SHERBOURNE Health Centre

Rainbow Health Ontario

Protocols for Hormone Therapy for Trans Clients

A quick reference guide for primary care providers

This quick reference guide was derived from Sherbourne Health Center's Guidelines and Protocols for Hormone Replacement Therapy and Primary Health Care for Trans Clients and is designed to be used in conjunction with the full Protocols.

KEY MESSAGES

- Prescribing hormone therapy for trans clients is **ideally situated in primary care**.
- The risks of **not providing** hormone therapy are often more substantial than the risks of treatment.

AN INDIVIDUAL APPROACH TO CARE

There is no single pathway for a trans person to follow in order to actualize the expression of their authentic self. Non-binary clients may also seek hormone therapy to modify their secondary sex characteristics.
Though hormones and/or surgery are medically necessary for many trans people, others may obtain relief of gender dysphoria through other means of modifying their self expression. The experience of regret after medical transition is very rare. There is no requirement of lived gender role experience prior to initiation of hormone therapy.

DECISION TO START HORMONES

The decision to initiate hormone therapy is a collaborative client-centered process that focuses on psychosocial readiness and informed consent. For each client seeking hormone therapy, it is important to not only consider the possible risks of treatment but to consider the often substantial risks of not undergoing hormonal therapy as part of the management plan for significant gender dysphoria.[1]

1. Raj R, Schwartz C. A collaborative preparedness and informed consent model: Guidelines to assess trans candidates for readiness for hormone therapy and supportive counselling throughout the gender transitioning process. International Journal of Transgenderism. 2015

TERMINOLOGY

Cis	refers to a state of alignment of one's gender identity with the gender assigned at birth
Trans	refers to a state of incongruence of one's gender identity with the gender assigned at birth
Non-binary	(e.g. gender queer, gender fluid, pangender, agender) may feel that their gender falls somewhere between "man" or "woman", is both, neither or in flux.
Gender non conformity	refers to the extent to which a persons gender identity, role or expression differs from the cultural norms prescribed for people of a particular sex.
Gender Dysphoria	refers to discomfort or distress that is caused by a discrepancy between a person's gender identity and their sex assigned at birth (and the associated gender role and/or primary and secondary sex characteristics). Only some gender nonconforming people experience gender dysphoria at some point in their lives.

INITIAL ASSESSMENT

The following is a tool to guide the assessment process with new (or newly transitioning) trans clients who have reached tanner stage V in pubertal development and are interested in hormone therapy.

It is more important that the tasks of the assessment period are completed, rather than a certain number of visits logged or period of time elapsed.

CRITERIA FOR HORMONE THERAPY

- ☐ Diagnosis of Gender Dysphoria (according to the DSM-V-TR*)[2]
- ☐ Psychosocial readiness to begin treatment
- ☐ Completion of a period of assessment including appropriate physical and laboratory investigations
- ☐ Absence of absolute contraindications
- ☐ Optimal mitigation of risks relating to pre-existing health conditions
- ☐ Client understanding of risks, precautions and side effects of treatment

CULTURAL COMPETENCE

As with many marginalized populations, care of trans clients requires cultural competence, which includes an understanding and awareness of the barriers to care. Wherever possible, it is advisable to make the clinic setting accessible to trans people. This may include staff training around common office issues that affect trans clients, such as the use of appropriate pronouns. These considerations can go a long way towards reducing stigmatization while increasing the comfort of trans clients in the medical setting.

For more information, please visit www.rainbowhealthontario.ca/trans-health-connection

GENDER-AFFIRMING SURGERY

Some trans clients may consider gender affirming surgery.

OHIP COVERED SURGERIES FOR TRANS WOMEN

- › orchiectomy
- › vaginoplasty

OHIP COVERED SURGERIES FOR TRANS MEN

- › chest reconstruction
- › hysterectomy +/- bilateral salpingoophorectomy
- › metoidioplasty
- › phalloplasty
- › scrotoplasty

2. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 5th edition (DSM-5). 2013. New York: American Psychiatric Pub

CLIENT HISTORY

- ☐ Discuss the rationale for assessment period:
  - › Establish rapport
  - › Ensure optimal readiness
  - › Educate client
- ☐ General medical intake & medical history

BASELINE DATA

- ☐ Vitals (incl. BP, Ht, Wt, Waist & Abdo circ.)
- ☐ Focused Physical Exam
- ☐ Blood work
- ☐ Health screening commensurate to age & risk profile

