

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

Sarcopenia

Public Meeting: April 6, 2017

Report Date: October 2017

Center for Drug Evaluation and Research (CDER)
U.S. Food and Drug Administration (FDA)

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Introduction

On April 6, 2017, the Food and Drug Administration (FDA) held a public meeting to hear perspectives from individuals who have sarcopenia (hereafter referred to as patients), caregivers, and other patient representatives. FDA conducted the meeting as part of the agency's Patient-Focused Drug Development (PFDD) initiative,¹ an FDA commitment under the fifth authorization of the Prescription Drug User Fee Act (PDUFA V) to systematically gather patients' perspectives on their condition and available therapies to treat their condition. As part of this commitment, FDA held 24 public meetings between Fiscal Years 2013 and 2017, each focused on a specific disease area.

More information on this initiative can be found at:

<https://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm527587.htm>

Overview of Sarcopenia

Sarcopenia is a term used to describe the loss of muscle mass, strength, and function that is associated with aging. Currently, there is no universally agreed-upon definition or method of diagnosis for sarcopenia. Sarcopenia is estimated to affect up to a third of individuals over the age of 60. The three primary types of methods currently used to document the presence of sarcopenia are based on: detecting the amount of muscle mass, either with body scans or imaging; testing muscle strength, such as by testing grip or lower body strength; and measuring muscle function, such as by testing walking speed or stair climbing ability.

The precise causes of sarcopenia are not known. There are numerous risk factors that are associated with muscle loss associated with aging, such as lack of exercise, decrease in muscle growth, or changes in nerves supplying muscles. Other illnesses may also be associated with muscle loss, particularly severe conditions such as cancer, heart disease, malnutrition or critical illness.

Sarcopenia may result in serious health outcomes in older adults. Muscle weakness may lead to falls, which can cause fractures and other serious injuries. Loss of muscle function is associated with slower walking speed. Decreased walking speed has been associated with a higher risk of mortality in population studies of older adults, especially those over age 75. Sarcopenia can also lead to disability and loss of patients' ability to care for themselves.

Currently, there are no FDA-approved medications for the treatment of sarcopenia. The effects of exercise and nutritional supplementation on patients with sarcopenia have been examined in numerous studies. Exercise has consistently demonstrated improved muscle strength and function in a wide range of populations, with inconsistent effects on improving muscle mass. Evidence of benefit from nutritional supplementation has been inconsistent, showing a range of impacts on muscle function, strength, and size.

¹ The Federal Register Notice for the Patient-Focused Drug Development Initiative can be found here: <https://www.gpo.gov/fdsys/pkg/FR-2015-07-02/pdf/2015-16359.pdf>

Meeting overview

The Sarcopenia PFDD meeting provided FDA with the opportunity to hear directly from patients and other patient representatives about their experiences and perspectives on managing their health or the health of the individuals they care for. The discussion focused on two key topics: 1) Disease symptoms and daily impacts that matter most to patients, and 2) Patients' perspectives on approaches to treating sarcopenia. The questions for the discussion (*Appendix 1*) were published in a [Federal Register notice](#) that announced the meeting.

A panel of patients (*Appendix 2*) shared comments to begin the dialogue. Panel comments were followed by large-group facilitated discussions inviting comments from other patients and patient representatives in the audience. Two FDA facilitators led the discussion, and a panel of FDA staff (*Appendix 2*) asked follow-up questions. Participants who joined the meeting via the live webcast (referred to in this report as web participants) also contributed comments. In addition, 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 and how many participants shared a particular perspective on a given topic.

Approximately 15 patients or patient representatives (including caregivers and patient advocates) attended the meeting in-person. Approximately 20 patients or patient representatives provided input through the live webcast. Patient participants in the room and on the webcast ranged in age from 50 to 80 years and older, and were split evenly between men and women. Approximately half of these participants had consulted a healthcare professional about sarcopenia. Approximately 70% of the participants reported experiencing some kind of comorbid condition, with the most common responses being arthritis, cardiovascular disease, and cancer. Although participants at this meeting may not fully represent the overall population of patients with sarcopenia, FDA believes that the input received reflects the burden that sarcopenia can have in some elderly patients.

