The **first** and **only** FDA-approved **oral** testosterone undecanoate (TU) is here for men with hypogonadism[1,2]

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, including BOXED WARNING on increases in blood pressure, on pages 1-8, and full Prescribing Information.

JATENZO®
(testosterone undecanoate)
Capsules CIII

In a 2020 survey, 82% of men wanted to learn more about oral TRT[3]*

The Harris Poll conducted a survey of 491 men who have been diagnosed with hypogonadism within the United States.

76% believe their **needs are not very well met** by currently available TRTs

2 in 5

(44%) patients say **finding TRT that works for them has been a challenge**

Of the 53% who do not always take TRT exactly as prescribed, **94% attribute this to challenges of non-oral TRTs**

82% are interested in **learning about oral TRT**

*The survey was conducted online within the United States by the Harris Poll on behalf of Clarus Therapeutics from May 6–June 5, 2020, among 491 US males ages 18+ who have been diagnosed with hypogonadism by a healthcare provider. Results were weighted by education, age, race/ethnicity, region, income, household size, marital status, and propensity to be online to align them with their actual proportions in the population.

TRT=testosterone replacement therapy.

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.

Please see Important Safety Information, including BOXED WARNING on increases in blood pressure, on pages 1-8, and full Prescribing Information.

A unique formulation for oral testosterone delivery

FORMULATED AS A LIPOPHILIC TESTOSTERONE PRODRUG[1,4]

- JATENZO bypasses first-pass hepatic metabolism without alkylation[1,4]
- No liver toxicity-related events observed with JATENZO in clinical trials[1,4]
- JATENZO is not known to cause hepatic adverse events[1]
  - Patients should report any signs or symptoms of hepatic dysfunction (eg, jaundice). If these occur, promptly discontinue JATENZO while the cause is evaluated

DESIGNED FOR ORAL DELIVERY

As an oral softgel, JATENZO offers your appropriate patients a treatment option with[5,6]:

- No injection pain, no procedures
- No mess, no drying time
- No transference to women/kids
- No skin irritation
- No gum irritation/disorders
- No nasal irritation

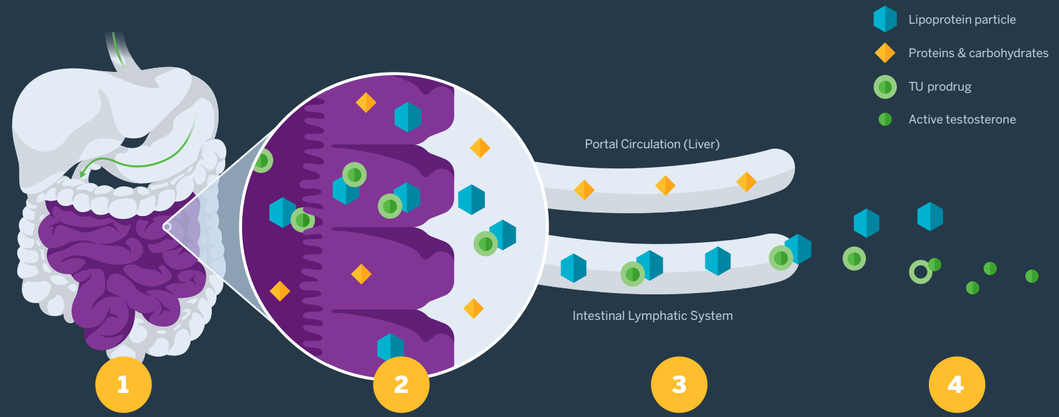
Important Safety Information *(continued)*

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.

JATENZO®
(testosterone undecanoate)
Capsules C-III

Pharmacokinetics[1,4,7]



Important Safety Information *(continued)*

WARNINGS AND PRECAUTIONS *(continued)*

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.

Please see Important Safety Information, including BOXED WARNING on increases in blood pressure, on pages 1-8, and full Prescribing Information.

1 JATENZO IS TAKEN **TWICE DAILY** WITH FOOD

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

2 TU IS CARRIED BY LIPOPROTEINS INTO THE **INTESTINAL LYMPHATICS**

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

3 JATENZO THEREFORE **BYPASSES THE FIRST-PASS HEPATIC METABOLISM** AND AVOIDS INACTIVATION

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

4 ONCE IN THE SYSTEMIC CIRCULATION, ESTERASES **RELEASE ACTIVE TESTOSTERONE** FROM THE TU PRODRUG

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

Important Safety Information *(continued)*

WARNINGS AND PRECAUTIONS *(continued)*

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.

