Transcript Details
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An Advancement in Oral Testosterone Replacement Therapy

Announcer:
This medical industry feature, titled "An Advancement in Oral Testosterone Replacement Therapy," is sponsored by Clarus Therapeutics, Inc., driven by a mission to help men overcome the symptoms of hypogonadism.

This program is intended for physicians.

Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
Although testosterone replacement therapy, or TRT for short, is a common therapeutic approach for men with certain forms of hypogonadism, treatment delivery options have remained static for years. That is, until now.

On today's program, we'll be taking a look at one of the most recent advancements in the TRT treatment landscape. This is ReachMD, and I'm your host, Dr. Jennifer Caudle. Joining me to discuss an available oral formulation for testosterone replacement therapy is Dr. Adrian Dobs, Professor of Endocrinology and Director of the Johns Hopkins Clinical Research Network, and Dr. Faysal Yafi, Assistant Clinical Professor of Urology and Medical Director of the Men's Health Program at UC Irvine Health.

Dr. Dobs and Dr. Yafi are paid consultants for Clarus Therapeutics, Incorporated.

Dr. Dobs and Dr. Yafi – welcome to you both.

Dr. Dobs:
Thank you, our pleasure to be here.

Dr. Yafi:
Excited about the conversation, thank you.

Dr. Caudle:
Before we dive into our discussion, let's review the indication and boxed warning for JATENZO, which will be the focus of today's program.

INDICATION
JATENZO® (testosterone undecanoate) capsules, CIII, is an androgen indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:

• Primary hypogonadism (congenital or acquired): testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins or (follicle-stimulating hormone or [FSH], luteinizing hormone or [LH]) above the normal range.
• Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone or (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

Limitation of use
Safety and efficacy of JATENZO in males less than 18 years old have not been established.

IMPORTANT SAFETY INFORMATION

WARNING: INCREASES IN BLOOD PRESSURE

• JATENZO can cause blood pressure or (BP) increases that can increase the risk of major adverse cardiovascular events or (MACE), including non-fatal myocardial infarction, non-fatal stroke and cardiovascular death.
• Before initiating JATENZO, consider the patient's baseline cardiovascular risk and ensure blood pressure is adequately controlled.
• Periodically monitor for and treat new-onset hypertension or exacerbations of pre-existing hypertension and re-evaluate whether the benefits of JATENZO outweigh its risks in patients who develop cardiovascular risk factors or cardiovascular disease on treatment.
• Due to this risk, use JATENZO only for the treatment of men with hypogonadal conditions associated with structural or genetic etiologies.

CONTRAINDICATIONS
JATENZO is contraindicated in men with carcinoma of the breast or known or suspected carcinoma of the prostate, in women who are pregnant, in men with a known hypersensitivity to JATENZO or its ingredients, or in men with hypogonadal conditions that are not associated with structural or genetic etiologies as JATENZO has not been established for these conditions and there is a risk of increased blood pressure with JATENZO that can increase the risk of MACE.

Dr. Caudle:
So, Dr. Dobs, it's an unfortunate reality that men often bear a sort of stigma associated with issues like hypogonadism. How do you most commonly see this stigma manifesting in clinical practice?

Dr. Dobs:
It's important to ask questions of a gentleman that comes in the door because some of the issues that may develop can be subtle and perhaps embarrassing to men. So we're looking for not only the symptoms and the signs, but also the blood tests, and it's crucial that a serum testosterone level be measured and repeated, to ensure that it's right, before any treatment would be contemplated.

Dr. Caudle:
And how about you, Dr. Yafi? What did you witness from your practice? And how do you address this issue with your patients?

Dr. Yafi:
Well, hypogonadism is a – is an important and prevalent condition that I encounter very frequently in – in my practice, on a daily basis. It can have some significant ramifications on patients, and as such, I always emphasize the importance of treating it appropriately, with FDA approved testosterone replacement therapy options, such as JATENZO, and to steer away from other, non-approved and non-proven, therapies.

Dr. Caudle:
And, as I understand it, Dr. Yafi, there's now an oral option in testosterone replacement therapy. Can you elaborate on what that option is, and who it's intended to treat?

