Erectile Dysfunction

Policy Number: AHS – G2132 – Erectile Dysfunction	Prior Policy Name and Number, as applicable:
Initial Presentation Date: 06/01/2021 Revision Date: N/A	

I. Policy Description

Erectile dysfunction (ED), or impotence, is defined as the inability to achieve or maintain an erection of sufficient rigidity to enable penetration and completion of the sexual act (Cunningham & Khera, 2018).

For guidance on hormonal testing in males, please refer to AHS-G2013 Hormonal Testing in Males.

II. Related Policies

Policy Number	Policy Title
AHS-G2013	Hormonal Testing in Males

III. Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request. Medical Policy Statements do not ensure an authorization or payment of services. Please refer to the plan contract (often referred to as the Evidence of Coverage) for the service(s) referenced in the Medical Policy Statement. If there is a conflict between the Medical Policy Statement and the plan contract (i.e., Evidence of Coverage), then the plan contract (i.e., Evidence of Coverage) will be the controlling document used to make the determination.

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request. If there is a conflict between this Policy and any relevant, applicable government policy [e.g. National Coverage Determinations (NCDs) for Medicare] for a particular member, then the government policy will be used to make the determination. For the most up-to-date Medicare policies and coverage, please visit their search website http://www.cms.gov/medicare-coverage-database/overview-and-quick-search.aspx?from2=search1.asp& or the manual website

1. The following lab tests **MEET COVERAGE CRITERIA** in the diagnosis of erectile dysfunction:

    a. Blood glucose (Fasting / HbA1c)

b. Complete blood count

c. Creatinine and Blood Urea Nitrogen

d. Hepatic panel

e. Lipid profile

f. Prostate specific antigen

g. Serum testosterone (Total / Free or Bioavailable)

h. Thyroid function studies

i. Urinalysis

The following does not meet coverage criteria due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of a patient's illness.

2. The following tests for the diagnosis of erectile dysfunction **DO NOT MEET COVERAGE CRITERIA** because their effectiveness has not been established:

   a. Angiotensin-converting enzyme insertion/deletion polymorphism testing

   b. Endothelial nitric oxide synthase polymorphism (4 VNTR, G894T, and T786C) testing for estimating risk of erectile dysfunction

   c. Iron binding capacity

   d. Prostatic acid phosphatase

IV. Scientific Background

It has been projected that approximately 150 million men in the world suffer from erectile dysfunction (ED), making it one of the most frequent chronic health problems in men over 40 years of age and a common reason for consultation of family physicians and specialists (Brotons et al., 2004; Cunningham & Khera, 2018). Najari and Kashanian (2016) report that ED is present in 1 of 2 men over the age of 40. However, men younger than 40 also seek medical help for new-onset ED. One study reports that one in four patients younger than 40 experience ED, with almost 50% of the young men complaining of severe ED (Capogrosso et al., 2013). ED may be an indicator for other underlying diseases, such as diabetes, hypertension or atherosclerosis, and thus merits investigation (Brotons et al., 2004; Najari & Kashanian, 2016; Yoshimura, Kato, Chencellor, Nelson, & Glorioso, 2010).

The development of an erection is a complex process that involves the brain, hormones, emotions, nerves, muscles, and blood vessels. A problem with any of these components (endocrine, cardiovascular, neurological, and so on) can result in ED. For example, low intracavernosal nitric oxide synthase, which is necessary for nitric oxide to maximize blood flow to the penis, is often found in low

levels in diabetic patients or patients with low testosterone. Any disruption of blood flow or nitric oxide synthesis may prevent intracavernosal blood pressure from rising enough to maintain acceptable rigidity for an erection (Cunningham & Khera, 2018). Other causes of erectile dysfunction may be penile trauma, spinal cord injuries, abnormalities of the penis (e.g., penile fibrosis and Peyronie's disease), veno-occlusive dysfunction or as a result of a radical pelvic surgery (e.g., radical prostatectomy or cystectomy) (Shindel, Brant, Bochinski, Bella, & Lue, 2014). Regardless of the cause, ED has a negative impact on the quality of life of both the patient and partner (Althof, 2002).

ED may be cured or improved simply by implementing lifestyle changes. Diet and weight loss plans may improve ED symptoms significantly. Patients are also recommended to reduce alcohol intake, avoid smoking, and eliminate illicit drug use (Najari & Kashanian, 2016). Further, if side effects from medication are the cause of ED, physicians may work with the patient to prescribe alternative medications. Psychotherapy may also be recommended if ED is caused by psychological factors.

