IS THE TREATMENT OF LOW T JUST ABOUT A NUMBER?

NATESTO® DELIVERS TESTOSTERONE DIFFERENTLY[1]

THE FIRST AND ONLY FDA-APPROVED INTRANASAL TESTOSTERONE REPLACEMENT THERAPY[1]

The nose offers an effective, efficient and well-established method of drug delivery due to its rapid absorption into the bloodstream[2,3]

Uses an ultra-thin layer of bioadhesive gel[2]

- Thickness comparable to the natural mucus layer in the nose
- Average time to apply NATESTO® approximately 10 seconds

Traditional topical gels exhibit high discontinuation rates[4]

65.3% discontinue in 6 months
84.6% discontinue in 12 months

80% were confident using NATESTO® within 2 days

nearly **70%** said they would switch to NATESTO®

In a survey of a subset of men from the Phase 3 Trial taking NATESTO® TID (n=66)[5]
TID=3 times daily

Minimizes concern about transference in Low T treatment

- Levels of testosterone have been shown to increase in female partners of topical testosterone users under certain conditions[6]
- Patients and their families have expressed concern about the unintentional transfer of TRT[6]

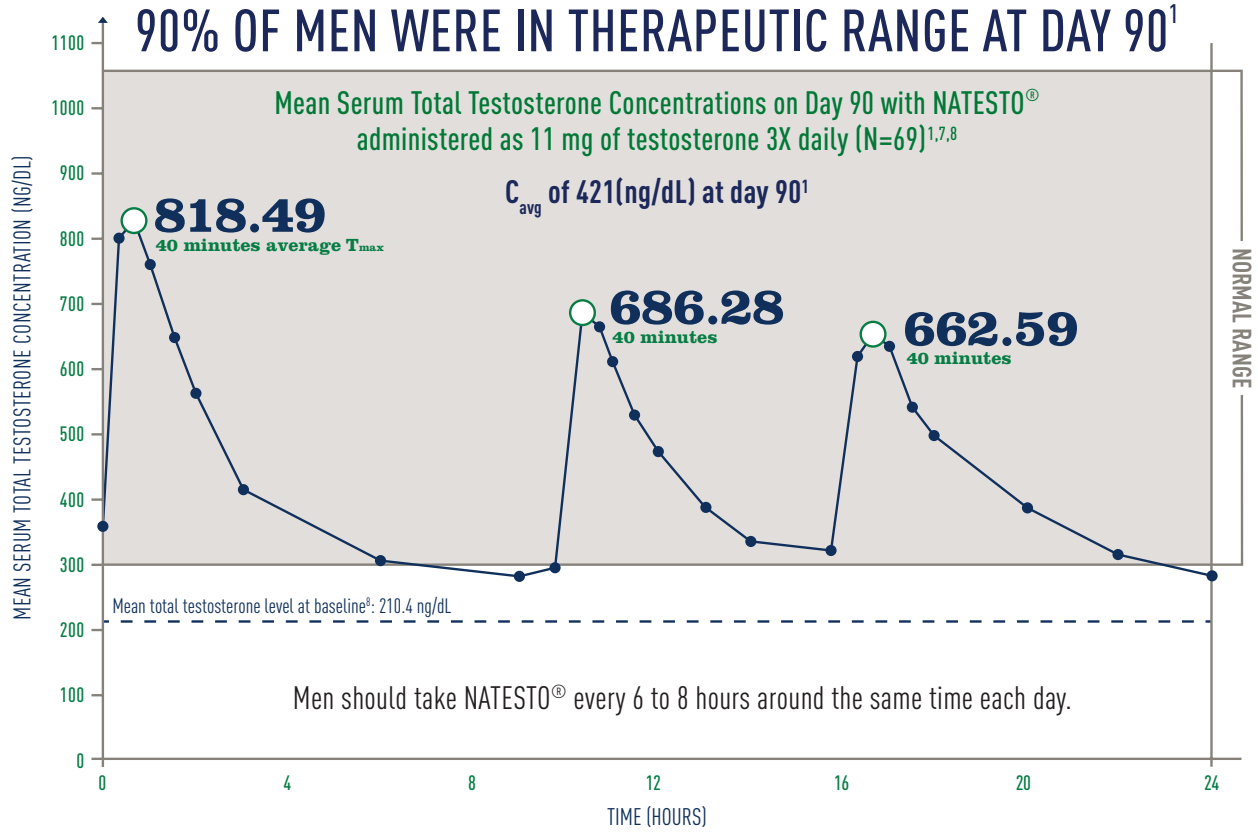
IMPORTANT SAFETY INFORMATION

Nasal adverse reactions, including nasopharyngitis, rhinorrhea, epistaxis, nasal discomfort, and nasal scabbing, were reported in the clinical trial experience with NATESTO®. Patients should be instructed to report any nasal symptoms or signs to their healthcare professional. In that circumstance, healthcare professionals should determine whether further evaluation or discontinuation of NATESTO® is appropriate.

Please see additional Important Safety Information on back cover and refer to accompanying complete prescribing information.

SYMPTOM RELIEF THROUGH A DIFFERENT PHARMACOKINETIC PROFILE[1]

90% OF MEN WERE IN THERAPEUTIC RANGE AT DAY 90[1]



