Xyosted™ (testosterone enanthate auto-injection)

Policy # 00667
Original Effective Date: 04/24/2019
Current Effective Date: 05/10/2021

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider Xyosted™‡ (testosterone enanthate auto-injection) for the treatment of hypogonadism to be **eligible for coverage**** when the patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility for Xyosted (testosterone enanthate auto-injection) will be considered when the following criteria are met:

- Patient has a diagnosis of hypogonadism (primary or secondary); AND
- Diagnosis of hypogonadism has been confirmed by serum testosterone measurements taken in the MORNING on TWO separate days BOTH showing levels BELOW the normal range; AND
- Patient is 18 years of age or older; AND
- Patient is a male; AND
- Patient has tried and failed (e.g., intolerance or inadequate response) BOTH prescription GENERIC testosterone enanthate vials for injection and prescription GENERIC testosterone cypionate vials for injection unless there is clinical evidence or patient history that suggests the use of the required products will be ineffective or cause an adverse reaction to the patient. *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

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When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Xyosted (testosterone enanthate auto-injection) when the patient has not tried and failed (e.g., intolerance or inadequate response) BOTH prescription GENERIC testosterone enanthate vials for injection and prescription GENERIC testosterone cypionate vials for injection to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Xyosted (testosterone enanthate auto-injection) when patient selection criteria are not met (except the criterion denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Xyosted is an androgen indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone. Safety and efficacy of Xyosted in adult males with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established. Safety and efficacy of Xyosted in males less than 18 years old have not been established. Prior to initiating Xyosted, the diagnosis of hypogonadism should be confirmed by ensuring that serum testosterone has been measured in the morning on at least two separate days and that these concentrations are below the normal range. The starting dose of Xyosted is 75 mg subcutaneously in the abdominal region once weekly. Xyosted should not be given via the intramuscular and intravascular route. Dose adjustments are based upon total testosterone trough concentrations (measured 7 days after most recent dose) obtained following 6 weeks of dosing and periodically thereafter. Xyosted is available in 50 mg, 75 mg, and 100 mg strengths in auto-injector form.

As mentioned, this product is approved for primary or secondary hypogonadism:

- Primary hypogonadism (congenital or acquired) – testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low

serum testosterone concentrations accompanied by gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range.

- Secondary hypogonadism (i.e., hypogonadotropic hypogonadism) (congenital or acquired) – idiopathic gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low serum testosterone concentrations without associated elevations in gonadotropins. Appropriate adrenal cortical and thyroid hormone replacement therapy may be necessary in patients with multiple pituitary or hypothalamic abnormalities.

Other forms of testosterone for injection (available in generic form) are indicated for hypogonadism. None of these versions of testosterone have been studied head to head versus Xyosted, so no superiority claims can be made between these products. Generic products offer a more cost effective, yet efficacious option for treatment.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Xyosted is an androgen indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.

Rationale/Source

Xyosted was evaluated in a 52-week, open-label study to evaluate its efficacy and safety when administered subcutaneously once weekly to 150 adult males with hypogonadism. The study included a Screening Phase, a Treatment Titration Phase, and an Extended Treatment Phase. Patients were trained on proper use of Xyosted to self-administer the initial dose of 75 mg once weekly on the same day of the week and at approximately the same time (7:00 am ± 2 hours). The dose was increased by 25 mg at Week 7 if the Week 6 serum total testosterone concentration at the end of the dosing interval (C_{trough}) was <350 ng/dL, and was decreased by 25 mg if the C_{trough} was ≥650 ng/dL.

The primary endpoint was the percentage of patients with a time-averaged serum total testosterone concentration (C_{avg}) over the 7-day dosing interval (0 to 168 hours) within the normal range (300 to 1100 ng/dL) at Week 12. Secondary endpoints were the percentage of patients with a maximum total testosterone concentration (C_{max}) above three predetermined limits: greater than 1500 ng/dL, between 1800 and 2500 ng/dL, and greater than 2500 ng/dL.

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Policy # 00667
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One hundred and thirty five (90%) of the 150 hypogonadal men who received Xyosted had a serum total testosterone concentration C_{avg}(0-168h) within the normal range (300 to 1100 ng/dL) at Week 12. There were no patients (0%) with C_{max} >1500 ng/dL at Week 12.

This policy is intended to ensure that this product is used per its FDA approved usage. Also it should be noted that other forms of testosterone for injection (available in generic form) are indicated for hypogonadism. None of these versions of testosterone have been studied head to head versus Xyosted, so no superiority claims can be made among these products. Generic products offer a more cost effective, yet efficacious option for treatment.

References

1. Xyosted [package insert]. Antares Pharma, Inc. Ewing, NJ 08628.
2. Male Hypoganadism. Merck Manual, 18th edition. p1944-1948.

Policy History

Original Effective Date: 04/24/2019
Current Effective Date: 05/10/2021
04/04/2019 Medical Policy Committee review
04/24/2019 Medical Policy Implementation Committee approval. New policy.
04/02/2020 Medical Policy Committee review
04/08/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/01/2021 Medical Policy Committee review
04/14/2021 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 04/2022

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2020 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of

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descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J3121, J3490, J3590
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

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B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.