CLIENT EDUCATION, READINESS AND SUPPORTS

- ☐ Allow client to articulate their transition goals
- ☐ Discuss risks, side effects, potential benefits and expected changes (reversible vs. irreversible) associated with treatment and ensure client demonstrates understanding
- ☐ Discuss effects on fertility and options available for preservation (see RHO fact sheet)
  - › Fertility may be **permanently** affected by hormone therapy.
- ☐ Discuss pregnancy risk and options for contraception & implement these if needed
- ☐ Review potential costs (e.g. medication, hair removal, fertility)
- ☐ Discuss psychosocial readiness
  - › Ensure supports are in place to facilitate healthy adjustment
  - › Refer to psychological support/counselling if necessary
- ☐ Ensure client expresses reasonable expectations
  - › Client understands timeline of changes
  - › Client understands limitations of hormone therapy
- ☐ Ensure client possesses capacity to consent
- ☐ Review medication options/treatment routes
- ☐ Submit EAP form (for clients on ODB)

RISK MANAGMENT

- ☐ Ensure absence of absolute contraindications
- ☐ Optimally manage precautions
- ☐ Manage psychiatric co-morbidity, if present
- ☐ If smoker, complete smoking cessation counseling

DIFFERENTIAL DIAGNOSIS

- ☐ Rule out other possible diagnosis (i.e. psychiatric disorders that could mimic gender dysphoria such as psychotic or dissociative disorders)
- ☐ Ensure client meets Criteria for Gender Dysphoria
- ☐ No evidence of intersex condition (e.g. ambiguous genitalia, abnormal baseline hormone profile)

NEXT STEPS

- ☐ Choose initial hormone regimen
- ☐ Client signs consent form
- ☐ Discuss interest in Gender Affirming Surgery
- ☐ Offer support for changing client's sex designation on Government ID

FEMINIZING HORMONE THERAPY

The goal of hormone therapy in trans women is to reduce the endogenous effects of testosterone and to induce female secondary sex characteristics. Physiologically, this requires a suppression of endogenous androgens and the addition of estrogen. This treatment results in both reversible and irreversible feminization.[3]

ABSOLUTE CONTRAINDICATIONS

- Unstable ischemic cardiovascular disease
- Estrogen-dependent cancer
- End stage chronic liver disease
- Psychiatric conditions which limit the ability to provide informed consent
- Hypersensitivity to one of the components of the formulation

ESTROGEN

Estrogen acts directly on estrogen receptors to initiate feminization. It is usually the focus of hormonal transition for trans women. At SHC, oral estradiol (Estrace) is prescribed most often because it has a preferable safety profile compared to conjugated estrogen (e.g. Premarin), and is covered by the ODB program with an EAP request. Some report faster breast development with injectable estrogens. The starting dose of estrogen can be maintained for 1-2 months, after which a dose increase can be considered barring any concerning effects. In clients over 50 years old who have been on estrogen for several years, doses may be reduced to those administered to post-menopausal cis women (ie. 0.025 – 0.05 mg patch).

RELATIVE SAFETY

Transdermal estradiol seems to be safer than oral estradiol, have fewer hepatic side effects and is thus recommended for clients over 40 or with risk factors for cardiovascular or thromboembolic disease. [4]

PRECAUTIONS

All reasonable measures should be taken to reduce the risks associated with estrogen therapy.[5] Suggested measures to minimize risks associated with listed precautions may be found in the *Guidelines and Protocols for Hormone Replacement Therapy and Primary Health Care for Trans Clients*.

PREVENTIVE CARE

Trans women maintained on feminizing hormone therapy have unique preventive care needs and recommendations. An Adapted Preventive Care Checklist for trans women that can be used at the point of care can be found in the *Guidelines and Protocols for Hormone Replacement Therapy and Primary Health Care for Trans Clients*.