* STUDY DESIGN Results from 73 hypogonadal men (morning testosterone ≤300 ng/dL) who received NATESTO® 11 mg 3 times daily (total daily dose: 33 mg) in a multicenter, open-label, 90-day clinical study (N=306) were included in the statistical evaluation of efficacy. The primary endpoint was the percentage of patients with an average serum total testosterone concentration (Cavg) within the normal range (300-1050 ng/dL) on Day 90[1]

Symptom relief is achievable with NATESTO® [9,10]

- Substantial increase in positive mood affect as early as day 30[9,10]
- Substantial decrease in negative mood affect as early as day 30[9,10]
- Significant improvement in sexual function as early as day 30[9,10]

Among all subjects (n=306) who received NATESTO®, the most common adverse events were prostate specific antigen increased, headache, rhinorrhea, epistaxis, nasal discomfort, nasopharyngitis, upper respiratory tract infection, sinusitis, bronchitis, and nasal scab[1]

<2% of patients who received NATESTO® at any dose in the 90-day clinical study and its 90- and 180-day extension periods discontinued during the study due to adverse events.

IMPORTANT SAFETY INFORMATION (cont)

- Edema, with or without congestive heart failure, may be a serious complication in patients with pre-existing cardiac, renal, or hepatic disease
- Administration of exogenous androgens, including NATESTO®, may lead to azoospermia through suppression of spermatogenesis; gynecomastia; sleep apnea (especially in patients with risk factors such as obesity and chronic lung disease); decreased concentrations of thyroxine-binding globulins; and changes in serum lipid profile
- NATESTO® should be used with caution in cancer patients at risk of hypercalcemia (and associated hypercalciuria)
- Periodic monitoring of prostate specific antigen (PSA), hematocrit, and lipid concentrations is recommended, as changes may require discontinuation of NATESTO®