To supplement the input gathered at the meeting, sarcopenia patients and others were encouraged to submit comments on the discussion topic to a public docket,² which was open until June 6, 2017. Eleven comments were submitted to the public docket, the majority by individual patients and patient advocacy organizations.

More information, including the archived webcast and meeting transcript, is available on the meeting website: <https://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm527587.htm>.

Report overview and key themes

This report summarizes the input shared by patients and patient representatives during the meeting, webcast, and through the public docket. To the extent possible, the terms used in this report to describe specific experiences with sarcopenia reflect the words used by in-person, web participants, or 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 related to sarcopenia that are not included in this report.

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.

The input from the meeting and docket comments reflect a range of patients' experiences with sarcopenia. Participants described the numerous ways their lives had been impacted by the physical, emotional, and social burden of sarcopenia. Several key themes emerged from this meeting:

- Patients experience a significant physical burden as a result of sarcopenia. Most participants described experiencing loss in muscle function and physical ability, resulting in inability to perform basic physical tasks such as standing and walking long distances. Participants also stated that they experienced health effects such as balance problems or falling, fatigue, and muscle pain, along with comorbid conditions, such as arthritis.
- Participants identified a range of factors that contributed to causing or worsening their sarcopenia, including sedentary lifestyles, inactivity due to injury and illness, and malnutrition. Patients described a cycle of inactivity and decline in function, resulting in progressive decline over time. Some participants stated that it was difficult for them to determine whether their symptoms were worsening as a result of sarcopenia or as a natural result of aging.
- Participants provided rich detail and insight into the toll that sarcopenia takes on their lives. In addition to physical limitations, participants described emotional impacts such as fear of injury and embarrassment from their physical limitations, limited social interactions and feelings of isolation, and difficulties caring for themselves and living independently.
- Participants shared the difficulty they encountered in maintaining a healthy, active lifestyle in order to manage their condition. Most participants focused on the importance of exercise and nutrition in maintaining muscle function and strength. Other participants also addressed the importance of communicating the benefit of exercise and physical activity to patients with sarcopenia and other seniors. Some of these participants emphasized the positive impact of exercise and physical activity, stating that they could help slow or prevent the onset of symptoms associated with sarcopenia.

The patient input generated through this Patient-Focused Drug Development meeting and the public docket comments strengthens FDA's understanding of how sarcopenia impacts the lives of people living with the condition. FDA staff carefully considers this input 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 medical products under review. This input may also be of value to the drug development process more broadly. For example, it may be useful to researchers and drug developers as they seek to better understand the impact that sarcopenia has on how patients feel or function. It may also help drug developers and others as they develop instruments that can measure the treatment benefit of potential therapies.

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

The first discussion topic gathered participants' perspectives on the impacts of sarcopenia on their health and on daily life. Four panelists (Appendix 2) provided comments to begin the dialogue. They included: an 85 year-old woman who had participated in an National Institutes of Health (NIH) study related to sarcopenia; an 85 year-old man who carefully manages his diet and exercise with the intent of

staving off any effects of sarcopenia; a registered dietician and nutrition program manager who works with seniors and patients with sarcopenia; and an 83 year-old man has also been dealing with the health effects of sarcopenia for decades.

Each panelist described their history with sarcopenia, including the progression of symptoms and their efforts to manage the condition. They also discussed the impact of sarcopenia on their daily lives or the lives of older adults they encountered. Panelists also touched on the emotional and social impact of sarcopenia, including isolation and feeling fragile or vulnerable after experiencing falls.

In the large-group facilitated discussion, participants conveyed similar perspectives to those expressed by the panelists, providing a vivid description of what it is like to live with sarcopenia, as well as factors that contributed to the worsening of their condition over time. The remainder of this section summarizes participants' comments on health effects of sarcopenia and the impact their condition has on daily life.

Perspectives on Sarcopenia

Participants identified significant challenges in their lives as a result of sarcopenia. Most patients felt their ability to live normally and to perform basic physical activities was limited by the effects of their condition. In a polling question (Appendix 3, Q5), participants were asked to identify the most bothersome impacts of sarcopenia on daily life. Participants highlighted reduced muscle strength or increased muscle weakness, fatigue, difficulty walking, and pain as the most significant effects of sarcopenia. Some participants, however, expressed difficulty in determining which health effects are caused by their condition, versus which are a result of natural decline in health due to aging.

