Public Meeting on Narcolepsy
Patient-Focused Drug Development

September 24, 2013

Welcome

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Agenda

- **Setting the context**
  - Opening Remarks
  - Overview of FDA's Patient-Focused Drug Development Initiative
  - Background on Narcolepsy and Therapeutic Options
  - Overview of Discussion Format
- **Discussion Topic 1**: Most significant symptoms of narcolepsy and their impact on daily life
- **Discussion Topic 2**: Patient perspectives on treating narcolepsy
- **Open Public Comment**
- **Closing Remarks**

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Opening Remarks

Ellis Unger, M.D.
Director, Office of Drug Evaluation I
Center for Drug Evaluation and Research
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FDA's Patient-Focused Drug Development Initiative

Theresa Mullin, PhD
Director, Office of Strategic Programs
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Basic Observations

- Patients are uniquely positioned to inform FDA understanding of the clinical context
- FDA could benefit from a more systematic method of obtaining patients' point of view on the severity of a condition, and its impact on daily life, and their assessments of available treatment options
- Current mechanisms for obtaining patient input are often limited to discussions related to specific applications under review, such as Advisory Committee meetings

Patient-Focused Drug Development under PDUFA V

- FDA is developing a more systematic way of gathering patient perspective on their condition and available treatment options
  - Patient perspective helps inform our understanding of the context for the assessment of benefit-risk and decision making for new drugs
  - Input can inform FDA analysis both during and outside of review
- Patient-Focused Drug Development is part of FDA commitments under the fifth reauthorization of the Prescription Drug User Fee Act (PDUFA V)
  - FDA will convene at least 20 meetings on specific disease areas over the next five years
  - Meetings will help develop a systematic approach to gathering input

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Which Disease Areas would be the Focus of PDUFA V Meetings? Criteria for Nomination

- Disease areas that are chronic, symptomatic, and affect functioning and activities of daily living
- Disease areas for which important aspects of that disease are not formally captured in clinical trials
- Disease areas for which there are currently no therapies or very few therapies, or the available therapies do not directly affects how a patients feels, functions, or survives
- Disease areas that reflect a range of severity
- Disease areas that have a severe impact on identifiable sub-populations (such as children or the elderly)
- Disease areas that represent a broad range in terms of size of the affected population

Identifying Disease Areas for the Patient-Focused Meetings

- **In September 2012, FDA announced a preliminary set of diseases as potential meeting candidates**
  - Public input on these nominations was collected through an online docket and at a public meeting held in October 2012
  - Over 4,500 comments were submitted, which addressed over 90 disease areas
  - FDA carefully considered these public comments and the perspectives of our drug review divisions at FDA

- **FDA selected a set of 16 diseases selected to be the focus of meetings for fiscal years 2013-2015; this set was published in the Federal Register in April 2013**
  - Another public process will be initiated in 2015 to determine the set for fiscal years 2016-2017

Disease Areas to be the focus of meetings for FY 2013

FY 2013

1. Chronic fatigue syndrome – April 25
2. HIV – June 14
3. Lung cancer – June 28
4. **Narcolepsy – September 24**

Disease Areas to be the focus of meetings for FY 2014-2015

FY 2014 – 2015

- Alpha-1 antitrypsin deficiency
- Breast cancer
- Chronic Chagas disease
- Female sexual dysfunction
- Fibromyalgia
- Hemophilia A, Hemophilia B, von Willebrand disease, and other heritable bleeding disorders
- Idiopathic pulmonary fibrosis
- Irritable bowel syndrome, gastroparesis, and gastroesophageal reflux disease with persistent regurgitation symptoms on proton-pump inhibitors
- Neurological manifestations of inborn errors of metabolism
- Parkinson's disease and Huntington's disease
- Pulmonary arterial hypertension
- Sickle cell disease

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Tailoring Each Patient-Focused Meeting

- **In planning the format and questions we consider unique characteristics of the disease context**
  - E.g., current state of drug development, specific interests of the FDA review division, and the needs of the patient population
  - Each meeting focuses on a set of questions that aim to elicit patients' perspectives on their disease and on treatment approaches
- **Three meetings to date: CFS/ME, HIV, and lung cancer**
  - CFS/ME Focus: Impact of disease on patients' daily lives and experience with current treatments
  - HIV Focus: Patients' experience with current treatments and perspectives on potential "cure research"
  - Lung Cancer Focus: Patients' perspectives on the importance of disease symptoms, benefits of treatment approaches, and possible cancer treatment side effects