3. Levy A, Crown A, Reid R Endocrine intervention for transsexuals. Clin Endocrinol 2003; 59(4):409-18
4. Van Kesteren PJ, Asscheman H, Megens JA, Gooren LJ. Mortality and morbidity in transsexual subjects treated with cross-sex hormones. Clinical endocrinology. 1997; 47(3):337-343. Hembree, WC, Cohen-Kettenis P, Delemarre- van de Waal HA, Goore LJ, Meyer WJ, Spack NP, Tangpricha V, Montori VM. Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline. J of Clin Endo & Metabolism. 2009; 94:3132-3154. doi: http://dx.doi.org/10.1210/jc.2009-0345
5. Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the women's health initiative randomized controlled trial. JAMA 2002; 288(3):321-333 doi:101001/jama2883 321

ANTI-ANDROGEN

Spironolactone has traditionally been used preferentially as it was thought to have a superior safety profile. This practice has recently come into question as it has been anecdotally noted that adequate anti-androgen effects are achievable at lower doses of cyproterone at which adverse effects are less likely. Thus the choice of anti-androgen should be made individually for each client based on their medical history and preference regarding respective side effect profiles. Following orchiectomy (+/- vaginoplasty), most trans women will not require androgen suppression. The androgen-blocker can be tapered over the course of 4-6 weeks.

Formulations and recommended doses of estrogens and anti-androgens

Formulations	Starting Dose	Maximum Dose	Cost* (4 weeks)
Spironolactone	50 - 100 mg OD	200 mg BID	$16.56[a] - $40.58[b]
Cyproterone	12.5 - 25 mg OD	50 mg OD	$32.98[c] - $101.92[d]
Conjugated Estrogen*	0.625 mg OD	1.25 mg OD	$20.01[e]
Estradiol (oral)*	1 - 2mg OD	4 mg OD	$18.53 - $40.14[f] **Covered by ODB with EAP request**
Estradiol Patch (transdermal) *[g]	0.1 mg OD / apply path 2x/week	0.2 mg OD / apply path 2x/week	$39.97 - $69.95[h]
Estradiol valerate injectable (IM)[i]**	10mg q 2/52	10mg q 1/52	$14.20 - $28.40

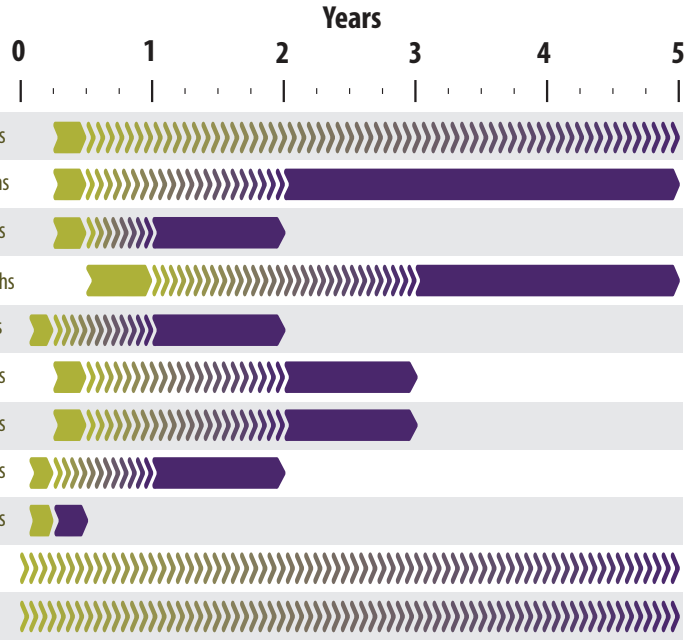
* Price quotes provided by www.pharmacy.ca. represent the price for 4 weeks' supply of a generic brand of medication where available (unless indicated otherwise). Prices include a usual and customary dispensing fee of $9.99 ($10.99 for Pace), which may vary from pharmacy to pharmacy. Accurate as of February 4th, 2015.
**estradiol valerate IM must be prepared by a compounding pharmacy, price quote provided by Pace Pharmacy

a) 50 mg OD given as 2x25 mg tablets OD;
b) 200 mg BID given as 2x100 mg tablets BID;
c) 25mg OD given as 1⁄2 x 50mg tablet OD;
d) 100mg OD given as 2x50 mg tablets OD;
e) The cost of 28 tablets of Premarin® 0.625 mg or 1.25 mg is the same
f) 4mg OD given as 2 x 2mg tablets
g) Estradot® brand
h) 0.2mg OD given as 2x100 mcg patches applied twice weekly(4 patches/week)
i) given as 1mL of 10mg/mL Estradiol valerate

EFFECTS AND EXPECTED TIME COURSE OF A REGIMEN CONSISTING OF AN ANTI-ANDROGEN AND ESTROGEN

The degree and rate of physical effects is dependent on the dose and route of administration[6], as well as client-specific factors such as age, genetics, body habitus and lifestyle.