Proprietary tests exist for the assessment of risk factors for ED. For example, Walk-In Lab offers an ED panel consisting of several biomarkers (thyroid stimulating hormone [TSH], complete blood count [CBC], luteinizing hormone [LH], and so on) (Walk-In, 2017). Genova offers a similar panel, which evaluates hormones, including testosterone, estradiol, PSA (prostate specific antigen), and DHEA (dehydroepiandrosterone) (GENOVA, 2019). Finally, GX Sciences offers a genetic "Men's Health Panel" that evaluates 15 gene variants proposed to play a significant role in "Testosterone conversion and breakdown, estrogen formation, risk of metabolic weakness, and risk of hypertension." Besides low sex drive and testicular atrophy, GX Sciences states that their genetic test can also be used to address "carbohydrate cravings," "slow recovery," and male pattern baldness (GXSciences, 2019). AccesaLabs has also developed an ED test panel which measures FSH, LH, prolactin, total testosterone and free testosterone levels (AccesaLabs, 2020).

Clinical Utility and Validity

The evaluation of male sexual dysfunction may include sexual history and physical examination, which have been reported to have a 95 percent sensitivity but only a 50 percent specificity in determining the cause of ED (Davis-Joseph, Tiefer, & Melman, 1995). Additional diagnostic tests include fasting glucose or glycated hemoglobin (A1C) to examine for diabetes or level of glucose control, complete blood count (CBC), comprehensive metabolic profile to assess liver and kidney function, thyroidstimulating hormone (TSH) to rule out thyroid disease, lipid profile to assess cardiac risk factors, and serum total testosterone to assess gonadal function (Cunningham & Khera, 2018; Hatzimouratidis et al., 2010; Qaseem et al., 2009).

Lane-Cordova, Kershaw, Liu, Herrington, and Lloyd-Jones (2017) performed a study assessing cardiovascular health with ED. The study included 1136 men who were divided into three categories of cardiovascular health (CVH, low, medium, high) and were assessed for ED. The researchers concluded that 58% of men with low CVH were found to have ED (233/387), 41% with moderate CVH (277/670), and 33% (26/79) with CVH. ED was also found to have a prevalence ratio of 0.75 with moderate CVH and 0.68 with high CVH (Lane-Cordova et al., 2017).

Brooke et al. (2014) conducted a study examining the association between testosterone levels in ED patients with type 2 diabetes. A total of 355 diabetic patients were evaluated, and on average,

patients with ED were found to have 9.1% lower SF-36 health questionnaire score, which correlated with lower total, bioavailable, and free testosterone (Brooke et al., 2014).

Kizilay, Kalemci, Simsir, and Altay (2020) researched predisposing factors for ED and response to treatment in young versus old men. Patients were divided in to two groups: <40 years (n=58, group I) and ≥40 years (n=73, group II). Participants completed both the International Index of Erectile Function-5 (IIEF-5) questionnaire, and Beck's Depression Inventory (BDI) questionnaire. Results seem to be typical. The researchers report higher morning rigidity and libido in group I. Further, "In multivariate analysis, the factors predicting the low IIEF-Erectile Function domain score in young men were testosterone level and BDI score (p = .026 and p = .034). Although psychogenic factors contribute significantly to the aetiology of ED, hormone profile is more preserved in young men than in older men (Kizilay et al., 2020)."

Huntingdon, Muscat, de Wit, Duracinsky, and Juraskova (2020) completed a systematic review for ED in men with and without HIV. Fourteen studies from 1997 to 2019 met the inclusion criteria. The researchers found that both age and depression were significantly associated with ED. Also, "Importantly, factors unique to HIV emerged as consistently significant across studies, including time on antiretroviral medication and protease inhibitor medication use (Huntingdon et al., 2020)." The authors concluded by suggesting that psychological factors such as fear of transmission or rejection by a sexual partner should be considered in future ED/HIV research.

V. Guidelines and Recommendations

American College of Physicians (ACP) (Qaseem, Horwitch, Vijan, Etxeandia-Ikobaltzeta, & Kansagara, 2020; Qaseem et al., 2009)

The ACP concluded that the evidence for the utility of hormonal blood tests in identifying and affecting therapeutic outcomes for treatable causes of ED is inconclusive. The ACP makes no recommendations either for or against routine use of hormonal blood tests or hormonal treatment in the management of patients with ED. Clinicians should make decisions to measure hormone levels on a case-by-case basis, in accordance with the patient's clinical presentation (Qaseem et al., 2009).

In 2020, the ACP published guidelines for testosterone treatment in adult men with age-related low testosterone levels. These guidelines mention that the "ACP suggests that clinicians discuss whether to initiate testosterone treatment in men with age-related low testosterone with sexual dysfunction who want to improve sexual function (conditional recommendation; low-certainty evidence) (Qaseem et al., 2020)." However, these guidelines do not give specific examples of recommended testing methods for men experiencing sexual dysfunction.

