Open Meeting: Nebulizers

Meeting Date & Time:	November 3, 2021, 10:00 a.m. ET
Facilitator:	Belinda Yandell
Location:	Virtual Meeting

Belinda Yandell (0:01): Good morning. My name is Belinda Yandell.

I'm a Senior Analyst with Provider Outreach and Education here at CGS, and I'll be moderating the meeting today.

For those of you that are scheduled to present your comments this morning, please make sure you have entered your audio PIN into your telephone keypad.

If you can hear my voice but you have not entered your audio pin, then you must hit the pound key and enter your audio PIN, and then hit the pound key once more.

Again, just as a note, the audio PIN is located in the audio pane.

That is to the right of the screen on the GoToWebinar app.

It is imperative that you do this so that we can unmute your line when it's your turn to speak.

Now I'm going to turn the meeting over to Doctor Robert Hoover.

Dr. Robert Hoover (0:51): Thank you for joining. The purpose of this meeting is to solicit public comments on the proposed Nebulizer Local Coverage Determination.

My name is Dr. Robert Hoover the CGS jurisdiction C DME Medical Director. And the here today with me also from CGS is Jurisdiction B's Medical Director, Dr. Stacey Brennan.

Dr. Smitha Ballyamanda and Dr. Peter Gurk represent Noridian Healthcare Solutions, the Medical directors for Jurisdictions A and D, respectively.

We look forward to hearing your comments today regarding the Nebulizers LCD.

Please put these comments in writing and send them to us via e-mail at NEBLCDComments (all one word), N-E-B-L-C-D-C-O-M-M-E-N-T-S at CGSadmin dot com.

We'll also have additional details at the end of the meeting for that.

There are also instructions on our websites for submitting comments.

Please remember that we can only respond to written comments.

And all comments are due by close of business on Saturday, November, the 13th.

Also, note that we'll be recording the meeting today, which will be posted on the DME MAC websites in the coming weeks.

You're giving your consent to the use of your recorded voice and comments by signing into this meeting.

We remind everyone to please be careful about sharing any personal health information in your verbal comments.

We have one commenter today who pre-registered to provide oral comments.

We're only permitting those pre-registered commenters to speak at today's meeting, but anyone can submit written comments to the e-mail address I mentioned earlier.

For those pre-registered comments, each person will have 10 minutes to present their oral comment.

Speakers should be prepared to begin their comments immediately when called on by our moderator.

So, turning to the proposed nebulizer LCD, this proposed LCD makes two changes first the change to the covered indications for inhaled treprostinil.

Earlier this year, an article was published in the New England Journal of Medicine detailing a multicenter, randomized, double-blind, placebo-controlled trial, aimed to determine the safety and efficacy of inhaled treprostinil for the treatment of pulmonary hypertension due to interstitial lung disease, also classified as World Health Organization Group 3 Pulmonary Hypertension.

Interstitial lung diseases represents a heterogeneous group of disorders that affect alveolar structures, the pulmonary interstitium, and small airways, leading to progressive scarring of the lungs.

Approximately two thirds of interstitial lung disease patients are idiopathic—the causes are idiopathic—with idiopathic interstitial pneumonias being the most common entities.

The prevalence of pulmonary hypertension associated with interstitial lung disease varies based on the underlying cause and severity of the lung disease, pulmonary hypertension, due to interstitial lung disease is associated with decreased exercise tolerance and quality of life, and the need for supplemental oxygen.

When approved by the FDA in March 2021, treprostinil inhalation solution became the first FDA approved treatment option for pulmonary hypertension due to interstitial lung disease, with an intent to improve exercise ability.

The second change in the proposed LCD is to remove coverage for iloprost and treprostinil inhalation solutions for the indication of chronic thromboembolic pulmonary hypertension, classified as World Health Organization Group 4.

After a review of FDA indications for iloprost and inhaled treprostinil solutions, neither drug has FDA approval for use in patients with chronic thromboembolic pulmonary hypertension. Therefore, pulmonary hypertension, secondary to thromboembolic disease of the pulmonary arteries will be removed from the covered indications for iloprost and treprostinil inhalation solutions in the Nebulizer LCD. The ICD 10 tables in the LCD-related policy article will be updated to reflect this change.

