TESTOSTERONE REPLACEMENT THERAPY

Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Medical Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as “Description” defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as “Criteria” defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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TESTOSTERONE REPLACEMENT THERAPY (cont.)

Description:

Testosterone therapy routes addressed in this guideline include buccal tablets, intramuscular injections, oral medications, topical gel and topical patches. Testosterone replacement therapy is the primary treatment for androgen deficiency in males when symptoms of hypogonadism are present. Testosterone therapy has been used in the absence or deficiency of endogenous testosterone. Testosterone is produced in males primarily by the testes in response to stimuli from the hypothalamic and pituitary glands. Low testosterone is caused by deficient production of the hormone, and is also known as androgen deficiency.

Definitions:

Adult: Age 18 years and older

Hypogonadism:
Hypogonadism is the clinical syndrome associated with androgen deficiency. Symptoms are dependent upon age, severity of androgen deficiency, duration of androgen deficiency, individual sensitivity to androgen, and comorbid illness.

More specific symptoms and signs of hypogonadism, as classified by the Endocrine Society include the following:

- Breast discomfort, gynecomastia
- Decreased spontaneous erections
- Height loss, low trauma fracture, low bone mineral density
- Hot flushes, sweats
- Inability to father children, low or zero sperm count
- Incomplete or delayed sexual development, eunuchoidism
- Loss of body (axillary and pubic) hair, reduced shaving
- Reduced sexual desire (libido) and activity
- Very small (especially <5 ml) or shrinking testes

Other less specific symptoms and signs of hypogonadism, as classified by the Endocrine Society include the following:

- Decreased energy, motivation, initiative, and self-confidence
- Diminished physical or work performance
- Feeling sad or blue, depressed mood, dysthyemia
- Increased body fat, body mass index
- Mild anemia (normochromic, normocytic, in the female range)
- Poor concentration and memory
- Reduced muscle bulk and strength
- Sleep disturbance, increased sleepiness
TESTOSTERONE REPLACEMENT THERAPY (cont.)

Definitions:

Chronic Steroid Treatment:
Men receiving ongoing treatment for manifestations of a chronic condition, as opposed to episodic treatment for an acute condition or acute flare of a chronic condition. The length of acute episodic steroid treatment may vary from several days to several months, but in most cases will be less than 4-6 weeks.

Criteria:

For testosterone therapy for gender dysphoria, see BCBSAZ Medical Coverage Guideline #O922, “Treatments for Gender Dysphoria”.

For subcutaneous hormone pellet therapy for males and females, see BCBSAZ Medical Coverage Guideline #O138, “Hormone Pellet Therapy”.

For criteria below, routes of administration include buccal tablets, intramuscular injections, oral medication, topical gel and topical patches.

➢ For male individuals, initiation of testosterone replacement therapy for existing members, and continuation of testosterone replacement therapy for members on testosterone replacement therapy prior to their BCBSAZ original effective date (OED) of coverage is considered medically necessary with documentation of ALL of the following:

1. **ONE** of the following diagnosis:
   - Adult male with androgen deficiency syndrome
   - HIV-infected male with documentation of weight loss
   - Adult male on chronic steroid treatment (use greater than 6 weeks)
   - Individual 14 years or older with delayed male puberty and pre-pubertal testes present
TESTOSTERONE REPLACEMENT THERAPY (cont.)

Criteria: (cont.)

- For male individuals, initiation of testosterone replacement therapy for existing members, and continuation of testosterone replacement therapy for members on testosterone replacement therapy prior to their BCBSAZ original effective date (OED) of coverage is considered medically necessary with documentation of ALL of the following: (cont.)

2. An established diagnosis of hypogonadism with persistently low testosterone levels defined as ANY of the following:
   - Baseline total testosterone level less than the reference lab’s normal value on two separate occasions
   - Baseline serum free testosterone level and total testosterone less than reference lab normal value on the same date

3. Androgen deficiency diagnosis is not made during an acute or subacute illness
4. Complete physical examination, including a digital prostate examination and PSA measurement, all done within the last 12 months. A digital prostate examination should be done periodically during therapy.
5. No contraindication present such as known or suspected carcinoma of the prostate or the male breast

- For male individuals, continuation of coverage for testosterone replacement therapy for members already approved by BCBSAZ, is considered medically necessary with documentation of a complete physical examination, including a digital prostate examination, both done within the last 12 months. Historical labs are not required.

- For male individuals, testosterone replacement therapy for all other indications not previously listed or if above criteria not met is considered experimental or investigational based upon:

1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
2. Insufficient evidence to support improvement of the net health outcome, and
3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
4. Insufficient evidence to support improvement outside the investigational setting.

These indications include, but are not limited to:

- Older men with low testosterone levels in the absence of clinical signs and symptoms of hypogonadism
TESTOSTERONE REPLACEMENT THERAPY (cont.)

Criteria: (cont.)

➢ For female individuals, initiation of testosterone replacement therapy for existing members, and continuation of testosterone replacement therapy for members on testosterone replacement therapy prior to their BCBSAZ original effective date (OED) of coverage is considered medically necessary with documentation of ALL of the following:

1. Diagnosis of metastatic/inoperable breast cancer
2. There are no contraindications present such as:
   • Woman of child bearing potential who is pregnant or not currently using effective contraception
   • Woman who is breast feeding an infant or child

➢ For female individuals, continuation of coverage for testosterone replacement therapy for members already approved by BCBSAZ, is considered medically necessary with documentation that there is no disease progression.