JATENZO®
(testosterone undecanoate)
Capsules CIII

Evaluating efficacy and safety in the phase 3 inTUne study[1]

JATENZO WAS EVALUATED AMONG 166 ADULT, HYPOGONADAL MEN IN A 4-MONTH, OPEN-LABEL STUDY

STARTING DOSE

237 mg twice daily (BID) with meals

DOSE ADJUSTMENTS

- Adjusted on Days 21 and 56 (minimum 158 mg BID; maximum 396 mg BID)
- Based on average testosterone concentration obtained over 24 hours post-morning dose

PRIMARY ENDPOINT

Patients (%) with mean plasma total testosterone concentration (C_{avg}) over 24 hours within the normal eugonadal range (plasma levels 252-907 ng/dL) on the final pharmacokinetic (PK) visit of the study

SECONDARY ENDPOINTS

Patients (%) with a maximum total testosterone concentration (C_{max}) above 3 predetermined limits: 1) ≤1500 ng/dL; 2) 1800-2500 ng/dL; 3) >2500 ng/dL

inTUne=**in**vestigational **t**estosterone **un**decanoat**e**.

Important Safety Information *(continued)*

WARNINGS AND PRECAUTIONS *(continued)*

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.

Please see Important Safety Information, including BOXED WARNING on increases in blood pressure, on pages 1-8, and full Prescribing Information.

Baseline demographics for the inTUne study[4]

AGE, MEAN YEARS	51.6
RACE	
NATIVE AMERICAN OR ALASKA NATIVE	0
ASIAN	3 (1.8%)
AFRICAN AMERICAN OR BLACK	29 (17.5%)
CAUCASION	133 (80.1%)
OTHER	1 (0.6%)
BMI (KG/M^2)	31.8
SERUM TESTOSTERONE (NG/DL)	190.2
DURATION OF HYPOGONADISM (MEAN YEARS)	5.9
TYPE 1 OR TYPE 2 DIABETES, %	24.1
HISTORY OF HYPERTENSION, %	52.4

Key inclusion criteria[4]

- Men 18 to 65 years of age, with a clinical diagnosis of hypogonadism
- Signs/symptoms consistent with hypogonadism for testosterone-naive subjects
- History of signs/symptoms for subjects who had received prior treatment
- Hypogonadal serum testosterone levels (2 morning total testosterone values <300 ng/dL)
- Naive to TRT or washed out of prior TRTs
- Stable doses of thyroid hormone and adrenal replacement hormones in subjects on replacement therapy for hypopituitarism or multiple endocrine deficiencies

Important Safety Information *(continued)*

WARNINGS AND PRECAUTIONS *(continued)*

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.

JATENZO®
(testosterone undecanoate)
Capsules CIII

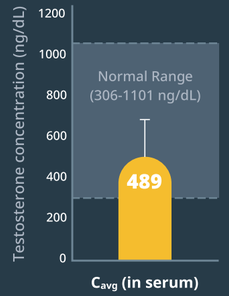
With JATENZO, 87% of men raised their T level to normal range[1]

PRIMARY ENDPOINT

87.3% of JATENZO patients were **in eugonadal range**[4]

FDA target: ≥75%[8]

JATENZO INCREASED TOTAL T INTO THE MID-NORMAL RANGE (AVERAGE CONCENTRATION: 489 NG/DL) FOR SOME MEN[1,9*]



*In the inTUne study, testosterone concentrations were measured in plasma isolated from blood collected into NaF-EDTA tubes. NaF was used to limit ex vivo conversion of TU to testosterone, which could artefactually raise measured testosterone levels. In a typical clinical setting, testosterone concentrations are measured in serum isolated from blood collected in plain tubes. To account for the lower testosterone concentrations measured in plasma vs serum, a conversion factor of 1.214 was determined and used to approximate the equivalent mean serum concentration of 489 ± 155 ng/dL from the mean NaF-EDTA plasma testosterone value of 403 ± 128 ng/dL in the inTUne study.[1,4,9]

T=testosterone.