Muscle Loss, Muscle Weakness, Frailty

Most in-person and web participants identified reduced muscle function and physical ability as their most burdensome health effects. Participants generally used the terms muscle loss, muscle weakness, and frailty when referring to these health effects. Participants provided in-depth perspectives on how their weakness affected parts of their body and their overall function, with particular emphasis on core muscle weakness, weakness in the quadriceps and lower-muscles, and loss of upper body strength. Some participants described themselves as feeling "very weak," "physically frail," "fragile," and like they "couldn't move anymore." One participant stated that she had lost so much muscle mass she felt like "skin on bones ... with a big belly and skinny little legs." Another participant stated she felt her limbs had "turned into little old lady limbs."

Other participants described challenges they faced in their lives and activities they were no longer able to participate in. Some participants stated that their loss in core muscle strength made it difficult to support themselves and led to them needing to sit down frequently. One participant stated that they couldn't walk for long distances because "I had the feeling if I kept going, I'd fall down because my core muscles wouldn't support me." Participants also described a number of impacts of lower-leg weakness; including being unable to stand unassisted, being unable to get out of cars, needing to crawl up stairs, and experiencing injuries such as sprained ankles. One participant described experiencing difficulties with standing while at the meeting, saying "I imagine at the end of the day today, people are going to help me stand up ... I frankly can't get out of a chair." Another participant shared a similar perspective, saying they were worried about their dogs "knock[ing] me over or break[ing] my leg ... because I can't

get up.” Other participants addressed their loss of upper body strength, stating that it left them unable to complete tasks such as opening cans of soda, juice cartons, or picking up grandchildren.

Balance Problems & Falling

Participants discussed their difficulties with balance and their experiences with falling. Multiple participants stated that they had fallen at least once in recent years and had experienced injuries as a result. These participants linked their falls to difficulties with maintaining balance while standing, being unable to catch themselves after accidentally bumping into things, and becoming tired after standing or walking. One participant said that they had a “hard fall” after tripping over an object behind him. Another shared that they had to be especially careful when standing or leaning on an object to support himself, stating that they had to check if objects are “sturdy enough so when I push on it to get up, it’s not going to turn over.” Another stated that lower leg weakness and balance problems led to “an inversion of my foot and an ankle sprain that had me end up in the emergency room.”

Fatigue

Some participants also mentioned fatigue when discussing their sarcopenia symptoms, stating that during the day they felt “weary,” “tired,” or simply “bad.” Participants described having difficulty summoning the energy to participate in activities such as buying groceries, preparing food, and taking care of themselves. One participant stated that they had to stop participating in volunteer work they found meaningful, because they were “just too tired” both physically and mentally.

Muscle Pain

Participants also identified pain as one of the health effects they experienced, generally focusing on muscle pain. For one participant, muscle pain was sometimes a result of overexertion creating “severe pain” in the affected muscle. Other participants described their pain as being constant and affecting multiple body parts, describing it as “stiffness and little aches and pains ... [that are] always there.”

Other Health Effects & Comorbid Conditions

Participants also mentioned a number of other health effects and comorbid conditions that they experienced which may be attributed or impacted by sarcopenia. A few participants noted that they experienced arthritis in their necks, backs, or other parts of the body. Some of the participants were unsure if their arthritis was connected to their sarcopenia. Other health effects and comorbid conditions mentioned included weight loss, skin cancer, cardiovascular disease, carpal tunnel syndrome, and lupus.

Causes & Progression

Many participants highlighted a range of factors that may have contributed to their loss in muscle function and strength. The most commonly mentioned factors were long periods of bedrest or a lack of physical activity, and malnutrition or improper diet. For several participants, long periods of inactivity were caused by illness or injury resulting in bedrest during treatment or rehab. These participants emphasized that even short periods of bedrest could have significant impact on muscle mass and strength. Other participants stated that they experienced a “general lack of exercise and a sedentary lifestyle” caused by a number of factors, including social isolation and limited mobility from other chronic conditions (such as arthritis and lupus). Participants also highlighted a lack of awareness about the importance of staying

active in everyday life and after periods of bedrest. Participants who mentioned malnutrition and improper diet highlighted problems such as insufficient protein consumption and overall caloric intake among elderly patients.