Tailoring Each Patient-Focused Meeting

- **We've been exploring different methods of gathering input: polling questions and interactive webcast options**
- **Common to all of the meetings:**
  - Patient, caretaker, and patient advocate perspectives were powerful and insightful
  - Patient stakeholder involvement was key to the success of past meetings

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Product of Patient-Focused Meetings

- **Each meeting will result in a meeting report that will be shared with FDA reviewers and posted on the FDA website**
  - The patient perspectives captured in these reports will provide helpful insights for FDA reviewers conducting benefit-risk assessment for drugs to treat that disease

Background on Narcolepsy and Therapeutic Options

Ronald Farkas, MD, PhD
Lead Medical Officer, Division of Neurology Products
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

Background on Rare Diseases

- Narcolepsy is the 1st rare disease being featured in our series of Patient-Focused Drug Development meetings

- Rare disease / orphan drug definition:
  - A disease or condition affecting less than 200,000 people in the US
  - Approximately 7,000 different rare diseases have been defined, affecting approximately 30 million Americans
  - So, almost 1 in 10 Americans suffer from rare diseases

Rare Disease Resources at FDA

- FDA Office of Health and Constituent Affairs
  - Contact info: PatientNetwork@fda.hhs.gov, (301) 796-8460
  - Liaison between FDA and stakeholder organizations
  - Runs the Patient Representative Program
    - Patient Representatives advise FDA at Advisory Committee meetings
- CDER Office of New Drugs Rare Disease Program
  - Supports the research, development, regulation, and approval of products for the treatment of rare disorders
- FDA Office of Orphan Products Development
  - Advances the evaluation and development of products that demonstrate promise for diagnosis or treatment of rare diseases
  - Provides incentives for sponsors to develop products for rare diseases

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Introduction

- Narcolepsy is an under-recognized and under-diagnosed condition
  - Estimated to affect more than 1 in 2,000 people in the U.S.
  - Fewer than 50,000 are diagnosed
- There are two general types of narcolepsy:
  - Narcolepsy without cataplexy
  - Narcolepsy with cataplexy
    - Narcolepsy with cataplexy is estimated to affect about 1 in every 3,000 Americans

Symptoms

- Symptoms start in childhood or adolescence, but may also occur later in life
  - Symptoms may first appear between the ages of 7 and 25 years
- Patients may experience symptoms including:
  - Excessive daytime sleepiness (EDS):
    - Permanent, steady sleepiness in waking hours
    - Decreased alertness throughout the day
    - In majority of cases, EDS is the first symptom to appear
  - Cataplexy:
    - Reduction or loss of muscle tone causing physical changes (e.g., slurred speech, weakness of muscles)
    - Uncontrollable; triggered by intense emotions (e.g., laughter, excitement, fear, surprise, anger)
    - Occurs in 60-90% of narcoleptic patients

Symptoms (cont'd)

- Hallucinations
  - *Hypnagogic hallucinations:* occur during sleep onset
  - *Hypnopompic hallucinations:* occur upon awakening
  - Occur in 40-80% of narcoleptic patients
- Sleep paralysis
  - Temporary inability to move, speak or breathe upon falling asleep or waking from REM (rapid eye movement) sleep
  - Occurs in 20-50% of narcoleptic patients
- Disrupted nocturnal sleep
  - Patients fall asleep rapidly, but have difficulty maintaining sleep
  - Occurs in 30-50% of narcoleptic patients
- Restless leg syndrome or periodic limb movement
  - Disorder characterized by an overwhelming urge to move the legs when they are at rest
  - Occurs in approximately 50% of narcoleptic patients

Symptoms (cont'd)

- Automatic behaviors
  - Continuing to perform ongoing action in a semiconscious way without remembering it, such as sleep walking.
- Other sleep disorders include:
  - REM sleep behavior disorder
    - Occurs in one-third of narcoleptic patients
  - Obstructive sleep apnea
- Other associated diseases include:
  - Obesity
  - Type 2 diabetes
  - Depression

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Treatment

- Symptoms of narcolepsy can be treated with drug treatments and lifestyle changes
- Drug treatments include:
  - Stimulants: modafinil, armodafinil, methylphenidate or amphetamines
  - Antidepressant drugs (off-label use)
  - Depressant: Sodium oxybate
- Lifestyle (behavioral) changes include:
  - Scheduled naps
  - Diet and exercise
  - Counseling and support groups

Common Side Effects of Treatment

- Common side effects of drug treatment may include:
  - Stimulants:
    - Irritability and nervousness
    - Shakiness
    - Disturbances in heart rhythm
    - GI problems: upset stomach, nausea
    - Nighttime sleep disruption
    - Anorexia
  - Anti-depressants:
    - Impotence
    - High blood pressure
    - Heart rhythm irregularities
    - GI problems
    - Headache and insomnia
  - Depressants
    - Drowsiness or sleepiness
    - Breathing problems
    - Depression
    - Hallucinations
    - Sleepwalking

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THANK YOU!