Important Safety Information *(continued)*

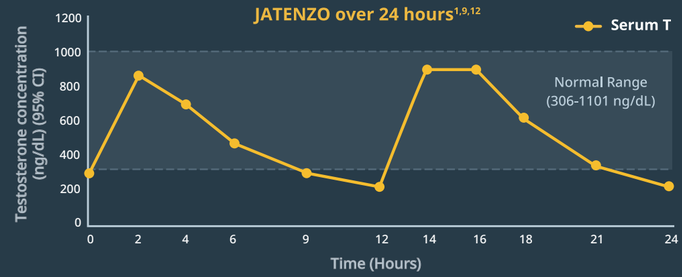
WARNINGS AND PRECAUTIONS *(continued)*

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.

Men reached steady state T levels as early as Day 7* and maintained stable levels† in PK studies[10,11]

Steady state by **Day 7**[10*]

JATENZO MAINTAINED NORMAL T LEVELS OVER EACH 12-HOUR DOSING INTERVAL[12‡]



*In a 28-day study, the results suggest that the initial transient effect is resolved by Days 5-7, and that if testosterone administration continues beyond that time, systemic concentrations remain essentially constant from at least Day 7 onward for the remainder of the study period.[10]

†In a 12-month study, the pharmacokinetics of oral TU were stable over an extended time period (>9 months) of chronic dosing. Steady state exposures for the oral TU treatment subjects did not change between Day 90 (after at least 1 month on the maintenance dose) and Day 365 (after at least 10 months on the maintenance dose).[11]

‡Note that the testosterone concentrations were not measured in serum but the effects of different sample preparation conditions were accounted for in data analysis of the results shown here. The titration scheme for use in clinical practice is based on serum total testosterone.[12]

CI=confidence interval.

Important Safety Information *(continued)*

WARNINGS AND PRECAUTIONS *(continued)*

JATENZO is not indicated for use in women.

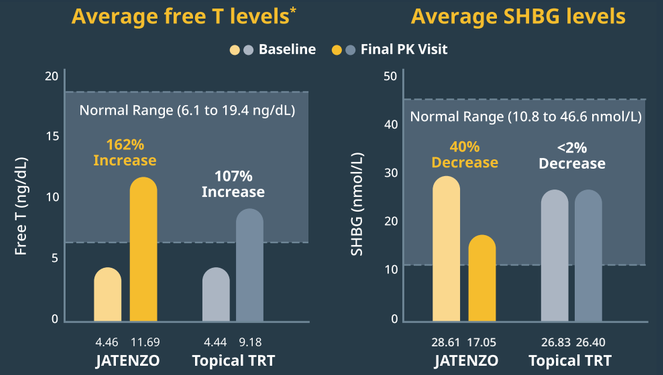
Large doses of androgens can suppress spermatogenesis by feedback inhibition of pituitary FSH. Inform patients of this risk before prescribing JATENZO.

Please see Important Safety Information, including BOXED WARNING on increases in blood pressure, on pages 1-8, and full Prescribing Information.

JATENZO®
(testosterone undecanoate) Capsules CIII

While on JATENZO, free T increased and SHBG decreased[4,13]

In the inTUne clinical study, 2% topical testosterone (T) solution was used as the active T reference arm. Testosterone C_{avg} was determined for each treatment group but topical T C_{avg} data are not included in the JATENZO labeling. The following analyses from the inTUne clinical study were exploratory. These data are provided to reflect known pharmacological actions of TRT but were not used to assess efficacy.



- SHBG tightly binds T in blood and thus limits the concentration of free T. Only free T (or its active metabolite, DHT) can bind to androgen receptors in tissues[14]

Topical TRT study design[4,13]: In the inTUne trial, subjects who met all eligibility criteria were randomly assigned in a 3:1 ratio to JATENZO (n=166) or topical TRT (n=56) for 3 to 4 months. The starting dose for topical TRT was 60 mg once daily (QD) in the AM. Doses were adjusted on Days 21 and 56 (minimum 30 mg QD; maximum 120 mg QD) based on average T concentration obtained over 24 hours post-morning dose. Beyond the primary objective of the inTUne study, other objectives included comparing JATENZO-treated subjects with topical TRT-treated subjects in terms of C_{avg} DHT concentration at Visit 7.