In addition to talking about contributing factors and causes of sarcopenia, several participants discussed the progressive nature of the condition. Some participants focused on the deterioration of certain body parts, such as one who shared that “upper-body strength went first ... legs lasted a little longer as I lost weight.” Others focused on a cycle of general weakening, due to inactivity, leading to muscle loss, and more inactivity. One participant described this as “downward spiral” leading to being bedbound or disabled. Some participants stated that this spiral could be “insidious” and difficult to detect, with patients often not realizing anything is wrong. One participant shared that patients often think it is “inevitable to get weak and wobbly as they get older” and don’t realize they may need to take action to address their weakness. Some participants acknowledged that it was difficult to determine if some of the progression of health effects they experienced were due to their underlying medical condition(s), or if they were the natural result of aging. Participants emphasized the need to maintain activity levels and proper diet to combat the progressive nature of the condition, especially after periods of bedrest.

Overall Impacts on Daily Life

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

- **Emotional impacts** – Participants provided insight into some of the emotional and psychological impacts of living with sarcopenia. Participants described feeling embarrassed by their physical limitations, including one participant who was injured throwing a party and ended up sitting on the couch “trying to conceal my pain and feeling really embarrassed to be such a poor hostess.” Another participant stated that they needed help getting out of chairs, saying it felt “embarrassing, frankly... I don’t want to have people hauling [me] up out of a chair and making a big fuss.” Other participants stated that they experienced psychological impacts as a result of their sarcopenia, including feeling fragile and afraid of injury. One participant stated that after experiencing a fall, the psychological effects were “worse and longer lasting than the physical effects,” and that they avoided activities where crowds might be present out of concern for another fall. One participant also highlighted the fear and anxiety that came after having fallen, sharing, “For weeks after the bruise had healed ... I was afraid someone would bump into me, knock me over, and injure me badly. I felt really quite fearful and fragile.”
- **Impact on ability to live independently** – Many participants shared their concerns about the impact of sarcopenia on their ability to care for themselves and live independently. Participants described feeling too weak or tired to carry groceries, prepare food, clean their home, shower, drive, and take transportation. One participant summarized the challenges of living independently with sarcopenia by sharing, “I no longer have the strength or stamina to handle the tasks I used to manage ... I want to remain independent, but if I push myself too hard, I injure myself and undermine that goal.”
- **Social impacts & isolation** – Several participants also addressed how the effects of sarcopenia restricted their ability to participate in social interactions. Participants stated that they had to step down from engaging with the community in volunteer work and local government, with

one participant calling it a “great loss.” Others described their challenges hosting or attending social engagements, given their fatigue and difficulty with physical activities such as lifting objects, cooking, and walking. Participants stated that after a year of being sick and bedridden, they stopped working and friends stopped visiting or calling. One participant shared the impact of this loss of social interaction, saying “The isolation becomes terrible ... there is a loss of community connection and just all of the everyday interactions that actually help keep you bright and alive.”

Topic 2: Patients’ perspectives on current approaches to treatment

The second topic discussion gathered patient perspectives on their approaches to managing their condition. The discussion primarily focused on patients’ experiences with non-drug therapies, perspectives on future treatments, and the need for better communication of treatment importance. These perspectives are summarized below.

Perspectives on treatment approaches

Most participants stated that their approaches to managing and treating their sarcopenia focused on non-drug therapies, including exercise, physical therapy, lifestyle and diet modification, and emotional support.

Exercise and physical therapy were the most commonly mentioned treatment approaches among meeting and web participants as well as docket commenters. These included water and pool exercises, cardio exercises, intense physical activity, and personalized physical therapy. Participants who underwent water exercises and swimming stated that it played a significant role in improving balance, strength, flexibility, and overall muscle function, while causing little stress on the joints. One participant stated that physical therapy helped improve difficulty walking, poor balance, pain, and muscle weakness, but that fatigue and lack of energy sometimes made it difficult to stay motivated. Another participant said that their exercise “kept them going” and allowed them to go on an international trip with their grandchildren. Some participants viewed exercise as a preventative tool for elderly patients at risk of sarcopenia. These participants stated that exercise helped prevent the onset of sarcopenia and the related health effects, and highlighted the importance of maintaining an active lifestyle at all ages.

In addition to exercise, participants emphasized the importance of proper diet, especially consuming sufficient protein and calories throughout the day. They also noted that proper diet can make exercise and physical therapy more effective in combatting the loss of muscle mass.