Dr. Yafi:
Why yes, we now have JATENZO, which is the first and only FDA-approved oral softgel testosterone undecanoate for testosterone replacement therapy in adult males, for conditions associated with a deficiency or absence of endogenous testosterone, due to certain medical conditions. JATENZO is indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone, and this could be due to primary hypogonadism, which is basically in the testicles, and that can be either congenital or acquired, and hypogonadotropic hypogonadism, which can also be congenital or acquired. JATENZO is not for use in men with hypogonadal conditions, such as age-related hypogonadism, that are not associated with structural or genetic etiologies.

Dr. Caudle:
That's interesting. Dr. Dobs, do you have anything to add to what Dr. Yafi just said?

Dr. Dobs:
When we – we talk about who this drug is intended to help, I want to include some important background. There are other options available for testosterone replacement therapy. However, we often see a cycle of discontinuation among those options, due to the problems with the methods of delivery, that is, either gels or injections. So, I'm very excited to have an oral option now available to my patients.

Dr. Caudle:
Sticking with you for just another moment, Dr. Dobs, what were the results of the clinical trial supporting JATENZO?

Dr. Dobs:
In an open label study of JATENZO, 87% of the patients reached testosterone levels within the normal eugonadal range at the end of the study. JATENZO was evaluated among 166 adults hypogonadal men, in the four month study, which was open label, and called the "inTUne" study. The starting dose was 237 milligrams, given twice daily, that is, b.i.d., with meals. The dose adjustments were made at day 21 and 56. The minimum dose was 158 milligrams b.i.d., and the maximum was 396 milligrams, b.i.d. So based on the average testosterone concentration, obtained at 24-hours, the post-morning dose, it turned out that 87% were able to obtain normal levels.

Dr. Caudle:
For those of you who are just tuning in, you're listening to ReachMD. I'm your host Dr. Jennifer Caudle, and here with me is Dr. Adrian Dobs and Dr. Faysal Yafi to discuss JATENZO, an oral formulation for testosterone replacement therapy.

So, Dr. Yafi, now that we have a better understanding of the clinical trials that investigated JATENZO, can you walk us through how JATENZO works to support appropriate testosterone levels?

Dr. Yafi:
Well, well let's look at the pharmacokinetics of JATENZO. It is taken orally, twice daily, once in the morning and once in the evening, with food. It's absorbed as a prodrug, and is carried by lipoproteins into the lymphatics, thus allowing it to avoid first pass hepatic metabolism. Then once in the circulation, the active testosterone component is released, and is thus available.

Dr. Caudle:
And based on your own experience, Dr. Yafi, why would you choose to prescribe JATENZO to your patients?

Dr. Yafi:
To me, JATENZO's key attributes include: it serves an unmet need as the first and only FDA approved oral testosterone undecanoate for appropriate patients with hypogonadism. Another feature is its unique formulation, with up to two softgel capsules taken twice daily with food, such as breakfast and dinner. It's available in 158, 198 and 237 milligram doses. The patients can take two pills of the 158 or two of the 198 milligrams, which allows us for five different doses, and this allows for appropriate dosage titration, based on the patient's serum testosterone concentration response.

Another reason is the normalization of testosterone levels. Actually, in the inTUne study, 87% of men treated with JATENZO achieved average circulating levels of testosterone in the normal range for men. It also allows avoiding certain testosterone administration challenges that are seen with other testosterone replacement options. It eliminates the worry for transference and skin irritation that is seen with topical testosterone, and pain that is seen with injections. Another reason is the absence of liver toxicity. If you look at the clinical trials, there were no liver toxicity related events that were reported, and this is because, as mentioned previously, JATENZO is absorbed into the intestinal lymphatic system, thereby bypassing the liver.

Finally, JATENZO has an established and robust safety profile. In that four-months open label study with JATENZO, adverse reactions were seen in less than 2% of patients.

Dr. Caudle:
And before we wrap up, Dr. Dobs, is there anything else physicians should know when considering JATENZO for their patients?