Adverse reactions occurring in >2% of subjects in the topical TRT arm[13]: headache=1 (1.8); hematocrit increased=0; upper respiratory tract infection=0; hypertension=0; high-density lipoprotein decreased=0; nausea=0; rash=2 (3.6); overdose=2 (3.6).

*Free T concentrations were calculated using the Vermeulen formula based on T, SHBG, and albumin concentrations.[13]

DHT=dihydrotestosterone; SHBG=sex hormone-binding globulin.

Important Safety Information *(continued)*

WARNINGS AND PRECAUTIONS *(continued)*

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.

Established safety profile[1]

NUMBER (%) OF PATIENTS WITH ADVERSE REACTIONS ≥2% IN A 4-MONTH STUDY WITH JATENZO

	OVERALL (N=166)
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 patients (1.8% of 166) had 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

Other Data

Important Safety Information *(continued)*

WARNINGS AND PRECAUTIONS *(continued)*

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.

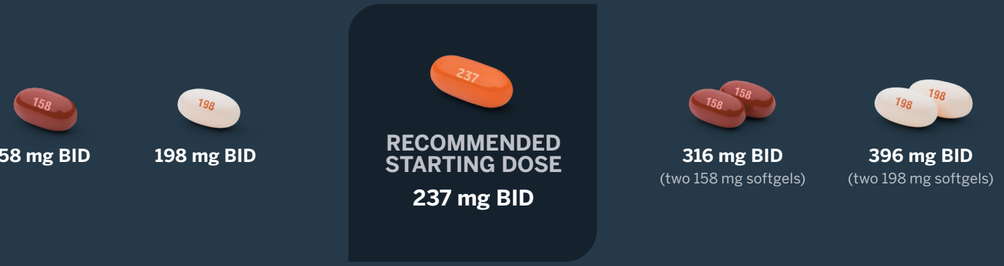
Please see Important Safety Information, including BOXED WARNING on increases in blood pressure, on pages 1-8, and full Prescribing Information.

JATENZO®
(testosterone undecanoate)
Capsules

Whether it's Kevin, Evan, or Devin, raising his T starts with 237 mg (BID with food)[1*†]

JATENZO IS DESIGNED TO PROVIDE BIOAVAILABILITY WITHOUT REQUIRING HIGH-FAT MEALS[4]

- Take JATENZO with food once in the morning and once in the evening[1]
- Individualize the dosage of JATENZO based on the patient's serum testosterone concentration response to the drug[1]



In the inTUne study, 72% of patients titrated up from the 237 mg starting dose[4‡]

*No need for dietary fat adjustment.
†Not actual patients. For illustrative purposes only.
‡JATENZO was taken orally at a starting dose of 237 mg twice daily with meals. The dose was adjusted on Days 21 and 56 between a minimum of 158 mg twice per day and a maximum of 396 mg twice per day on the basis of the average testosterone concentration obtained over 24 hours post-morning dose. Data shown represent the percentage of patients on each JATENZO dose at the end of the study. Of the 155 patients, 39 did not require dose adjustment, 52 required 1 dose adjustment, and 64 required 2 dose adjustments.

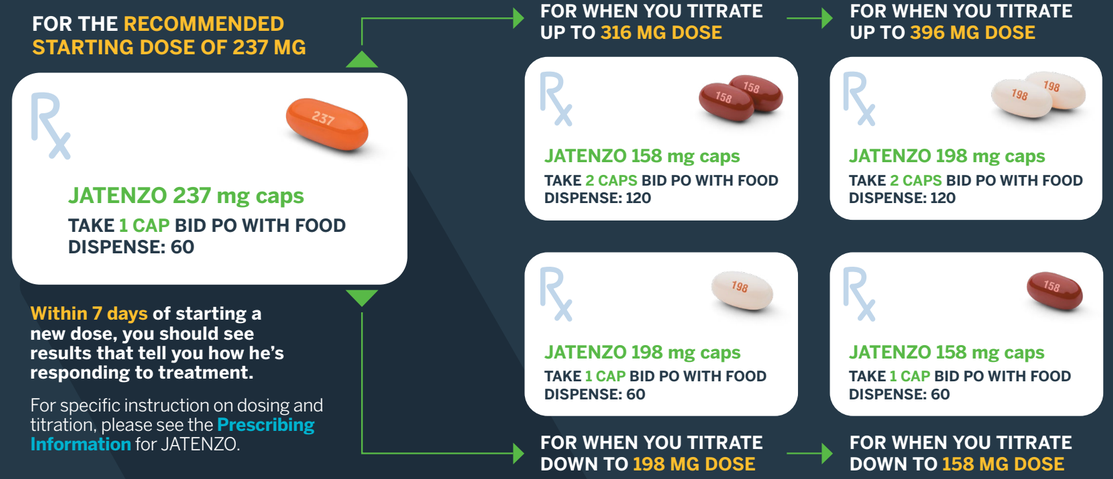
Important Safety Information *(continued)*

WARNINGS AND PRECAUTIONS *(continued)*

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.

