficulties  
   d. Fever or night sweats  
   e. Loss of appetite  
   f. Weight loss  
   g. Fatigue or lack of energy  
   h. Pain, such as chest pain, or shoulder pain  
   i. Other symptoms not mentioned

**Questions for Topic 2**

8. Have you **ever** used any of the following drug therapies to treat the nontuberculous mycobacterial lung infection? Check all that apply.

   a. Oral antibacterial (such as clarithromycin, azithromycin, rifampin or rifabutin, ethambutol, ciprofloxacin, levofloxacin, moxifloxacin, linezolid, clofazimine)  
   b. Intravenous antibacterial (such as imipenem, cefoxitin, amikacin, tigecycline)  
   c. Steroids (inhaled or oral)  
   d. Inhaled therapies (such as nebulizers)  
   e. Other prescription medicine (such as pain medication)  
   f. Other drug therapies not mentioned  
   g. I'm not taking any drug therapies

9. Besides your drug therapies, **what else are you doing** to manage any symptoms you have experienced because of your NTM lung infection? Check all that apply.

   a. Cough medicines  
   b. Supplemental oxygen  
   c. Pulmonary rehabilitation  
   d. Breathing, exercise or relaxation techniques  
   e. Dietary supplements  
   f. Diet modifications
g. Complementary or alternative therapies
h. Other therapies not mentioned
i. I am not doing or taking any therapies to treat symptoms
Appendix 4: Meeting Scenario Questions

Scenario: What thoughts and questions come to mind as you hear this scenario?

Imagine that...

- You have been invited to participate in a clinical trial to study an experimental antibiotic treatment for NTM lung infections
- The purpose of the study is to better understand how well this treatment works and its safety
- This clinical study lasts 2 years, and clinical visits will occur every month for 2 years, in addition to regular doctor’s visits
- Visits will involve monthly sputum collections, lab tests, lung function tests, and other laboratory tests as needed
- Treatments may involve either IV medication (administered via catheter) or inhaled therapy (administered for 1-2 hours)
- Treatment is given in addition to standard of care
Appendix 5: Incorporating Patient Input into a Benefit-Risk Assessment Framework for Non-Tuberculous Mycobacterial Lung Infections

Introduction

Over the past several years, FDA has developed an enhanced structured approach to benefit-risk assessment in regulatory decision-making for human drugs and biologics. The Benefit-Risk Assessment Framework involves assessing five key decision factors: Analysis of Condition, Current Treatment Options, Benefit, Risk, and Risk Management. When completed for a particular product, the Framework provides a succinct summary of each decision factor and explains FDA’s rationale for its regulatory decision.

In the Framework, the Analysis of Condition and Current Treatment Options rows summarize and assess the severity of the condition and therapies available to treat the condition. The assessment provides an important context for drug regulatory decision-making, including valuable information for weighing the specific benefits and risks of a particular medical product under review.

The input provided by patients and patient representatives through the Non-tuberculous mycobacterial Patient-Focused Drug Development meeting and docket comments will inform our understanding of the Analysis of Condition and Current Treatment Options for this disease.

The information in the top two rows of the sample framework for Non-tuberculous mycobacterial lung infection below draws from various sources, including what was discussed at the Non-tuberculous mycobacterial Patient-Focused Drug Development meeting held on October 15, 2015. This sample framework contains the kind of information that we anticipate could be included in a framework completed for a drug under review for NTM. This information is likely to be added to or changed over time based on a further understanding of the condition or changes in the treatment armamentarium.

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3 Commitments in the fifth authorization of the Prescription Drug User Fee Act (PDUFA V) include further development and implementation of the Framework into FDA’s review process. Section 905 of the FDA Safety and Innovation Act also requires FDA to implement a structured benefit-risk framework in the new drug approval process. For more information on FDA’s benefit-risk efforts, refer to http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm326192.htm.
### Sample Benefit-Risk Framework NTM: Analysis of Condition and Current Treatment Options

<table>
<thead>
<tr>
<th>Decision Factor</th>
<th>Evidence and Uncertainties</th>
<th>Conclusions and Reasons</th>
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</thead>
<tbody>
<tr>
<td><strong>Analysis of Condition</strong></td>
<td></td>
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<td></td>
<td>− Non-tuberculous mycobacterial (NTM) lung infection is a rare, chronic, progressive lung disease that occurs as a result of inhalation of <em>Mycobacteria</em> from exposure to environmental sources.</td>
<td>NTM cause chronic and devastating lung disease with debilitating symptoms that can ultimately lead to lung deterioration. Over time, it takes a physical and emotional toll on patients, which has a detrimental effect on their quality of life and ability to live a normal life.</td>
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<td>− There are about 50,000 to 90,000 people with NTM pulmonary disease in the United States, with a higher frequency in older adult women than men.</td>
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<td>− Disease progression varies, but progressive bronchiectasis ultimately leads to lung deterioration.</td>
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<td>− NTM is characterized by a range of symptoms, including persistent cough, shortness of breath when active, fatigue, sputum production, low-grade fever, night sweats, and weight loss. Symptoms can develop slowly early on, and worsen over time.</td>
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<td>− NTM symptoms cause a significant detrimental impact on a patient’s life, their ability to perform certain activities, and their social life.</td>
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<td>− <em>See the Voice of the Patient report for a more detailed narrative.</em></td>
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<td><strong>Current Treatment Options</strong></td>
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<td>− Current treatment attempts to slow down the progression of the disease, while killing the bacteria and improving lung function. The response to treatment varies.</td>
<td>There is a continuing need for additional treatment options that are effective in slowing down disease progression in addition to stopping lung deterioration. In addition, there is a need for earlier and better diagnosis to increase the chances of treatment being more effective.</td>
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<td>− Treatment requires the use of multiple antibiotics for an extended period of time. Combination of antibiotic drugs administered orally, intravenously, nebulized or inhaled is used to treat NTM. The most common treatment includes a three drug cocktail consisting of Biaxin (clarithromycin), Myambutol (ethambutol), and Rifadin (rifampin).</td>
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<td>− Amikin (amikacin) is used in the treatment of NTM.</td>
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<td>− Serious side effects include neuropathy, numb toes, severe vertigo, hearing loss, optic nerve damage, vision loss, sensitivity to stimuli, nausea, acid reflux, kidney and liver damage, and tinnitus.</td>
<td>Although most treatments are beneficial in slowing down disease progression, their toxicity and side effects can have a significant detrimental impact on patients’ lives. Emerging targeted therapies such as stem cell research, precision medicine and personalized therapy may be explored.</td>
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<td>− Pain medicines, antidepressants, antifungals, and medicines for acid reflux are used to manage the symptoms of NTM.</td>
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<td>− Patients can develop resistance to the antibiotics after extended use, making some treatments less effective over time.</td>
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<td>− Other therapies include exercise, pulmonary rehabilitation, dietary changes, acupuncture, massage, meditation and prayer.</td>
<td>Patients’ treatment decisions often require making difficult tradeoffs between increasing the chance to prolong life and preserving quality of life.</td>
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