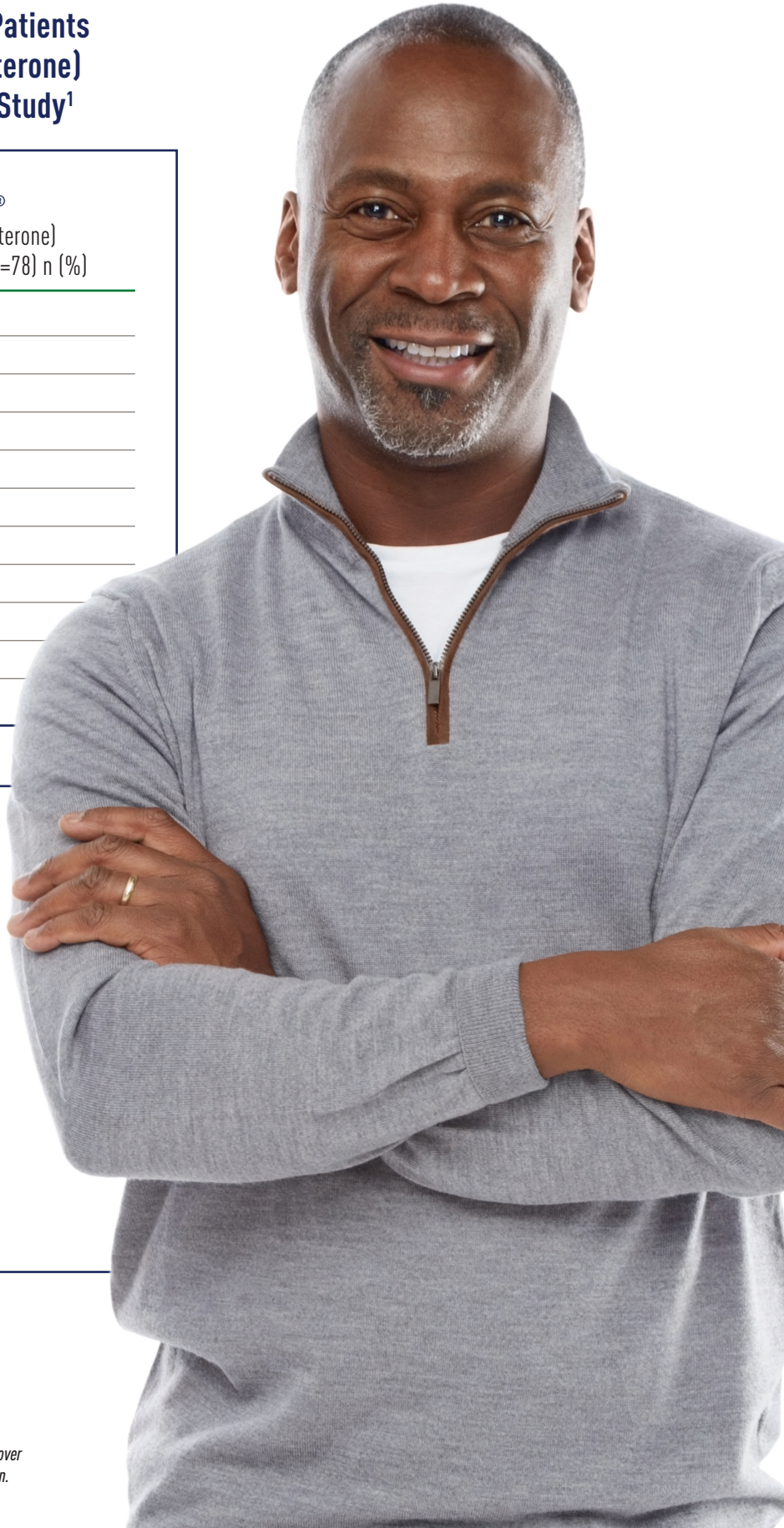
Please see additional Important Safety Information on back cover and refer to accompanying complete prescribing information.

Natesto®
(testosterone) nasal gel

NATESTO® HAS A FAVORABLE SAFETY PROFILE

Adverse Reactions Reported by ≥3% of Patients Treated with NATESTO® (11 mg of testosterone) Three Times Daily in the 90-Day Clinical Study[1]

Adverse Reactions	NATESTO® (11 mg of Testosterone) Three Times Daily (N=78) n (%)
PSA increased	4 (5.1)
Headache	3 (3.8)
Rhinorrhea	3 (3.8)
Epistaxis	3 (3.8)
Nasal discomfort	3 (3.8)
Nasopharyngitis	3 (3.8)
Bronchitis	3 (3.8)
Upper respiratory tract infection	3 (3.8)
Sinusitis	3 (3.8)
Nasal scab	3 (3.8)