Participants also highlighted the impact that emotional support played in motivating them to continue with their treatment approaches. One participant said that the socialization aspect of their water exercises kept them “getting out of bed at 5:00 and into the pool at 6:30 three mornings a week.” Others stated that they encouraged themselves by focusing on goals, such as wanting to pick up grandchildren or building up muscles after heart surgery. One participant also noted that undergoing functional movement assessments can serve to motivate and plan for treatment approaches and for the future in general.

In addition to non-drug therapies, participants listed some drug therapies and medical procedures they had taken to treat the effects of sarcopenia or one of their comorbid conditions. These included

ibutamoren, creatine, fluconazole, interferon, teriparatide, etanercept, and surgery related to arthritis, cancer, and cardiovascular disease.

Considerations regarding future treatment

FDA was also interested in understanding the factors patients take into account when making decisions about treatments for sarcopenia. In a polling question (Appendix 3, Q8) participants were asked what benefits they would consider most meaningful in a new treatment. The majority of participants, around 65%, indicated that improved muscle strength or reduced muscle weakness would be most meaningful. To help guide the discussion, participants were asked to imagine a scenario in which a new medication for sarcopenia was recently approved by FDA (see full text in Appendix 3). Their doctor believes that they may be a good candidate for this medication. In the clinical studies, one-half of older adults taking this medication achieved a 20% increase in walking speed within three months. Common side effects include fatigue, headaches and weight gain. The medication is also believed to cause rare, but serious side effects, such as liver problems and cancer.

Participants were asked to comment on the first thoughts that came to mind as they heard this scenario. Most participants stated that they would likely not be interested in trying this hypothetical treatment. Some participants expressed concern about the potential for serious side effects. Others stated that the effect of 20% increase in walking speed seemed like a minor benefit, and that it did not outweigh potential downsides. One participant said that the increase in walking speed was not meaningful, but that if it reversed even a part of the muscle wasting, they would take it as they would do “anything to remain independent and fully functional.”

A few participants also provided some perspectives on areas they would like to see further progress in drug development for sarcopenia. One participant stated that they hoped products would focus on treating the underlying reduction in muscle mass, and not the related health effects. Another participant stated that they would like treatments to avoid causing side effects like muscle cramping, as they cause inability to exercise and bed rest, both of which are harmful to patients with sarcopenia.

Other Medical Issues

Several participants identified the lack of better understanding about sarcopenia and its treatment methods as being a major issue in the medical community. Some participants said that most of the doctors that they had encountered “don’t even have the knowledge of what sarcopenia means.” Participants stated that this resulted in little to no conversations with the doctor about the proper treatment options such as physical therapy and nutrition. One participant stated that they had avoided some of the worst health effects of sarcopenia by beginning exercise and physical therapy at an earlier age than most, but that they had to do their own research to get enough information to make that decision. Others said they felt like sarcopenia was not treated as a recognized medical condition or a “real disease,” resulting in less development from pharmaceutical companies.

Conclusion

Sarcopenia appears to have a significant impact on the physical, emotional and social aspects of patients' lives. The condition may be under recognized or treated and new approaches are needed to address the challenges that patients living with sarcopenia experience.

Patient perspectives play an important role when considering how to best facilitate drug development for sarcopenia. FDA recognizes that patients have unique insights into their condition and these valuable insights contribute to FDA's understanding of the impact of the condition on a patient's life. This is important to our role, and that of others, in the drug development process. The information from this meeting has helped FDA better understand how the condition impacts the lives of patients who live with it and what patients most want in the therapies that aim to improve the condition.

FDA is grateful to the patients and caregivers who thoughtfully and generously provided such personal experiences on living with loss of muscle mass, weakness, and strength related to aging. FDA shares the patient community's desire and commitment to advancing the development of safe and effective treatment options for managing sarcopenia.