Now I'll turn the meeting back over to our moderator Belinda Yandell from CGS who will open the line for oral comment speakers.

Belinda Yandell (5:18): Thank you, Dr. Hoover.

Our first presenter today, Steven Nathan, MD.

Dr. Nathan, you have 10 minutes. If you just let me know when you are ready for me to advance the slides—let me find you here, online.

There you are. I am unmuting your line. Can you hear me, Doctor—Dr. Nathan?

Dr. Steven Nathan (5:41): Yeah, can you hear me?

Belinda Yandell (5:43): Yes. Got you loud and clear.

Dr. Steven Nathan (5:44): I actually called in. That's because I wasn't sure I was in. So I'm going to hang up on my cell phone and hopefully I'll still be good here.

I'm probably echoing, so I'm going to hang up on the one line.

Belinda Yandell (5:55): Okay.

Dr. Steven Nathan (5:55): Can you still hear me?

Belinda Yandell (5:56): I can now.

Dr. Steven Nathan (5:58): Excellent, OK, I'm ready to go. And you'll just advance the slides for me, correct?

Belinda Yandell (6:03): Yes.

Dr. Steven Nathan (6:05): OK, so you can see my title there. I am the Medical Director of the Advanced Lung Disease and Lung Transplant Program at Inova Fairfax Hospital, and I'm here today as on behalf of the United Therapeutics. Next slide, please.

On March 31st of this year, Tyvaso which is inhaled treprostinil became the first FDA approved treatment for pulmonary hypertension due to interstitial lung disease, with a labeling to improve exercise ability.

The study which was the INCREASE study, established the effectiveness, predominantly, included patients with etiologies of idiopathic interstitial pneumonias, which included the prototypical illness idiopathic pulmonary fibrosis, also included patients with combined pulmonary fibrosis and emphysema, as well as connective tissue disease patients with interstitial lung disease.

This is the second FDA approved indication for Tyvaso which was first approved in July of 2009. The treatment of PAH, Pulmonary arterial hypertension, also to improve exercise ability.

United Therapeutics has requested updates to the LCD on Nebulizers L33370 and the accompanying LCA A52466 to accommodate this new indication. Next slide please.

Pulmonary hypertension is a common complication of most forms of interstitial lung disease and its associated with a significantly worse prognosis, worsened functional status, reduced quality of life, greater oxygen needs, and increased mortality, as shown on the curve for the survival curve to the right, where it's shown in relation to idiopathic pulmonary arterial hypertension, the prognosis being significantly worse.

If you look just there at one year, the mortality is about 40%. And certainly going at five years very few patients will survive once they get interceding primary hypertension.

Next slide please.

The INCREASE study was a randomized, controlled clinical trial. It's the largest study to date in group 3 pulmonary hypertension with patients randomized equally to inhaled Treprostinil four times a day, versus placebo. The primary endpoint was a change in the six minute walk test distance at 16 weeks. There are a number of secondary endpoints, including the biomarker NT-proBNP, composite endpoints of time to clinical worsening, peak six minute walk at 12 weeks, as well as a trough six minute walk at 15 weeks.

And then we also looked at various safety endpoints, which has shown to the right.

Next slide please.

This is the primary output from this study. This was a positive study based on the primary endpoint of six minute walk distance, with the placebo corrected difference of 31 meters at 16 weeks, and we also hit on the various secondary endpoints of six minute walk at 12 weeks, as well as the trough six minute walk at 16 weeks.

Next slide, please.

Significant differences were observed for our biomarker, the NT-proBNP, in the placebo arm it went up, in the treatment arm it went down, indicating less right ventricular strain and stress.

We also hit on the important secondary endpoint of time to clinical worsening with a 39% percent relative reduction, which was statistically significant.

And as I mentioned, the various looks at the six minute walk distance at various times, including the trough, were also positive. So, hit on the primary, hits on pretty much all the secondaries as well.

Next slide please.