NATESTO® maintains key hormones within their normal respective reference ranges[11,12]

- Follicle Stimulating Hormone (FSH)[11]
- Luteinizing Hormone (LH)[11]
- Estradiol (E2)[12]
- Dihydrotestosterone (DHT)[12]

No clinically significant change in hematocrit and hemoglobin after NATESTO® treatment[13]

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NATESTO DIRECT

OFFERS COPAY SAVINGS† AND PRIOR AUTHORIZATION ASSISTANCE

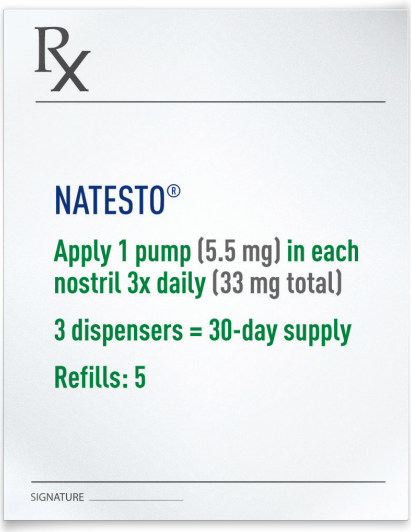
1-833-NATESTO

1-833-628-3786

Dedicated services to help your patients with Benefits Investigation, Prior Authorizations, copay assistance† and dispensing pharmacy

GET PATIENTS STARTED TODAY

HOW TO PRESCRIBE NATESTO®



Patients can download a card at natesto.com

IT'S TIME TO TREAT LOW T DIFFERENTLY

† Eligibility and Restrictions: On each valid NATESTO® prescription or refill, pay as low as $10 copay on all prescriptions (minimum of 2 dispensers with a maximum of 3 dispensers per Rx), maximum benefits apply per use, for up to 12 refills. Cash paying patients pay no more that $199 (3 dispensers), max benefits apply per use, for up to 12 refills. To access the Cash benefit please call 1.833.NATESTO (628.3786). Patient is responsible for any remaining balance, and for reporting receipt of this coupon benefit to any insurer, health plan, or other third party who pays for or reimburses any part of the prescription filled using the coupon, as may be required. Patient, pharmacist, and prescriber agree not to seek reimbursement for all or any part of the benefit received by the patient through this offer.

Offer only valid for male patients over age 18 who have private health insurance. Offer not valid for uninsured patients or for patients eligible for Medicaid, Medicare, TRICARE, Veterans Affairs or any other state or federal healthcare program (including state prescription drug programs). Offer good only in the USA and void where prohibited by law, taxed, or restricted. Aytu BioScience reserves the right to rescind, revoke, or amend this offer without notice. Card is limited to one per person, is not transferrable and cannot be reproduced.

This card is not health insurance.

