

EXHIBIT 7

From: Neil Fisher <NFisher@wexfordhealth.com>
Sent: Tuesday, April 12, 2016 10:55 AM
To: Shicker, Louis
Cc: Thomas Lehman; Donna Jasko; Michelle Marrone; Helen Feinstein
Subject: Guidelines for Medical Management of Transgender Adults
Attachments: Guidelines for Medical Management of Transgender Adults 4-2016.docx

Dr. Shicker - Awhile ago you asked me at a Illinois P&T meeting about the Medical Management of Transgender Adults.

Dr. Feinstein had worked on this months ago but I forgot to forward it to you.

We have updated the pricing of the medications and the references.

This is for your review.

Thanks!

Neil

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"R.A.I.S.E. the Standard."

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Guidelines for Medical Management of Transgender Adults

Part I. Male to Female Transition - Transfemale Patient¹⁻⁴

1. Prior to starting hormone therapy, ensure that the following conditions are **adequately managed** with pharmacological therapy:
 - Hypertension
 - Hyperlipidemia, obesity
 - Diabetes
 - Psychiatric disorders
2. The following conditions represent **absolute contraindications** to estrogen therapy:
 - Active or recent thromboembolic disease, including history of DVT or PE
 - Breast or other estrogen-dependent cancer
 - Liver dysfunction
 - Uncontrolled hypertension or diabetes
 - Abnormal genital bleeding
 - Pregnancy, known or suspected
3. Estrogen therapy is **not recommended** if the patient has documented
 - Endometriosis or endometrial cancer
 - Ovarian cancer
 - Gallbladder disease requiring surgery
 - Metabolic syndrome
 - Refractory migraine or focal migraine
 - Seizure disorder
 - Is an active smoker
 - Drug addiction (alcohol, prescription drugs, or illicit substances)
4. Prior to starting therapy ensure that the patient is enrolled in **smoking cessation** program.
5. Prior to starting therapy ensure that the patient is participating in **active exercise** program.
6. **Therapy goals:**
 - Achieve serum estradiol level of <200 pg/ml
 - Suppress testosterone to <55 ng/dl
 - Achieve and maintain physical changes such as breast growth, decreased muscle mass, body fat redistribution, and decreased body/facial hair
7. Treatment Options
 - **Anti-androgen Therapy-**
 - Purpose: estrogen-sparing initial regimen to block peripheral androgen receptors and inhibit testosterone secretion; used during initial preparation for conversion only
 - Drug: Spironolactone 100mg po daily, adjusted weekly by 50mg increments, maximum dose is 400mg/day in divided doses or as a whole dose in AM
 - i. Contraindicated in hyperkalemia and moderate to severe renal impairment
 - ii. Must monitor potassium levels

- **Estrogen therapy** (green-preferred choice; orange-secondary alternative)

Formulation	Dosage	Advantages	Drawbacks	Cost Per Month
Oral estradiol	1-4mg/day	Easy to administer, inexpensive, improves physical characteristics	Higher thromboembolic risk	\$3
Transdermal estradiol patch	0.1-0.4 mg dose as patches applied twice a week	Easy to apply, bypasses liver metabolism, lower thromboembolic risk, preferred in individuals over 40, smokers, or patients with diabetes and liver disease	Skin reactions, adhesion problems, slower onset of action	\$92-\$366
Intramuscular estradiol	5-20 mg IM q 2 weeks		Levels may fluctuate, requires medical personnel, only available in multi-dose vials that are stable for a month when opened	\$104
Conjugated estrogens (Menest)	0.625-1.25mg/daily	Less expensive than IM estradiol	Limited clinical data, higher thromboembolic risk, lack of monitoring	\$57-80

- Progesterone is not recommended in current guidelines and has not shown clinical benefit in studies of male-to-female transition patients. Use of progestin is associated with increased risk of depression, mood fluctuations, weight gain, and lipid abnormalities.