Dr. Dobs:
JATENZO was approved with a black box warning for increases in blood pressure. As with any medication, there is always this risk benefit. It is probably a class effect, due to the potential risk of the increased blood pressure, JATENZO should only be used to treat men with hypogonadal conditions associated with structural or genetic causes. Liver toxicity, as Dr. Yafi already mentioned, was not observed with JATENZO in clinical trials. There was a mild decrease in HDL, and an increase in LDL, that was observed, but did not lead to any drug discontinuation. And finally, mild gastrointestinal adverse events were observed with JATENZO, but they were all manageable and did not lead to discontinuation.

Dr. Caudle:
Thanks for sharing that, Dr. Dobs. And Dr. Yafi, you get the final word.

Dr. Yafi:
Thanks. I'd just like to reiterate how exciting it is to have this important, oral, safe and effective testosterone replacement therapy in JATENZO, for patients with hypogonadism seeking medical treatment. Lastly, I would like to encourage physicians to visit JATENZO.com for full prescribing information.

Dr. Caudle:
Thank you both for those comments, which does bring us to the end of today's program. I'd like to thank Dr.'s Adrian Dobs and Faysal

Yafi for introducing JATENZO as an advancement in oral testosterone replacement therapy. Dr. Dobs, Dr. Yafi, it was great speaking with you both today.

Dr. Dobs:
Thank you.

Dr. Yafi:
Thank you, my pleasure.

Announcer:
And now, here's some important safety information.

INDICATION

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• Primary hypogonadism (congenital or acquired): testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins or (follicle-stimulating hormone or [FSH], luteinizing hormone or [LH]) above the normal range.
• Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone or (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

Limitation of use

Safety and efficacy of JATENZO in males less than 18 years old have not been established.

IMPORTANT SAFETY INFORMATION

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• Periodically monitor for and treat new-onset hypertension or exacerbations of pre-existing hypertension and re-evaluate whether the benefits of JATENZO outweigh its risks in patients who develop cardiovascular risk factors or cardiovascular disease on treatment.
• Due to this risk, use JATENZO only for the treatment of men with hypogonadal conditions associated with structural or genetic etiologies.

CONTRAINDICATIONS

JATENZO is contraindicated in men with carcinoma of the breast or known or suspected carcinoma of the prostate, in women who are pregnant, in men with a known hypersensitivity to JATENZO or its ingredients, or in men with hypogonadal conditions that are not associated with structural or genetic etiologies as JATENZO has not been established for these conditions and there is a risk of increased blood pressure with JATENZO that can increase the risk of MACE.

WARNINGS AND PRECAUTIONS

• JATENZO can increase blood pressure, which can increase the risk of MACE, with greater risk in patients with established cardiovascular disease or risk factors for cardiovascular disease. Before initiating JATENZO, consider the patient's baseline cardiovascular risk and ensure blood pressure is adequately controlled. Monitor blood pressure approximately 3 weeks after initiating, increasing the dose, and periodically while on JATENZO, and treat any new or exacerbations of hypertension. Re-evaluate benefits and risks of continued treatment with JATENZO in patients who develop cardiovascular risk factors or disease. JATENZO is contraindicated in men with hypogonadal conditions such as "age-related hypogonadism" because the efficacy of JATENZO has not been established for these conditions and the increases in BP can increase the risk of MACE.
• Polycythemia may require a lower dose or discontinuation of JATENZO. Check hematocrit prior to initiation and every 3 months while a patient is on JATENZO and if hematocrit becomes elevated, stop JATENZO until hematocrit decreases to an acceptable level. If hematocrit increases after JATENZO is restarted, stop permanently.
• Some studies, but not all, have reported an increased risk of major adverse cardiovascular events or (MACE) in association with use of testosterone replacement therapy in men. Long-term clinical safety trials have not been conducted to assess the cardiovascular outcomes of testosterone replacement therapy in men. Patients should be informed of this possible risk when deciding whether to use