References: 1. Natesto® (Prescribing Information). Aytu Bioscience, Inc. Englewood, CO 12/2017. **2.** Pires A, Fortuna A, Alves G, Falcão A. Intranasal drug delivery: how, why and what for? J Pharm Sci. 2009;12(3):288-311. **3.** Bitter C, Suter-Zimmermann K, Surber C. Nasal drug delivery in humans. Curr Probl Dermatol. 2011;40:20-35. **4.** Schoenfeld MJ, Shortridge E, Cui Z, Muram D, Medication adherence and treatment patterns for hypogonadal patients treated with topical testosterone therapy: a retrospective medical claims analysis. J Sex Med. 2013 May;10(5):1401-9. doi: 10.1111/jsm.12114. Epub 2013 Mar 6. **5.** Patient Market Research. Post-Phase III trial survey results. January 2014. **6.** de Ronde W. Hyperandrogenism after transfer of topical gel: case report and review of published and unpublished studies. Hum Reprod. 2009;24(2):425-428. **7.** Data on file, DOF-NT-02. Aytu BioScience, Inc. 2017. **8.** Data on file, DOF-NT-04. Aytu BioScience, Inc. 2017. **9.** Clinical Study Report TBS-1-2011-03. NATESTO®, a novel testosterone nasal gel, normalizes androgen levels in hypogonadal men. Trimel Biopharma SRL. May 28, 2013 (Final 2.0). **10.** Lipshultz L, Westfield G, Guidry M, Bryson N, Khera M. Clinical Improvements in Erectile Function and Mood in Hypogonadal Men Treated with 4.5% Nasal Testosterone Gel. Presented at the American Urological Association 2017. **11.** Conners W, Morgentaler A, Guidry M, Westfield G, Bryson N, Goldstein I. Preservation of Normal Concentrations of Pituitary Gonadotropins Despite Achievement of Normal Serum Testosterone Levels in Hypogonadal Men treated With a 4.5% Nasal Testosterone Gel. Presented at the American Urological Association 2017. **12.** Rogol A, Guidry M, Bryson N, Westfield G, Dobs A, Intranasal Testosterone Therapy (TTh) Produces Normal, Not High, Estradiol (E2) And Dihydrotestosterone (DHT) Levels In Hypogonadal Men. Presented at the 2018 Endocrine Society Conference (ENDO). **13.** Guidry M, Westfield G, Rogol A, Bryson N. One-Year Hematologic Safety of Natesto® (Testosterone) Nasal Gel In Men with Hypogonadism. Presented at ENDO Expo 2017.

Please see additional Important Safety Information on back cover and refer to accompanying complete prescribing information.

Natesto® (testosterone) nasal gel

IT'S TIME TO TREAT LOW T DIFFERENTLY

- 90% of men were within therapeutic range at day 90[1]
- Improvement in mood and sexual function as early as day 30[10]
- Rapid absorption and high bioavailability through the nasal membranes[2,3]
- Application in seconds
- Minimizes the risk of unintentionally transferring testosterone to others[6]
- Favorable safety profile
- NatestoDirect offers Prior Authorization assistance, copay savings† and a dispensing pharmacy
- Get started today with NATESTO DIRECT 1-833-NATESTO *(628-3786)*

INDICATION

What is NATESTO® (testosterone) Nasal Gel?

NATESTO® is a prescription medicine that contains testosterone and is used to treat adult males who have low or no testosterone due to certain medical conditions. Your doctor will test the testosterone level in your blood before you start and while you are using NATESTO®.

NATESTO® should not be used by men with breast cancer or known or suspected prostate cancer. NATESTO® should not be used by women.

It is not known if NATESTO® is safe or effective to treat men who have low testosterone due to aging.

Safety and effectiveness of NATESTO® have not been established in children younger than 18 years old and NATESTO® should not be used by children. NATESTO® use by children may affect bone growth.

NATESTO® is a controlled substance (CIII) because it contains testosterone that can be a target for people who abuse prescription medicines. Never give your NATESTO® to anyone else.

Please see accompanying complete prescribing information.