8. Treatment Monitoring

- **Baseline** - Blood Pressure, Weight, lipids, CMP, CBC, serum estradiol, serum testosterone, prolactin, PT/INR & PTT (when DVT risk exists)
- **Every 3 months after starting estrogen during first year**—Serum testosterone, estradiol, CBC, hemoglobin, lipids, LFTs, Weight, Blood Pressure.

- **Every 6-12 months after first year of therapy** - Blood Pressure, Weight, CBC, CMP, lipids, serum testosterone, estradiol, prolactin

Part II. Female-to-Male Transition - Transmale Patient¹⁻⁴

1. The following conditions represent **absolute contraindications** to testosterone therapy
 - Uncontrolled hypertension or coronary artery disease
 - Uncontrolled diabetes
 - Hepatic disease
 - Pregnancy
 - Active cancer
 - Active psychosis
2. Testosterone therapy is **not recommended** if the patient has documented
 - Dyslipidemia
 - Malignancy
 - Obesity
 - Chronic lung disease-increased risk of sleep apnea
 - Nasal disorders or mucosal inflammatory disorders
3. **Precautions** to consider when starting testosterone therapy
 - Decreases insulin sensitivity
 - Increases cardiovascular risk by
 - worsening lipid profile
 - increased erythropoiesis
 - potential lowering of homocysteine levels
4. **Goals of therapy:** testosterone level 320-1000 ng/dl, increased virilization, male pattern hair growth, voice changes, cessation of menses, and male body contour.
5. Treatment Options
 - **Testosterone**

Formulation	Dosage Range	Advantages	Drawbacks	Cost Per Month
Depo-testosterone IM	100-200 mg IM q 2 weeks	Inexpensive, longer duration between doses, achieves therapeutic levels and changes physical attributes faster	Requires injections, fluctuations in serum testosterone levels, mood disturbances	\$78 per MDV
Testosterone transdermal patch (Androderm)	2-6 mg daily	Ease of application, mimics physiological levels	Lower serum testosterone levels, skin irritation, used for maintenance after virilization	\$227-\$455

			achieved with injection, high cost	
Testosterone gel	2.5-10 g/day (25-100 mg of testosterone)	Easy to apply, flexible dosing, well tolerated, corrects symptoms	Secondary exposure, hypersensitivity, odor, high cost	\$283-520

- Medroxyprogesterone (Depo Provera)
Purpose: Supplemental therapy to stop menstruation, reduces estrogen levels to concentrations found biologically in men
Dosing: Medroxyprogesterone 150mg IM q 3 months up to 3 doses total; limit exposure to reduce risk of endometrial hyperplasia
Cost: \$53/injection

6. Treatment Monitoring

- **Baseline** – Blood Pressure, Weight, Lipids, BMP, CBC, serum testosterone, BMD (consider if osteoporosis risk exists)
- **Every 3 months after starting testosterone for first year** – Blood Pressure, Weight, Serum testosterone, estradiol (for 6 months after cessation of menses), CBC, lipids, CMP
- **Every 6 - 12 months after 1st year of therapy**— Blood Pressure, Weight, CBC, CMP, lipids, serum testosterone
- **Desired/undesired effects:** worsening of acne, increased muscle mass, increased hair growth, clitoral enlargement, vaginal atrophy, aggressive behavior; rare cases of ovarian cancer

References:

1. Knezevich EL, Viereck LK, Drincic AT. “Medical management of adult transsexual patients”, *Pharmacotherapy* 2012; 32(1): 54-66. www.medscape.com/viewarticle/757128_print, accessed April 6, 2015.
2. Sherbourne Health Centre. “Guidelines and protocols for comprehensive primary health care for trans clients”. Toronto, 2009, <http://www.sherbourne.on.ca/PDFs/Trans-Protocols.pdf>, accessed March 30, 2015.
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4. Micromedex® 2.0, (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: <http://www.micromedexsolutions.com>. Accessed April 6, 2015.