Appendix 1: Public Meeting on Patient-Focused Drug Development for Sarcopenia

April 6, 2017

12:00 – 1:00 pm	Registration
1:00 – 1:05 pm	Welcome Meghana Chalasani <i>Office of Strategic Programs (OSP), Center for Drug Evaluation and Research (CDER), FDA</i>
1:05 – 1:10 pm	Opening Remarks Jean-Marc Guettier, MD <i>Director, Division of Metabolism and Endocrinology Products (DMEP), CDER, FDA</i>
1:10 – 1:20 pm	Overview of Sarcopenia and Current Treatment Options John Sharretts, MD <i>DMEP, CDER, FDA</i>
1:20 – 1:30 pm	Overview of FDA’s Patient-Focused Drug Development Meeting Sara Eggers, PhD <i>OSP, CDER, FDA</i>
1:30 – 2:00 pm	Setting the Context on Patients’ Experiences and Perspectives A panel of patients and patient representatives will provide comments related to Topic 1 and Topic 2 (next page) to kick-off the facilitated discussions on these topics.
2:00 – 2:30 pm	Large-Group Facilitated Discussion Patients and patient representatives in the audience will be invited to add to the dialogue.
2:30 – 2:45 pm	Break
2:45 – 3:30 pm	Large-Group Facilitated Discussion: Continued Patients and patient representatives in the audience will be invited to add to the dialogue.
3:30 – 3:50 pm	Open Public Comment
3:50 – 4:00 pm	Closing Remarks Jean-Marc Guettier, MD <i>Director, DMEP, CDER, FDA</i>

Discussion Questions

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 difficulty walking, feeling unsteady and falling frequently, having a decreased level of activity etc.)
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 participation in social activities, household chores, daily hygiene, etc.)
3. How do your symptoms and their negative impacts affect your daily life on the **best days**? On the **worst days**?
4. How have your condition and its symptoms **changed over time**?
 - a) Would you define your condition today as being well managed?
5. What **worries you most** about your condition?

Topic 2: Patients' perspectives on current approaches to treatment

1. **What are you currently doing** to help treat your condition or its symptoms? (Examples may include prescription medicines, over-the-counter products, and other therapies including non-drug therapies such as diet modification.)
 - 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 control your condition?
 - a) How well do your treatments address specific activities that are important to you in your daily life?
 - b) 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 going to the hospital or clinic for treatment, time devoted to treatment, etc.)
4. What specific things would you look for in an **ideal treatment** for your condition?
 - a) What would you consider to be a meaningful improvement (for example symptom improvements or functional improvements) in your condition that a treatment could provide?

Docket Information

We encourage you to submit your written comments to the docket by June 6, 2017:

<https://www.regulations.gov/document?D=FDA-2016-N-4198-0001> or go to www.regulations.gov and search for: **sarcopenia patient-focused drug development**.

Appendix 2: Patient and FDA Panel Participants

Patient Panel

- Greta Dersheimer
- Fred Bartlit
- Rose Clifford
- Ray Lipicky

FDA Panel

- Jean-Marc Guettier, MD, Director, FDA Division Of Metabolic And Endocrinology Products (DMEP), CDER
- John Sharretts, MD, DMEP, CDER
- Shannon Sullivan, MD, DMEP, CDER
- Silvana Borges, MD, DMEP, CDER
- Wen-Hung Chen, MD, Clinical Outcomes Assessment Staff, Office Of New Drugs, CDER
- Theresa Mullin, Office Director, Office of Strategic Programs, CDER

Appendix 3: Meeting Polling Questions

Demographic Questions

The following questions are intended for older adults affected by loss of muscle mass and function, OR a caregiver who is representing an older adult affected by loss of muscle mass and function.

1. Have you ever consulted a healthcare professional about age related loss of muscle mass, strength and/or function (i.e. sarcopenia)?
 - a. Yes
 - b. No
2. What is your/your loved one's age?
 - a. Younger than 40
 - b. 40 – 49
 - c. 50 – 59
 - d. 60 – 69
 - e. 70 – 79
 - f. 80 or greater
3. Are you:
 - a. Male
 - b. Female
4. Do you/your loved one currently have any of the following conditions? **Check all that apply.**
 - a. Arthritis or Osteoporosis
 - b. Cancer
 - c. Cardiovascular disease (CVD)
 - d. Kidney disease
 - e. Lung disease (such as COPD)
 - f. Neurological conditions (such as stroke, cognitive impairment)
 - g. Psychiatric conditions (such as anxiety, depression)
 - h. Other comorbid condition(s) not mentioned
 - i. I do not have any comorbid conditions that I am aware of

Question for Topic 1

5. Of all the symptoms you have experienced because of sarcopenia, which do you consider to have the most significant impact on your daily life? **Please choose up to three symptoms.**
 - a. Pain
 - b. Fatigue or lack of energy
 - c. Poor balance
 - d. Difficulty walking
 - e. Reduced muscle strength or increased muscle weakness
 - f. Depression
 - g. Other symptoms not mentioned

6. What do you find to be the most bothersome impacts of your symptoms on your daily life?

Please choose up to three impacts.