➢ For female individuals, testosterone replacement therapy for all other indications not previously listed or if above criteria not met is considered experimental or investigational based upon:

1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
2. Insufficient evidence to support improvement of the net health outcome, and
3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
4. Insufficient evidence to support improvement outside the investigational setting.

➢ Bioidentical hormone replacement therapy, including compounded products, for men and women is considered experimental or investigational based upon:

1. Lack of final approval from the Food and Drug Administration, and
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
3. Insufficient evidence to support improvement of the net health outcome, and
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
5. Insufficient evidence to support improvement outside the investigational setting.
TESTOSTERONE REPLACEMENT THERAPY (cont.)

Resources:

Literature reviewed 08/21/18. We do not include marketing materials, poster boards and non-published literature in our review.

The BCBS Association Medical Policy Reference Manual (MPRM) policy is included in our guideline review. References cited in the MPRM policy are not duplicated on this guideline.

4. External Consultant Review. SW Pediatric Endocrinology. 05/06/2006.
6. UpToDate. Preparations for menopausal hormone therapy. 05/14/2018, 03/22/2017.

Initial Approval Duration:
12 months

Renewal Approval Duration:
12 months
TESTOSTERONE REPLACEMENT THERAPY (cont.)

Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ’s Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ’s Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html

Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un intérprete, llame al 602-864-4884.

Navajo: Díí kwe’é atah niilínígíí Blue Cross Blue Shield of Arizona haadí yit’éegi bina’ídíiłkidí éí doodago Háida bijá aniłyeedííígi t’áadoo le’é yina’idílkkidí beehaz’áánii hóół díí t’áa hazaad’ehjí háká a’dowolgo be hæz’á doo bąąl ilínígíí. Aťa’haine’ígí kojí bích’į’ hodilinhíí 877-475-4799.

Chinese: 如果您，或是您正在協助的對象，有關於插入項目的名稱 Blue Cross Blue Shield of Arizona 方面的問題，您有權利免費以您的母語得到幫助和訊息。洽詢一位翻譯員，請撥電話 在此插入數字 877-475-4799.

Vietnamese: Nếu bạn quí, hãy gọi người mà quí đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quí vị sẽ có quyền được giúp và có thể thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thợ dịch viên, xin gọi 877-475-4799.

Arabic: إن كنت لديك أو لأدي شخص تساعده أسلحة بخصوص Blue Cross Blue Shield of Arizona الضرورية بقليل من دون أي تكلفة، للتحدث مع مترجم التصل ب 877-475-4799.
TESTOSTERONE REPLACEMENT THERAPY (cont.)

Multi-Language Interpreter Services: (cont.)

Tagalog: Kung ikaw, o ang iyong tinitulungan, ay mga maya mga katanungan tungkol sa Blue Cross Blue Shield of Arizona, may karapatan ka na makakuha ng tulong at impormasyon sa iyong wika ng walang gastos. Upang makausap ang isang tagasalin, tumawag sa 877-475-4799.

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona에 관해서 질문이 있다면 귀하는 그러한 도움과 정보를 귀하의 언어로 이용 무담없이 얻을 수 있는 권리가 있습니다. 그렇게 통역사와 얘기하기 위해서는 877-475-4799로 전화하십시오.

French: Si vous, ou quelqu’un que vous êtes en train d’aider, a des questions à propos de Blue Cross Blue Shield of Arizona, vous avez le droit d’obtenir de l’aide et l’information dans votre langue à aucun coût. Pour parler à un interprète, appelez 877-475-4799.

German: Falls Sie oder jemand, dem Sie helfen, Fragen zum Blue Cross Blue Shield of Arizona haben, haben Sie das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Um mit einem Dolmetscher zu sprechen, rufen Sie bitte die Nummer 877-475-4799 an.

Russian: Если у вас или лица, которому вы помогаете, имеются вопросы по поводу Blue Cross Blue Shield of Arizona, то вы имеете право на бесплатное получение помощи и информации на вашем языке. Для разговора с переводчиком позвоните по телефону 877-475-4799.

Japanese: ご本人様、またはお客様の身の回りの方でも、Blue Cross Blue Shield of Arizonaについてご質問がございましたら、ご希望の言語でサポートを受けたり、情報を入手したりすることができます。料金はかかりません。通訳とお話される場合、877-475-4799までお電話ください。

Farsi: اگر شما یا کسی که شما به وی کمک می‌کنید، سوال‌های مربوط به Blue Cross Blue Shield of Arizona را داشته باشید، حق دارید اطلاعاتی در مورد آنها در زبان خود را به طور رایگان دریافت کنید. تماس حائز نمایندگان ترجمه.

Assyrian: بزو کرا کدی که کا کمکی کرا کرا و چکک می‌کاند، سەواکە دەوە مبادێکردنەوە، دەگەیە دەوە، لەسەوە، ماما سەیە. 877-475-4799

Serbo-Croatian: Ukoliko Vi ili nekoome Vi pomazete imo pitanje o Blue Cross Blue Shield of Arizona, imate pravo da besplatno dobijete pomoć i informacije na Vašem jeziku. Da biste razgovarali sa prevodijem, nazovite 877-475-4799.

Thai: หากคุณ หรือคนที่คุณช่วยเหลือเกี่ยวกับ Blue Cross Blue Shield of Arizona คุณมีสิทธิ์ได้ความช่วยเหลือและข้อมูลภาษาของคุณได้โดยไม่ค่าใช้จ่าย ติดต่อที่ โทร 877-475-4799