European Association of Urology (EAU) (Hatzimouratidis, 2016)

In 2016, EAU published revised guidelines for the diagnosis and treatment of patients suffering from erectile dysfunction. It recommended that laboratory testing must be ordered based on the patient's complaints and risk factors. It recommended that "patients may need a fasting blood glucose or HbA1C and lipid profile if not recently assessed. Hormonal tests include an early morning total testosterone. If indicated, bioavailable or calculated-free testosterone may be needed to corroborate total testosterone measurements." It further recommended that additional laboratory testing may be

considered in some patients (for example, prostate-specific antigen, prolactin and luteinizing hormone) (Hatzimouratidis, 2016).

American Urological Association (AUA) (Burnett et al., 2018)

The AUA recommends measuring morning serum total testosterone in men with ED. The AUA also states that "with the possible exception of serum testosterone, glucose/hemoglobin A1c, and in some cases serum lipids, no routine serum study is likely to alter ED management", but list "serum BUN/Cr, fasting lipids, fasting glucose or hemoglobin A1c, morning testosterone, thyroid function studies (i.e. thyroid-stimulating hormone, free T4) and PSA" as potentially appropriate tests for men with ED (Burnett et al., 2018).

American Association of Clinical Endocrinologists (AACE) (Guay et al., 2003)

The AACE guidelines (Guay et al., 2003) state that "chemistry testing should evaluate for anemia, increased plasma glucose levels, or impaired renal function. Thyroid testing should be done if clinically indicated. Other hormone screening should include serum testosterone and prolactin levels". The AACE concluded that free or bioavailable testosterone assays were preferred over measurement of the total testosterone level. AACE further recommended that "if the testosterone level is low, or even borderline, a serum LH level should be obtained to distinguish primary from secondary hypogonadism."

American Society of Clinical Oncology (ASCO) (Carter et al., 2018)

The ASCO published guidelines (Carter et al., 2018) which state that "Clinicians should check testosterone levels, even if the patient has a cancer that is not typically associated with hormone changes in men reporting decreased sexual functioning and satisfaction."

British Society for Sexual Medicine (BSSM) (Hackett et al., 2018)

The BSSM recommends the following lab testing for ED: "fasting glucose and/or glycated hemoglobin, lipid profile, and fasting testosterone level in all cases." Serum PSA may also be considered if "clinically indicated." The BSSM also notes that if serum testosterone is borderline or low, the test should be repeated together with serum LH and prolactin (Hackett et al., 2018).

VI. State and Federal Regulations, as applicable

FDA prescribing information for drugs that treat erectile dysfunction contraindicate their use in patients with severe renal impairment, hepatic impairment or if sexual activity is inadvisable due to cardiovascular status or any other reason.

FDA approved methods for fasting glucose or glycated hemoglobin (A1C), complete blood count, comprehensive metabolic profile to assess liver and kidney function, thyroid-stimulating hormone (TSH) to rule out thyroid disease, lipid profile to assess cardiac risk factors, and serum total testosterone are available in most CLIA certified laboratories.

Additionally, many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). As an LDT, the U. S. Food and Drug Administration has not approved or cleared this test; however, FDA clearance or approval is not currently required for clinical use.

VII. Applicable CPT/HCPCS Procedure Codes

Billing applicable codes is not a guarantee of payment; see Section III for indications and limitations of coverage that may affect payment

Code Number	Code Description
80061	Lipid Panel
80076	Hepatic function panel
81002	Urinalysis, by dip stick or tablet reagent for bilirubin, glucose, hemoglobin, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, any number of these constituents; non-automated, without microscopy

Code Number	Code Description
81003	Urinalysis, by dip stick or tablet reagent for bilirubin, glucose, hemoglobin, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, any number of these constituents; automated, without microscopy
81005	Urinalysis; qualitative or semiquantitative, except immunoassays
81400	Molecular Pathology - *Angiotensin-converting enzyme insertion/deletion polymorphism testing*

81479	Unlisted molecular pathology procedure - *Endothelial nitric oxide synthase polymorphism (4 VNTR, G894T, and T786C)*
82565	ASSAY OF CREATININE
82570	ASSAY OF URINE CREATININE
82947	Glucose; quantitative, blood (except reagent strip)
83036	Hemoglobin; glycosylated (A1C)
83550	Iron binding capacity
84066	Phosphatase, acid; prostatic
84153	Prostate specific antigen (PSA); total
84402-84403	Testosterone Code Range
84410	Testosterone; bioavailable, direct measurement (eg, differential precipitation)
84520	Urea nitrogen; quantitative
Code Number	**Code Description**
84540	Urea nitrogen, urine
84439	Thyroxine; free
84443	TSH
85025	Blood count; complete (CBC), automated (Hgb, Hct, RBC, WBC and platelet count) and automated differential WBC count
85027	Blood count; complete (CBC), automated (Hgb, Hct, RBC, WBC and platelet count)

VIII. Evidence-based Scientific References

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IX. Revision History

Revision Date	Summary of Changes
06-01-2021	Initial presentation