Hormone treatment results in both reversible and irreversible feminization.



PHYSICAL EFFECTS	REVERSIBILITY	ONSET
Softening of skin/decreased oiliness	Reversible	3 - 6 months
Body fat redistribution	Reversible/Variable	3 - 6 months
Decreased muscle mass/strength[b]	Reversible	3 - 6 months
Thinned/slowed growth of body/facial hair[c]	Reversible	6 - 12 months
Male Pattern Baldness[d]	Reversible	1 - 3 months
Breast growth	Irreversible	3 - 6 months
Decreased testicular volume	Variable	3 - 6 months
Decreased libido	Variable	1 - 3 months
Decreased spontaneous erections	Variable	1 - 3 months
Decreased sperm production	Variable	variable
Erectile Dysfunction	Variable	variable

a) Estimates represent published and unpublished clinical observations
b) Significantly dependent on amount of exercise
c) Complete removal of male facial and body hair requires electrolysis, laser treatment, or both
d) No regrowth, loss stops

Expected Onset Expected Maximum Effect[a]

MONITORING STRATEGIES & DOSE ADJUSTMENTS

Standard monitoring of estrogen administration should be employed at baseline, 1, 3, 6, and 12 months. This should include a functional inquiry, targeted physical exam, bloodwork, and health promotion/ disease prevention counselling as indicated.

Testosterone level may be the most useful test for monitoring in trans women; for many clients, the goal will be to achieve the suppression of testosterone into the female range.

That said, the client may have clinically relevant results without total suppression of testosterone because of androgen blockade, which is not easily measured[7].

Estradiol levels are of variable utility in monitoring feminizing therapy given the wide cyclical variation in cis women. Most clients attain considerable feminization at estradiol levels between 200-500 pmol/L. According to the Endocrine Society Guidelines, serum estradiol levels should not exceed the mean daily level for cis women (approximately 700 pmol/L).

Clinical effects are the goal of therapy, not specific lab values

6. Feldman J, Safer J Hormone Therapy in Adults:Suggested Revisions to the Sixth Version of the Standards of Care , Intl J of Transgenderism 2009;11(3)146-182, DOI: 101080/15532730903383757

7. Tom Waddell Health Centre. Protocols for Hormonal Reassignment of Gender [Internet] San Francisco, CA 2013

HORMONE MONITORING SUMMARY FOR TRANS WOMEN

EXAM/ INVESTIGATION	BASELINE	MONTH 1	MONTH 3	MONTH 6
	Full Phyical Exam, measure: height, weight, waist & abdo circ., +/- breast, hips as per client preference, EKG if over 40, EKG + cardiac stress test if additional risk factors	BP, weight, waist & abdo circ., abdominal exam including liver palpation, extremity exam	BP, weight, waist & abdo circ., abdominal exam including liver palpation, extremity exam, measure breast and hips as per client preference	
BLOODWORK				
CBC	✓	✓	✓	✓
ALT/AST[a]	✓	✓	✓	✓
Creatinine/Lytes/Urea[b]	✓	✓	✓	
Fasting Glucose	✓			
LDL/HDL/TG	✓			
Testosterone (+/- Estradiol)	✓	✓	✓	✓
Prolactin[c]	✓	✓	✓	✓
LH[d]	✓	✓	✓	✓
Other	Hep A, B, C			

a) for Ontario providers who may be restricted in ordering OHIP- covered AST ,evels, ALT alone may be u.ed to screen for liver dysf.nction
b) Elevated LH post-gonadectomy may have implications regarding bone mineral density (See Osteoporosis and BMD Screening in Protocols)
c) Prolactin should be monitored at least yearly, and more frequently if elevation noted
d) Elevated LH post-gonadectomy may have implications regarding bone mineral density (See Osteoporosis and BMD Screening in Protocols)

MASCULINIZING HORMONE THERAPY

The cornerstone of hormone therapy for trans men is testosterone. The goal of treatment is virilization – development of masculine secondary sexual characteristics. This treatment results in both reversible and irreversible masculinization.[3]