- a. Ability to perform work or hobbies
- b. Ability to care for self independently
- c. Ability to leave the home
- d. Risks to safety of self or others
- e. Impact on relationships with family and friends
- f. Emotional impacts
- g. Other impacts not mentioned

Questions for Topic 2

7. Have you ever used any of the following therapies to treat your sarcopenia? **Check all that apply.**

- a. Exercise routine
- b. Physical therapy, massage, or acupuncture
- c. Dietary and herbal supplements
- d. Over the counter products (such as aspirin, ibuprofen, etc.)
- e. Experimental/investigational therapies (such as hormone supplements)
- f. Other prescription medicine (such as pain medication)
- g. Other therapies not mentioned
- h. I am not doing or taking any therapies to treat my symptoms

8. When considering a new treatment for sarcopenia, which **ONE** of the following benefits would you consider to be most meaningful? **Please choose one.**

- a. Reduced pain
- b. Reduced fatigue or lack of energy
- c. Improved balance
- d. Increased endurance during physical activity
- e. Increased mobility (such as walking across a room, getting out of a chair)
- f. Improved muscle strength or reduced muscle weakness
- g. Other

SCENARIO:

FDA has approved a new monthly injectable medication indicated to increase walking speed. Your doctor believes that you may be a good candidate for this medication.

In the clinical studies, one-half of the adults taking this medication achieved a 20% increase in walking speed within three months.

This medication's common side effects include fatigue, headaches and weight gain. The drug is also believed to cause rare, but serious side effects, such as liver problems and cancer.

What first thoughts come to mind as you hear this scenario? What questions would you ask your doctor about this treatment? Would this be a meaningful benefit to you?

Appendix 4: Incorporating Patient Input into a Benefit-Risk Assessment Framework for Sarcopenia

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 biologics³. 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 Patient-Focused Drug Development Public Meeting on Sarcopenia 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 Sarcopenia below draws from various sources, including what was discussed at the Patient-Focused Drug Development Public Meeting on Sarcopenia on April 6, 2017. This sample framework contains the kind of information that we anticipate could be included in a framework completed for a drug under review for Sarcopenia. 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.

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>.

Dimensions	Evidence and Uncertainties	Conclusions and Reasons
Analysis of Condition	- Sarcopenia is a term used to describe the loss of muscle mass, strength, and function that is associated with aging. - Sarcopenia affects up to a third of individuals over the age of 60. The actual rate of this condition in the population depends on several factors, including what definition of sarcopenia is used, the methods to diagnose it, the geographical location, and other factors. Currently, there is no universally agreed-upon definition or method of diagnosis for sarcopenia. - Possible effects of sarcopenia include muscle weakness, loss of function, frailty, and osteoporosis. Muscle weakness may lead to falls, which can cause fractures and other serious injuries in older adults. - Loss of muscle function may also lead to slow walking speed, which is known to be associated with a higher risk of dying, especially in people who are older than age 75. - <i>See the Voice of the Patient report for a more detailed narrative.</i>	Sarcopenia may result in serious health outcomes for patients who experience it. Loss of muscle strength and loss of muscle function can also lead to disability and loss of patients' ability to care for themselves.
Current Treatment Options	- Currently, there are no medications that are approved by the FDA for the treatment of sarcopenia. - The effects of exercise and nutritional supplementation on patients with Sarcopenia have been examined in numerous studies. Exercise has consistently shown that it improves muscle strength and muscle function in different populations, with inconsistent effects on muscle mass. - Nutritional supplementation has been more inconsistent, showing a range of impacts on muscle function, strength, and size. - <i>See the Voice of the Patient report for a more detailed narrative.</i>	New approaches are needed to target the underlying loss of muscle mass and strength in patients with sarcopenia. In addition, new approaches are needed to investigate the impact of nutritional supplementation on patients with sarcopenia.