How to write his prescription[1]



PO=by mouth.

Important Safety Information *(continued)*

WARNINGS AND PRECAUTIONS *(continued)*

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.

Please see Important Safety Information, including BOXED WARNING on increases in blood pressure, on pages 1-8, and full Prescribing Information.

JATENZO®
(testosterone undecanoate)
Capsules

Offer him savings from the start

JATENZO GO

ELIGIBLE PATIENTS WITH COMMERCIAL INSURANCE MAY PAY AS LITTLE AS $0 FOR THEIR MONTHLY PRESCRIPTION OF JATENZO.*

Restrictions may apply. A maximum benefit per calendar year will be applied.

To learn more or download a Savings Card online, visit JATENZO.com.

*Eligibility criteria and limitations apply. This offer is valid in the United States and Puerto Rico. Offer not valid for prescriptions reimbursed under Medicaid, a Medicare drug benefit plan, TRICARE, or other federal or state health programs (such as medical assistance programs). Cash Discount Cards and other non-insurance plans are not valid as primary under this offer. See JATENZO.com for more details.

Important Safety Information *(continued)*

WARNINGS AND PRECAUTIONS *(continued)*

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

References

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JATENZO®
(testosterone undecanoate)
Capsules CIII

Offer him the first and only FDA-approved oral TU designed for men with hypogonadism[1,2]

With JATENZO, **87% of men reached normal testosterone levels** at the end of the phase 3 inTUne trial[1*]

The safety profile was established in the inTUne study

Avoid certain administration challenges of non-oral TRTs (no mess, no injection pain, no transfer risk, no irritation, no procedures)[5,6]

Eligible patients with commercial insurance **may pay as little as $0 for their monthly prescription of JATENZO†**

When prescribing, remember the recommended starting dose: 237 mg caps; take 1 cap BID PO with food[1‡]

*The open-label, 4-month clinical study included 166 adult, hypogonadal men.
†Eligibility criteria and limitations apply. See JATENZO.com for more details.
‡No need for dietary fat adjustment.

To see if JATENZO may be right for your patients, visit JATENZO.com.

Select Important Safety Information

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%).

Please see Important Safety Information, including BOXED WARNING on increases in blood pressure, on pages 1-8, and full Prescribing Information.

clarus THERAPEUTICS

JTZ-US-2041 01/2021

JATENZO®
(testosterone undecanoate)
Capsules C-III

OTHER DATA FROM INTUNE STUDY

Changes in hematocrit, blood pressure, and liver function

In the inTUne clinical study, 2% topical testosterone (T) solution was used as the active T reference arm. Testosterone C_{avg} was determined for each treatment group but topical T C_{avg} data are not included in the JATENZO labeling. The following analyses from the inTUne clinical study were exploratory. These data are provided to reflect known pharmacological actions of TRT but were not used to assess efficacy.

Topical TRT study design[1,2]: In the inTUne trial, subjects who met all eligibility criteria were randomly assigned in a 3:1 ratio to JATENZO (n=166) or topical TRT (n=56) for 3 to 4 months. The starting dose for topical TRT was 60 mg once daily (QD) in the AM. Doses were adjusted on Days 21 and 56 (minimum 30 mg QD; maximum 120 mg QD) based on average T concentration obtained over 24 hours post-morning dose. Beyond the primary objective of the inTUne study, other objectives included comparing JATENZO-treated subjects with topical TRT-treated subjects in terms of C_{avg} DHT concentration at Visit 7.

Adverse reactions occurring in >2% of subjects in the topical TRT arm[1]: headache=1 (1.8); hematocrit increased=0; upper respiratory tract infection=0; hypertension=0; high-density lipoprotein decreased=0; nausea=0; rash=2 (3.6); overdose=2 (3.6).