ABSOLUTE CONTRAINDICATIONS

- Pregnancy or breast feeding
- Active known androgen-sensitive cancer
- Unstable ischemic cardiovascular disease
- Active endometrial cancer
- Poorly controlled psychosis or acute homicidality
- Psychiatric conditions which limit the ability to provide informed consent
- Hypersensitivity to one of the components of the formulation

TESTOSTERONE

In Ontario, options for testosterone administration include injectable and transdermal preparations (patch or gel). Injectable formulations are most commonly used, both because of their superior efficacy and lower price.
Nurse practitioners (NPs) in Ontario are unable to prescribe testosterone due to its classification as a controlled substance; NPs providing trans care may opt to work collaboratively with a physician to overcome this restriction.

PRECAUTIONS

All reasonable measures should be taken to reduce the risks associated with testosterone therapy. Suggested measures to minimize risks associated with listed precautions may be found in the *Guidelines and Protocols for Hormone Replacement Therapy and Primary Health Care for Trans Clients*..

PREVENTIVE CARE

Trans men maintained on masculinizing hormone therapy have unique preventive care needs and recommendations.
An Adapted Preventive Care Checklist for trans men that can be used at the point of care can be found in the *Guidelines and Protocols for Hormone Replacement Therapy and Primary Health Care for Trans Clients*.

RELATIVE SAFETY

Gel formulations have the risk of inadvertent exposure to others who come into contact with the client's skin. This is of particular importance for clients with young children and/or with intimate partners who are pregnant or considering pregnancy.

Testosterone therapy does **not prevent pregnancy** even if amenorrhea is achieved. Testosterone is a **teratogen** thus reliable contraception may be required depending on sexual practices.

Formulations and recommended doses of testosterone

Formulations	Starting Dose	Maximum Dose	Cost Per Unit	Approx. Cost* (4 weeks)
Testosterone enanthate (IM)	50mg q week or 100 mg q 2 weeks	100mg q week or 100 mg q 2 weeks	$69.03 per vial (each vial contains 200mg/mL x 5mL = 1000mg)	$13.81 - $27.60 **Generally approved by ODB with EAP request**
Testosterone cyponiate (IM)	50mg q week or 100 mg q 2 weeks	100mg q week or 100 mg q 2 weeks	$43.31 per vial (each vial contains 100mg/mL x 10mL = 1000mg)	$8.66- $17.32 **Generally approved by ODB with EAP request**
Testosterone Patch (transdermal)	2.5 - 5 mg OD	5 - 10 mg OD	$159.27 / 60 x 2.5mg patches $159.27 / 30 x 5mg patches	$74.33 - $297.30
Testosterone Gel (transdermal)[i]	2.5 - 5g OD (2-4 pumps, equivalent to 25-50 mg testosterone)	5 - 10g OD (4-8 pumps, equivalent to 50-100 mg testosterone)	$85.90 / 30 x 2.5g patches $147.29 / 30 x 5g patches $167.55 / 2 pump bottles[j] **Only gel in packets (not in pump form) covered by ODB**	Sachets $80.17 - $274.94 Bottles $78.19 - 312.76
Testosterone Gel (transdermal, axillary)[k]	1.5 - 3g OD (1-2 pumps, equivalent to 30-60 mg testosterone)	3 - 4.5mL OD (2-3 pumps, equivalent to 60-90 mg testosterone)	$166.89 / pump bottle[l] **Only gel in packets (not in pump form) covered by ODB**	$77.88[a] - $233.65 **Axiron not covered by ODB**

*Price quotes provided by www.pharmacy.ca. The above-mentioned prices are accurate as of February 4th, 2015 and represent the price of the generic brand of medication where available (unless otherwise indicated). Prices include a usual and customary dispensing fee of $9.99, which may vary from pharmacy to pharmacy.

i) Androgel® 1% gel
j) each pump bottle provides 60 doses of 1.25g (=12.5mg testosterone)
k) Axiron™ 2% solution
l) each pump bottle provides 60 doses of 1.5 mL (=30mg testosterone)