IMPORTANT SAFETY INFORMATION

- NATESTO contains testosterone, a Schedule III controlled substance in the Controlled Substances Act.
- NATESTO is contraindicated in men with carcinoma of the breast or known or suspected prostate cancer and in women who are, or may become, pregnant or who are breastfeeding. NATESTO may cause fetal harm when administered to a pregnant woman and serious adverse reactions in nursing infants.
- Nasal adverse reactions, including nasopharyngitis, rhinorrhea, epistaxis, nasal discomfort, and nasal scabbing, were reported in the clinical trial experience with NATESTO. Patients should be instructed to report any nasal symptoms or signs to their healthcare professional. In that circumstance, healthcare professionals should determine whether further evaluation or discontinuation of NATESTO is appropriate.
- Due to lack of clinical data on safety or efficacy in the following patient populations, NATESTO is not recommended for use in patients with a history of nasal disorders, nasal or sinus surgery, nasal fracture within the previous 6 months or nasal fracture that caused a deviated anterior nasal septum, mucosal inflammatory disorders (e.g., Sjogren's syndrome), and sinus disease.
- Monitor patients with benign prostatic hyperplasia (BPH) for worsening of signs and symptoms of BPH. Patients treated with androgens may be at increased risk for prostate cancer. Evaluation of patients for prostate cancer prior to initiating and during treatment with androgens is recommended.
- Increases in hematocrit, reflective of increases in red blood cell mass, may require discontinuation of NATESTO.
- There have been postmarketing reports of venous thromboembolic events including deep vein thrombosis (DVT) and pulmonary embolism (PE), in patients using testosterone products such as Natesto. Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE) have been reported in patients using testosterone products. Evaluate patients with signs or symptoms consistent with DVT or PE. If a venous thromboembolic event is suspected, discontinue treatment with Natesto and initiate appropriate workup and management.
- Some postmarketing studies have shown an increased risk of myocardial infarction and stroke associated with use of testosterone replacement therapy.
- Long-term clinical safety trials have not been conducted to assess the cardiovascular outcomes of testosterone replacement therapy in men. To date, epidemiologic studies and randomized controlled trials have been inconclusive for determining the risk of major adverse cardiovascular events (MACE), such as nonfatal myocardial infarction, non-fatal stroke and cardiovascular death, with the use of testosterone compared to non-use. Some studies, but not all, have reported an increased risk of MACE in association with use of testosterone replacement therapy in men. Patients should be informed of the possible risk when deciding whether to use or to continue to use NATESTO.
- Testosterone has been subject to abuse, typically at doses higher than recommended for the approved indication and in combination with other anabolic androgenic steroids. This type of testosterone abuse can lead to serious cardiovascular and psychiatric adverse reactions.
- If testosterone abuse is suspected, check serum testosterone concentrations to ensure they are within therapeutic range. Counsel patients concerning the serious adverse reactions associated with testosterone and anabolic androgenic steroid abuse. Conversely, consider the possibility of testosterone and anabolic androgenic steroid abuse in patients who present with serious cardiovascular or psychiatric adverse events.
- Due to lack of controlled studies in women and potential virilizing effects, NATESTO is not indicated for use in women.
- Serious hepatic adverse effects (peliosis hepatis, hepatic neoplasms, cholestatic hepatitis, and jaundice) have been associated with prolonged use of high doses of oral methyltestosterone. NATESTO is not known to cause these adverse effects. Nonetheless, patients should be instructed to report any signs or symptoms of hepatic dysfunction (e.g., jaundice). If these occur, promptly discontinue NATESTO while the cause is evaluated.
- Edema, with or without congestive heart failure, may be a serious complication in patients with pre-existing cardiac, renal, or hepatic disease.
- Administration of exogenous androgens, including NATESTO, may lead to azoospermia through suppression of spermatogenesis; gynecomastia; sleep apnea (especially in patients with risk factors such as obesity and chronic lung disease); decreased concentrations of thyroxine-binding globulins; and changes in serum lipid profile.
- NATESTO should be used with caution in cancer patients at risk of hypercalcemia (and associated hypercalciuria).
- Periodic monitoring of prostate-specific antigen (PSA), hematocrit, and lipid concentrations is recommended, as changes may require discontinuation of NATESTO.
- The most common adverse reactions reported by ≥3% of patients were: PSA increased, headache, rhinorrhea, epistaxis, nasal discomfort, nasopharyngitis, bronchitis, upper respiratory tract infection (URI), sinusitis, and/or nasal scab.
- Changes in insulin sensitivity or glycemic control may occur in patients treated with androgens and may necessitate a decrease in the dose of anti-diabetic medication. Changes in anticoagulant activity may be seen with androgens. The concurrent use of testosterone with corticosteroids may result in increased fluid retention and requires monitoring particularly in patients with cardiac, renal, or hepatic disease.

Please see accompanying full Prescribing Information.

AYTU BioScience

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Natesto® (testosterone) nasal gel C

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