Overview of Discussion Format

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Discussion Format

- **We will first hear from a panel of patients and representatives**
  - The purpose is to set a good foundation for our discussion
  - Panel members include patients and advocates
  - They reflect a range of experiences with narcolepsy

- **We will then broaden the discussion to include other patients and patient representatives in the audience**
  - The purpose is to build on the experiences shared by the panel
  - The facilitator will ask follow up questions, inviting participants to raise hands to comment

Discussion Format, continued

- **Periodically, we will invite in-person and web participants to respond to specific "polling" questions**
  - The purpose is to aid discussion by seeing how many participants share a particular perspective
  - In-person participants can use the "clickers" to respond to a question
  - Web participants can respond to the poll through the webcast
  - We're looking for responses from patients and patient representatives
- **Those participating by live webcast can add additional comments through the webcast comment box**
  - Although they may not all be read or summarized today, they will be considered part of the public record

Public Docket

- **We invite all attendees to submit written or electronic comments to the docket**
  - The docket will be open until November 25, 2013
  - Go to http://www.regulations.gov/#!submitComment;D=FDA-2013-N-0815-0001 to submit your comments on today's discussion topics

Discussion Ground Rules

- We encourage patients, caregivers and other patient representatives to contribute to the dialogue
- The FDA panel is here to listen, and may periodically ask follow up questions during the discussion
- Discussion will focus on understanding the common ground regarding narcolepsy symptoms, impacts on daily life, and treatment approaches
- Your feedback on the meeting is important to us; evaluation forms are at the registration desk
- The views expressed today are personal opinions; respect for one another is paramount

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

Have you ever been diagnosed as having narcolepsy?

A. Yes
B. No

Are you:

A. Male
B. Female

Age:

A. Younger than 10
B. 11 – 20
C. 21 – 30
D. 31 – 40
E. 41 – 50
F. 51 – 60
G. 61 or greater

What is the length of time since your diagnosis?

A. Less than 5 years ago
B. 5 years ago to 10 years ago
C. 10 years ago to 20 years ago
D. More than 20 years ago
E. I'm not sure

Discussion Topic 1

Disease symptoms and daily impacts that matter most to patients

Soujanya Giambone
Facilitator

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Topic 1 Panel Participants

- Kerry Lenzi
- Brandon Coonrod
- Fran Rosen
- Joseph Poplawski
- Carrie Bollino

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

- Of all the symptoms that you experience because of your condition, which 1-3 symptoms have the most significant impact on your life?
- 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?
- How have your symptoms changed over time?

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

A. Cataplexy
B. Daytime sleepiness
C. Hallucinations while waking up or falling asleep
D. Sleep paralysis
E. Difficulty sleeping
F. Restless leg syndrome
G. Activity while sleeping, such as sleepwalking
H. Other symptoms not mentioned

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

- Of all the symptoms that you experience because of your condition, which 1-3 symptoms have the most significant impact on your life?
- 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?
- How have your symptoms changed over time?

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BREAK

Discussion Topic 2

Patients' perspectives on current approaches to treating narcolepsy

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Topic 2 Panel Participants

- Allison Greenstein
- LaShun Ray
- Casey Thompson
- Sharon O'Shaughnessy
- Justin Greene

Topic 2 Discussion: Patient perspectives on treating narcolepsy

- What are you currently doing to help treat your condition or its symptoms?
- How well does your current treatment regimen treat the most significant symptoms of your disease?
- What are the most significant downsides to your current therapies, and how do they affect your daily life?
- Assuming there is no complete cure for your condition, what specific things would you look for in an ideal therapy for your condition?

Have you ever used any of the following drug therapies to help reduce your symptoms of narcolepsy? **(check all that apply)**

A. Modafinil, armodafinil, methylphenidate, amphetamine
B. Anti-depressant drugs (off label use)
C. Xyrem (Sodium oxybate)
D. Other drug therapies not mentioned
E. I'm not sure

Besides your drug therapies, what therapies have you used to help reduce your symptoms of narcolepsy?

A. Naps
B. Dietary modifications
C. Exercise
D. Counseling and support groups
E. Other therapies not mentioned
F. I'm not using any additional therapies

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Open Public Comment Period

Closing Remarks

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