

PRIOR AUTHORIZATION POLICY

- POLICY:** Erectile Dysfunction – Alprostadil for injection
- Caverject® (alprostadil for injection – Pharmacia & Upjohn [Pfizer])
 - Caverject Impulse® (alprostadil for injection – Pharmacia & Upjohn [Pfizer])
 - Edex® (alprostadil for injection – Auxilium Pharmaceuticals, Inc.)
 - MUSE® (alprostadil urethral suppository – MEDA Pharmaceuticals)

TAC APPROVAL DATE: 8/22/2018

OVERVIEW

Alprostadil belongs to the family of prostaglandins (specifically prostaglandin E₁ [PGE₁]), which are naturally occurring lipids with various pharmacological effects, including vasodilation and inhibition of platelet aggregation.¹⁻⁴ They are naturally present in the seminal vesicles and cavernous tissue of males.⁵ As a smooth muscle relaxant, alprostadil has demonstrated efficacy for the treatment of erectile dysfunction (ED). It binds to specific receptors in the human penile tissue, and induces erection by relaxation of trabecular smooth muscle and by dilation of cavernous arteries.³ This leads to an expansion of the lacunar spaces and entrapment of blood by compressing the venules, a process referred to as the corporal veno-occlusive mechanism.

The available injectable alprostadil products are: Caverject, Caverject Impulse (disposable, single-dose, dual chamber syringe system), and Edex. MUSE is a single-use, medicated transurethral system for the delivery of alprostadil directly in the urethra.⁴ It is suspended in polyethylene glycol and is formed into a medicated pellet. MUSE is administered by inserting the applicator stem into the urethra after urination. All of the alprostadil products are indicated for the treatment of ED due to neurogenic, vasculogenic, psychogenic, or mixed etiology.¹⁻⁴ Additionally, intracavernosal Caverject may be used adjunct to other diagnostic tests in the diagnosis of ED.¹

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of alprostadil injections and suppository administered via intracavernous or intraurethral routes, respectively. Intravenous (IV) or other routes of administration of alprostadil is not covered by this policy. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of alprostadil injections (e.g., Edex, Caverject) and suppository (e.g., MUSE) is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Erectile Dysfunction (ED).** Approve for 1 year.

Alprostadil injections and MUSE are indicated for the treatment of ED.¹⁻⁴

Other Uses with Supportive Evidence

2. **Prophylaxis after Radical Prostatectomy (Early Penile Rehabilitation).** Approve for 1 year in treatment-naïve patients if they meet both of the following criteria (A and B).
 - A) Therapy will be started within 6 months of surgery; AND
 - B) Alprostadil (e.g., Edex, Caverject, MUSE) is prescribed by or in consultation with an urologist

The treatments most studied for penile rehabilitation are alprostadil (injections or intraurethral suppository) and oral phosphodiesterase type 5 (PDE5) inhibitors.⁸ Alprostadil may help the recovery of erectile function by promotion of cavernosal oxygenation levels. Several studies have demonstrated the efficacy of alprostadil injections and MUSE for early penile rehabilitation post radical prostatectomy.⁹⁻¹⁵

3. **Patient with a History of Radical Prostatectomy who is Continuing Alprostadil Therapy (e.g., Edex, Caverject, MUSE).** Approve for 1 year if patient was started on therapy post-operatively and is currently continuing therapy.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Alprostadil products (Caverject, Caverject Impulse, Edex, MUSE) have not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Caverject® [prescribing information]. New York, NY: Pharmacia and Upjohn Company (Pfizer); November 2017.
2. Caverject Impulse® [prescribing information]. New York, NY: Pharmacia and Upjohn Company (Pfizer); October 2016.
3. Edex® [prescribing information]. Chesterbrook, PA: Auxilium Pharmaceuticals, Inc.; March 2015.
4. MUSE [prescribing information]. Somerset, NJ: Meda Pharmaceuticals; August 2014.
5. Clinical Pharmacology [database online]. Tampla, FL: Gold Standard, Inc.; 2010. Available at <http://www.clinicalpharmacology-ip.com/default.aspx>. Accessed August 14, 2018. Search term: Caverject.
6. Segal R, Burnett AL. Erectile preservation following radical prostatectomy. *Ther Adv Urol.* 2011;3:35-46.
7. McCullough AR, Hellstrom WG, Wang R, et al. Recovery of erectile function after nerve sparing radical prostatectomy and penile rehabilitation with nightly intraurethral alprostadil versus sildenafil citrate. *J Urol.* 2010;183:2451-2456.
8. Kim ED. Local therapies to heal the penis: Fact of fiction? *J Androl.* 2009;30:384-390.
9. Montorsi F, Guazzoni G, Strambi LF, et al. Recovery of spontaneous erectile function after nerve-sparing radical retropubic prostatectomy with and without early intracavernous injections of alprostadil: Results of a prospective, randomized trial. *J Urol.* 1997;158:1408-1410.

10. Yiou R, Cunin P, de la Taille A, et al. Sexual rehabilitation and penile pain associated with intracavernous alprostadil after radical prostatectomy. *J Sex Med.* 2011;8:575-582.
11. Raina R, Lakin MM, Thukral M, et al. Long-term efficacy and compliance of intracorporeal (IC) injection for erectile dysfunction following radical prostatectomy: SHIM (IIEF-5) analysis. *Int J Impot Res.* 2003;15(5):318-322.
12. Claro J, Aboim J, Maringolo M, et al. Intracavernous injection in the treatment of erectile dysfunction after radical prostatectomy: an observational study. *Sao Paulo Med J.* 2001;119:135-137.
13. Raina R, Pahlajani G, Agarwal A, et al. The early use of transurethral alprostadil after radical prostatectomy potentially facilitates an earlier return of erectile function and successful sexual activity. *BJU Int.* 2007;100:1317-1321.
14. Raina R, Agarwal A, Ausmundson S, et al. Long-term efficacy and compliance of MUSE for erectile dysfunction following radical prostatectomy: SHIM (IIEF-5) analysis. *Int J Impot Res.* 2005;17:86-90.
15. Raina R, Nandipati KC, Agarwal A, et al. Combination therapy: Medicated urethral system for erection enhances sexual satisfaction in sildenafil citrate failure following nerve-sparing radical prostatectomy. *J Androl.* 2005;26:757-760.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	No criteria changes	11/11/2015
selected revision	Approval duration changed back to 1 year for all indications	12/02/2015
Selected revision	Added new automation for male erectile dysfunction; ICD-9 and ICD-10 codes for ED will be used when available for automation. This new automation will be in effect 4/1/2016.	03/16/2016
Early annual revision	Removed “Men with” from ED indication and changed treatment-naïve “men” to “patients.” Also deleted Pulmonary Arterial Hypertension and Premature Ejaculation from Conditions Not Recommended for Approval due to lack of new data/appeals info. Post-TAC also deleted automation with ICD9/10 codes and changed it to “None,” since it’s not going to be operationalized.	08/03/2016
Annual revision	No criteria changes	08/09/2017
Annual revision	No criteria changes	08/22/2018

TAC – Therapeutic Assessment Committee; * For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>; ED – Erectile dysfunction.