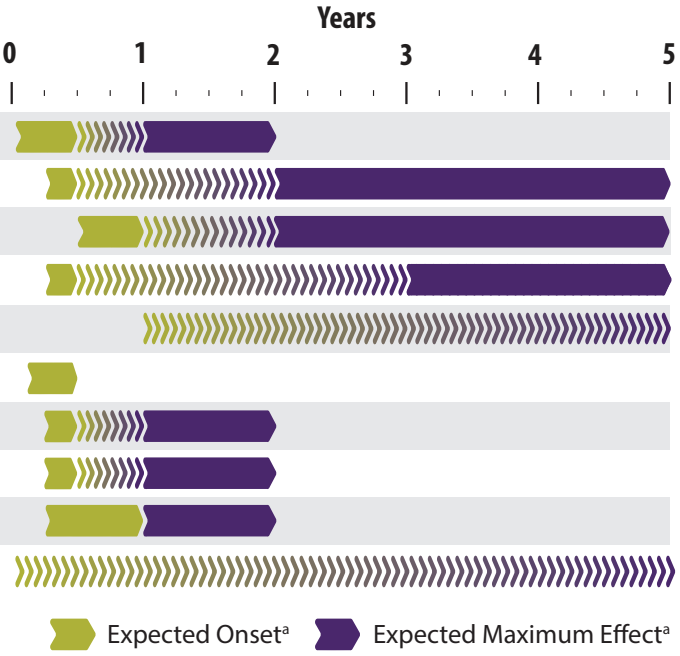
For more information, please visit www.rainbowhealthontario.ca/trans-health-connection

EFFECTS AND EXPECTED TIME COURSE OF A REGIMEN CONSISTING OF TESTOSTERONE

The degree and rate of physical effects is dependent on the dose and route of administration[6], as well as client-specific factors such as age, genetics, body habitus and lifestyle.

Hormone treatment results in both reversible and irreversible masculinization.

PHYSICAL EFFECT	REVERSIBILITY	ONSET
Skin oiliness/acne	Reversible	1 - 6 months
Body fat redistribution	Reversible/Variable	3 - 6 months
Increased muscle mass/strength[b]	Reversible	6 -12 months
Facial/body hair growth	Irreversible	3 - 6 months
Scalp hair loss	Irreversible	variable
Cessation of menses	Reversible	2 - 6 months
Clitoral enlargement	Irreversible	3 - 6 months
Vaginal atrophy	Reversible	3 - 6 months
Deepened voice	Irreversible	3 - 12 months
Infertility	Irreversible	variable



a) Estimates represent published and unpublished clinical observations
b) Significantly dependent on amount of exercise

MONITORING STRATEGIES & DOSE ADJUSTMENTS

As with treatment for trans women, monitoring should be done at 1, 3, 6 and 12 months after starting therapy. This should include a functional inquiry, targeted physical exam, bloodwork, and health promotion/disease prevention counselling as indicated. Titration of doses will occur in the early phases of treatment (i.e. after bloodwork done at 1 or 3 months).

There may be utility varying the timing of bloodwork (ie. trough vs. midcycle) to gather information regarding serum levels throughout the injection cycle. For clients seeking maximum masculinization, the target dose will bring the free and total testosterone levels into the physiologic male range. Dose reduction is warranted if supraphysiologic doses are measured at mid-cycle or trough.

Once menstrual cessation is achieved, any vaginal bleeding without explanation (e.g. missed dose(s) or lowered dose of testosterone) warrants a full workup for endometrial hyperplasia and cancer including endometrial biopsy.

Clinical effects are the goal of therapy, not specific lab values

HORMONE MONITORING SUMMARY FOR TRANS MEN

	BASELINE	MONTH 1	MONTH 3	MONTH 6
EXAM/ INVESTIGATION	Full Physical Exam with PAP if indicated, include height, weight, waist & abdo circ. EKG if over 40, EKG + cardiac stress test if additional risk factors	BP, weight, waist & abdo circ., abdominal exam including liver palpation		BP, weight, waist and abdo circ., abdominal exam including liver palpation
BLOODWORK				
CBC	✓	✓	✓	✓
ALT/AST[a]	✓	✓	✓	✓
Fasting Glucose	✓			✓
LDL/HDL/TG	✓			✓
Testosterone (+/- Estradiol)	✓	✓	✓	✓
LH[b]	✓			
Other	Hep A, B, C Pregancy test (before first injection)			

a) for Ontario providers who may be restricted in ordering OHIP- covered AST levels, ALT alone may be used to screen for liver dysfunction
b) Elevated LH post-gonadectomy may have implications regarding bone mineral density (See Osteoporosis and BMD Screening)