or to continue to use JATENZO. JATENZO can increase blood pressure, which can increase the risk of MACE.
• Monitor patients with benign prostatic hyperplasia or (BPH) treated with androgens due to an increased risk for worsening signs and symptoms of BPH. Patients treated with androgens may be at increased risk for prostate cancer and should be evaluated prior to initiating and during treatment with androgens. Monitor prostate-specific antigen or (PSA) levels periodically.
• Postmarketing reports of venous thromboembolic events or (VTE), including deep vein thrombosis or (DVT) and pulmonary embolism (PE), have been reported in patients using testosterone replacement products like JATENZO. Evaluate patients with signs or symptoms consistent with DVT or PE and, if a VTE is suspected, discontinue JATENZO and initiate appropriate workup and management.
• Testosterone has been subject to abuse, typically at doses higher than recommended for the approved indication and in combination with other anabolic androgenic steroids. Anabolic androgenic steroid abuse can lead to serious cardiovascular and psychiatric adverse reactions. If abuse is suspected, check testosterone levels to ensure they are in the therapeutic range. Counsel patients concerning the serious adverse reactions associated with abuse of testosterone and anabolic androgenic steroids. Conversely, consider the possibility of testosterone and anabolic androgenic steroid abuse in suspected patients who present with serious cardiovascular or psychiatric adverse events.
• JATENZO is not indicated for use in women.
• Large doses of androgens can suppress spermatogenesis by feedback inhibition of pituitary FSH. Inform patients of this risk before prescribing JATENZO.
• Prolonged use of high doses of methyltestosterone has been associated with serious hepatic adverse events. JATENZO is not known to cause these adverse events; however, patients should be instructed to report any signs of hepatic dysfunction and JATENZO should be discontinued while the cause is evaluated.
• Androgens, including JATENZO, may promote retention of sodium and water. Edema, with or without congestive heart failure, may be a serious complication in patients with pre-existing cardiac, renal, or hepatic disease. In addition to discontinuation of the drug, diuretic therapy may be required.
• Gynecomastia may develop and persist in patients being treated for hypogonadism.
• The treatment of hypogonadal men with testosterone may potentiate sleep apnea in some patients, especially those with risk factors such as obesity or chronic lung disease.
• Changes in the serum lipid profile may require dose adjustment of lipid-lowering drugs or discontinuation of testosterone therapy. Monitor the lipid profile periodically, particularly after starting testosterone therapy.
• Use JATENZO with caution in cancer patients at risk of hypercalcemia. Monitor serum calcium concentration regularly during treatment with JATENZO in these patients.
• Androgens, including JATENZO, may decrease concentrations of thyroxine-binding globulin, resulting in decreased total T4 serum concentrations and increased resin uptake of T3 and T4. Free thyroid hormone concentrations remain unchanged, however, and there is no clinical evidence of thyroid dysfunction.
• Depression and suicidal ideation have been reported in patients treated with JATENZO in clinical trials. Advise patients and caregivers to seek medical attention for manifestations of new-onset or worsening depression, suicidal ideation or behavior, anxiety, or other mood changes.

ADVERSE EVENTS

The most common adverse events of JATENZO (incidence ≥2%) are headache (5%), increased hematocrit (5%), hypertension (4%), decreased HDL (3%), and nausea (2%).

DRUG INTERACTIONS

• JATENZO can cause changes in insulin sensitivity or glycemic control. Androgens may decrease blood glucose and may require a decrease in the dose of antidiabetic medications.
• Anticoagulant activity may be affected by androgens. More frequent monitoring of international normalized ratio or (INR) and prothrombin time are recommended in patients taking warfarin, especially at initiation and termination of androgen therapy.
• Use of testosterone and corticosteroids concurrently may increase fluid retention and requires monitoring in patients with cardiac, renal, or hepatic disease.
• Some prescription and nonprescription analgesic cold medications contain drugs known to increase blood pressure and concomitant use of these medications with JATENZO may lead to additional increases in blood pressure.

USE IN SPECIFIC POPULATIONS

The safety and efficacy of JATENZO in pediatric patients less than 18 years old have not been established. Improper use may result in acceleration of bone age and premature closure of epiphyses.

There have not been sufficient numbers of geriatric patients involved in controlled clinical studies utilizing JATENZO to determine

whether efficacy or safety in those over 65 years of age differs from younger subjects. There is insufficient long-term safety data in geriatric patients utilizing JATENZO to assess the potentially increased risk of cardiovascular disease and prostate cancer.

Please visit jatenzo.com/hcp for full prescribing information, including BOXED WARNING on increases in blood pressure.

This program was brought to you by Clarus Therapeutics. If you missed any part of this discussion, visit ReachMD.com. This is ReachMD. Be part of the knowledge.