Treatment with Tyvaso was well tolerated. Safety profile was consistent with previous studies of inhaled treprostinil. Most of the adverse events were mild to moderate.

There was an equivalent number of discontinuations between the placebo and the treatment arms. Serious adverse events were almost—were more or less equivalent between the placebo and the treatment arms, as well, and 26% of patients receiving inhaled treprostinil had an exacerbation of the underlying lung disease versus 38% of the placebo patients. This was actually a safety endpoint but it went directionally unfavorably towards treprostinil, so certainly treprostinil appears to have a benefit also an acute exacerbations of the underlying lung disease. There were no treatments related to changes in pulse oximetry or increasing need for supplemental oxygen, when you compare the inhaled treprostinil to the placebo on either.

Next slide, please.

So in conclusion, INCREASE is the largest and most comprehensive study of patients with ILDPH to date.

There were significant improvements in exercise capacity, which was sustained throughout the 16 week treat—16 week treatment period.

Patients demonstrated improvements in other clinically meaningful benefits—outcomes rather—including the NT-proBNP, reduce risk of clinical worsening, as well as reduce risk of acute exacerbations of the underlying interstitial lung disease.

The treatment was generally well tolerated. There was no evidence of worsening oxygenation of the V/Q mismatch.

And these results support an additional treatment avenue and does, indeed, herald a shift in the clinical management of patients with interstitial lung disease.

Next slide, please.

So the summary of proposed changes are shown here.

They are to expand coverage for treprostinil inhalation solution and nebulizer to include PH ILD subject to specific criteria—adding the ICD 10 diagnosis code of I27.23, which is pulmonary hypertension due to lung disease and hypoxia, for PH ILD and then to remove coverage of inhaled treprostinil, as well as iloprost, for chronic thromboembolic pulmonary hypertension or CTEPH (which is Group 4 pulmonary hypertension) since neither drug has an FDA approved indication for CTEPH.

United Therapeutics agrees with all these proposed changes, including proposed coverage criteria for PH ILD in accordance with the INCREASE clinical trial inclusion criteria, and the addition of ICD 10 Code I27.23, and removal of I27.24, we believe, is also appropriate. So in agreement with that, as well. And I believe that is the last slide.

Oh, sorry. Last slide.

In conclusion, once again PH ILD is a serious, progressive disease characterized by very poor survival. Treprostinil inhalation solution is the only FDA approved treatment for PH ILD. Medicare patients will be best served if the DME MACs provide the proposed coverage as soon as possible.

And I'll stop there, and I'm not sure if we're opening this up to questions, but happy to take any questions, as well.

Belinda Yandell (13:07): Thank you, Dr. Nathan.

I am going to mute your line and turn it back over to Dr. Hoover for the time being.

Dr. Robert Hoover (13:16): Thank you, Dr. Nathan, and to answer your question, we don't have a Q and A session on this, officially. If there are questions that the medical directors have of a presenter, there have been occasions when we've asked questions but, in your case, I'd don't know if any of the other medical directors have any questions, but I suspect not so—. We would like to thank all members of the public and the stakeholders that attended today's open meeting, and especially thank you Dr. Nathan for taking the time out to present your oral comments.

Once again, please remember to send your comments in writing.

If you have any full text peer reviewed articles to help support your comments that are not included in the proposed LCD's bibliography, please send them along as well.

As a reminder, as I mentioned earlier, the comment period will end on Saturday, November the 13th, 2021.

Once again, the e-mail address for sending comments is NEBLCDcomments (that's plural) at CGSadmin dot com, NEBLCDcomments@ (at symbol) CGSadmin dot com.

Once we have considered and collated all the written comments received during the comment period, we'll consider any changes necessary to the proposed LCD. In addition, the DME MACs will address comments, in a response to comments document that will come out with the final LCD. For any updates, please refer to the DME MAC website.

I would encourage you to sign up for our Listservs, and that information is available on each of the DME MAC websites for doing that.

Thanks to everyone for their participation today, and we will adjourn the meeting at this time.

Thank you, Belinda.

Belinda Yandell (15:07): Thank you, Dr. Hoover.