DHT=dihydrotestosterone; inTUne=**in**vestigational **t**estosterone **un**decanoat**e**; TRT=testosterone replacement therapy.

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, including BOXED WARNING on increases in blood pressure, throughout the following pages, and full Prescribing Information.

JATENZO®
(testosterone undecanoate)
Capsules CIII

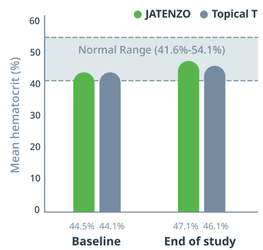
Detailed results for each treatment group

Hematocrit levels increased but stayed within normal range for 97% of patients[1]

With JATENZO, no increases in hematocrit led to premature discontinuation[4]

Evaluate hematocrit approximately every 3 months while the patient is on JATENZO.[4] All testosterone therapies, including JATENZO, require ongoing monitoring of hematocrit levels.[4,5]

Mean hematocrit 4-month clinical trial[2,3]



JATENZO increased mean cuff systolic blood pressure by 2.8 mmHg (increase in ABPM by 4.9 mmHg)[1,2,4]

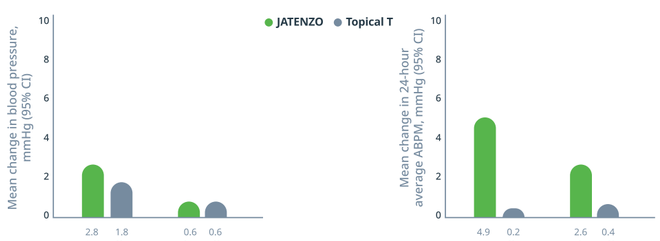
Instruct patients about the importance of monitoring blood pressure periodically while on JATENZO.[4]

Please see Important Safety Information, including BOXED WARNING on increases in blood pressure.

CI=confidence interval.

Change in blood pressure cuff from baseline to Day 139

Ambulatory blood pressure monitoring (ABPM) change from baseline to Day 139



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.

No clinically significant change in liver function tests were observed with JATENZO[1,2]

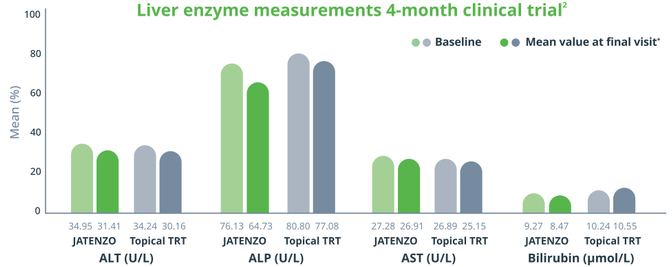
Additional details

Two oral TU patients experienced increases in AST or ALT that were <2x the upper normal limit (UNL) and one oral TU patient experienced an elevation of AST (<2x UNL) that returned to normal during continued oral TU treatment.[1]

*Final visit was defined as either Visit 7 or date of last data collection if terminated early.

ALP=alkaline phosphatase; ALT=alanine aminotransferase; AST=aspartate aminotransferase.

Liver enzyme measurements 4-month clinical trial[2]



Important Safety Information *(continued)*

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.

Please see Important Safety Information, including BOXED WARNING on increases in blood pressure, throughout the following pages, and full Prescribing Information.

JATENZO®
(testosterone undecanoate)
Capsules CII

Important Safety Information *(continued)*

WARNINGS AND PRECAUTIONS *(continued)*

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

Safety Profile

References

1. Swerdloff RS, et al. *J Clin Endocrinol Metab.* 2020;105(8):dgaa238. doi:10.1210/clinem/dgaa238
2. Data on file. Clinical Study Report: CLAR-15012. Clarus Therapeutics, Inc.
3. Swerdloff R, et al. Efficacy and safety of a new oral testosterone undecanoate (TU) formulation in hypogonadal men: results from the 'inTUne' trial. Presented at: Endocrine Society Annual Meeting (ENDO 2018); March 18, 2018; Chicago, IL. Abstract SUN-249.
4. JATENZO. Prescribing information. Clarus Therapeutics, Inc.; 2019.
5. Bhasin S, et al. *J Clin Endocrinol Metab.* 2018;103(5):1715-1744.

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Capsules