JATENZO®
(testosterone undecanoate) capsules, CIII

What is JATENZO?

JATENZO is the first and only FDA-approved oral testosterone undecanoate for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.[1,2]

The U.S. Food & Drug Administration (FDA) approved JATENZO on March 27, 2019.[3]

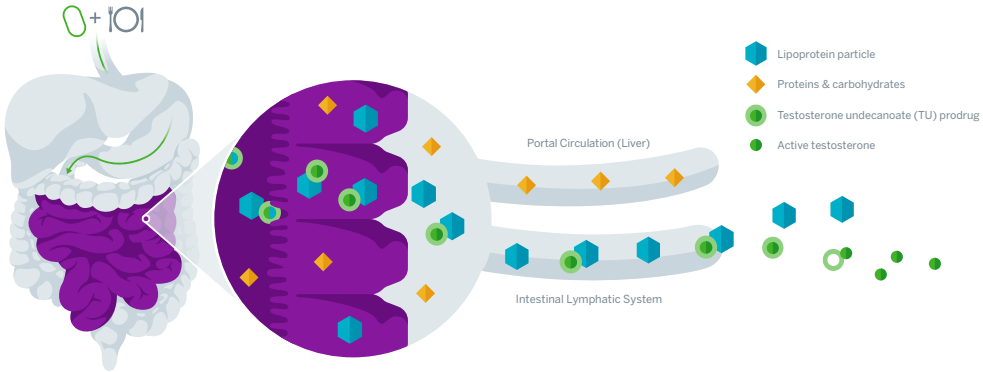
JATENZO has a Boxed Warning on the risk that the drug can cause increases in blood pressure, increasing the risk of heart attack, stroke and cardiovascular death. Please continue to read the full Important Safety Information.[1]

JATENZO Clinical Results

JATENZO was approved based on the efficacy results from the Phase 3 inTUne trial.[1]

For more information about JATENZO, please visit **JATENZO.com/HCP.**

Pharmacokinetics[1,4,5]



1 Taken orally with food

Each JATENZO softgel contains testosterone undecanoate (TU), a prodrug formed by attaching a fatty acid to testosterone, which the body naturally cleaves off to release testosterone.

2 Carried by lipoproteins into lymphatics

Once in the intestine, this lipophilic prodrug combines with lipoprotein particles, allowing absorption through the intestinal lymphatic system. In contrast, carbohydrates and proteins are absorbed into the portal circulation.

3 Avoids first-pass hepatic metabolism

JATENZO passes into the intestinal lymphatic system **(therefore bypassing the liver)** as testosterone awaits activation.

4 Release of active testosterone in circulation

After TU releases from lipoprotein particle, endogenous esterases liberate testosterone from TU. Fatty acid is metabolized like dietary fatty acids.

References:

[1]JATENZO (testosterone undecanoate) [prescribing information]. Clarus Therapeutics, Inc.

[2]US Food & Drug Administration. FDA Approved Drug Products. Available at: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=206089. Accessed October 1, 2019.

[3]US Food & Drug Administration. FDA approves new oral testosterone capsule for treatment of men with certain forms of hypogonadism. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-new-oral-testosterone-capsule-treatment-men-certain-forms-hypogonadism. Accessed October 1, 2019.

[4]Data on file. Clinical Study Report: CLAR-15012. Clarus Therapeutics, Inc.

[5]Data on file. BRUDAC Presentation; January 9, 2018. Clarus Therapeutics, Inc.

[6]Shoskes JJ, Wilson MK, Spinner ML. Pharmacology of testosterone replacement therapy preparations. *Transl Androl Urol.* 2016;5(6):834-843.

Please see Important Safety Information throughout and accompanying full Prescribing Information.

Why JATENZO?

Serves an unmet medical need:

First and only FDA-approved oral testosterone undecanoate for appropriate patients with hypogonadism.[1,2]

Unique formulation:

Up to 2 softgel capsules taken twice daily with food—such as breakfast or dinner. Available in 158 mg (red softgel), 198 mg (white softgel), and 237 mg (orange softgel), allowing for dose personalization.[1]

Normalized T-levels:

In the pivotal *inTUne* (**in**vestigational **t**estosterone **u**ndeca**n**oat**e**) study, 87% (n=166) of men treated with JATENZO achieved average circulating levels of testosterone in the normal range for men.[1]

Avoids certain administration challenges:

Eliminates the worry of gel transference, skin irritation from patches, or pain from injections that other testosterone treatments carry.[6]

No liver toxicity-related events have been observed in clinical trials:

JATENZO passes into the intestinal lymphatic system (thereby bypassing the liver).[4]

JATENZO® (testosterone undecanoate) Capsules CIII

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Efficacy results[1]

JATENZO was evaluated among 166 adult, hypogonadal men in the 4-month, open-label inTUne study. The starting dose was 237 mg twice-daily (BID) with meals. Dose adjustments were made on Days 21 and 56 (minimum 158 mg BID; maximum 396 BID), based on average testosterone concentration obtained over 24 hours post-morning dose. The primary endpoint was the percentage of patients with mean plasma total testosterone concentration (C_{avg}) over 24 hours within the normal eugonadal range on the final pharmacokinetic (PK) visit of the study. Please visit JATENZO.com/HCP for full inclusion criteria.

In the inTUne trial, 87% of patients reached testosterone levels within normal eugonadal range at the end of the study.

The secondary endpoints were the percentage of patients who received JATENZO and had C_{max} less than or equal to 1500 ng/dL, between 1800 and 2500 ng/dL, and greater than 2500 ng/dL at the final PK visit were 83%, 3%, and 3%, respectively.

In pharmacokinetic studies, steady state testosterone concentration was achieved by Day 7 and was stable over an extended time person (>9 months).

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 (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range.
- Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone (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 (BP) increases that can increase the risk of major adverse cardiovascular events (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.**

Please see Important Safety Information throughout and accompanying full Prescribing Information.

Established Safety Profile for JATENZO[1]

In a 4-month study with JATENZO (n=166), the following adverse reactions were seen in ≥2%.[1]

Number (%) of patients with adverse reactions

PREFERRED TERM	OVERALL (n=166) n (%)
HEADACHE	8 (4.8)
HEMATOCRIT INCREASED	8 (4.8)
HYPERTENSION	6 (3.6)
HIGH-DENSITY LIPOPROTEIN DECREASED	5 (3.0)
NAUSEA	4 (2.4)

Three of the 166 patients (1.8%) in the 4-month study experienced adverse reactions that led to premature discontinuation from the study, including rash (n=1) and headache (n=2).

Adverse reactions were reported in >2% of patients in all Phase 2 and 3 JATENZO trials combined (N=569):

- Polycythemia, diarrhea, dyspepsia, eructation, peripheral edema, nausea, increased hematocrit, headache, prostatomegaly, and hypertension.

JATENZO® CII
(testosterone undecanoate) Capsules

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IMPORTANT SAFETY INFORMATION (continued)

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 (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 (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 (PSA) levels periodically.
- Postmarketing reports of venous thromboembolic events (VTE), including deep vein thrombosis (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 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 inpatients 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.

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Capsules

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IMPORTANT SAFETY INFORMATION (continued)

- 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 (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 see accompanying full Prescribing Information, including BOXED WARNING on increases in blood pressure.

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Capsules