

Female Infertility

Prohibited Substances: Clomiphene, letrozole

1. Introduction

Female infertility may be caused by a range of medical conditions including ovulatory dysfunction, blocked fallopian tubes, endometriosis, and abnormalities of the uterus or cervix. In turn, ovulatory dysfunction can be caused by hypothalamic dysfunction, polycystic ovary syndrome (PCOS), hyperprolactinemia, thyroid dysfunction, or premature ovarian insufficiency (POI).

Female infertility may also be unexplained or due to factors related to the other partner, including male fertility problems or same sex partnerships. These guidelines are also applicable to athletes with diminished ovarian reserve or other scenarios, such as fertility preservation, that may require treatments to enhance oocyte (egg) production for oocyte retrieval.

For PCOS-related infertility treatments specifically, please refer to the [TUE Physician Guidelines for PCOS](#).

2. Diagnosis

a. Medical history

The athlete's *relevant* medical history should be included in the application. Where applicable, details of menstrual cycle regularity, cycle length, previous pregnancy or miscarriage, sexually transmitted disease, gynaecological medical conditions or surgery should be included. Furthermore, history or symptoms of endocrine disturbance such as hirsutism, acne, galactorrhea, hot flushes and sweating, or fatigue should be considered.

The reason for fertility treatment should be included in the medical documentation from the treating specialist. For athletes who require a prohibited treatment for assisted reproductive techniques, such as in vitro fertilization (IVF), the details of the procedure (e.g., physician, location, time) should be included in the TUE application.

b. Physical examination

Findings from a physical examination that are relevant and related to the cause/reason for fertility treatment should be included in the medical documentation from the treating specialist and should be provided in the TUE application.

c. Imaging and other investigations

Imaging and other investigations should be tailored to the individual and may include:

- i) Gynaecological examination, including vaginal ultrasound, is performed for the assessment of uterus and ovaries in relation to menstrual cycle phase and age. Antral follicle count (AFC) is measured, and the development of the preovulatory follicle, with its transformation to corpus luteum, could be monitored using an ultrasound. Furthermore, the specific changes of the endometrium could be determined.
- ii) Hystero-salpingo contrast sonography (HyCoSy) or hysterosalpingography (HSG) are used to evaluate the uterine cavity and for diagnosing tubal occlusion. Importantly, use of an iodine contrast medium such as Lipiodol may also be therapeutic as well as diagnostic in checking tubal patency. However, there is a potential risk of infection by these methods.
- iii) Laparoscopy is the best method for diagnosing tubo-peritoneal pathology related to, for instance, previous infection or endometriosis. However, there is a risk of complications such as damage to vessels, the intestine, and the urinary tract, which is why laparoscopy is rarely done when non-invasive tests can suffice.
- iv) Hysteroscopy can be used as a diagnostic tool and as a therapy, as it can be used therapeutically to remove intrauterine abnormalities such as uterine polyps or fibroids.

d. Laboratory testing

Depending on the underlying cause of female infertility, laboratory tests may be required, including serum analysis of anti-mullerian hormone (AMH), luteinizing hormone (LH), estradiol, thyroid stimulating hormone (TSH and free T4), prolactin, testosterone, and sex hormone-binding globulin (SHBG). Copies of relevant investigations should be included with the application.

3. Treatment

The management of female infertility, including fertility preservation, in athletes should adhere to established international clinical guidelines. Treatment regimens must be individualized, recognizing that access to specific interventions may vary geographically.

Ovulation induction may involve oral or injectable agents such as clomiphene citrate, letrozole, inositol, metformin, or gonadotropins (follicle stimulating hormone (FSH) or human menopausal gonadotrophins) to facilitate in vivo conception.

Controlled ovarian stimulation may be undertaken for oocyte retrieval in IVF or fertility preservation procedures, utilizing agents such as clomiphene, letrozole, metformin, gonadotropins (FSH, LH), and gonadotropin-releasing hormone (GnRH) agonists or antagonists.

In vitro fertilization protocols may differ depending on the patient's predicted ovarian response and clinical objectives.

Each treatment cycle typically lasts two to three weeks, with multiple cycles often required to achieve the desired outcome.

a. Names of prohibited substances

- i) **Letrozole** (aromatase inhibitor) 2.5 mg - 10 mg per day orally for five days (cycle day 3 to 7) is used for ovulation stimulation.
- ii) **Clomiphene** 50 mg - 150 mg orally per day for five days (cycle day 5 to 9) is an alternative for ovulation stimulation.

There is no scientific evidence to support adjuvant androgenic supplements such as testosterone or DHEA in IVF or other female fertility-related treatments.

4. Non-prohibited alternative treatments

- A. **Gonadotropins** (FSH or FSH/LH).
- B. **Gonadotropin-Releasing Hormones (GnRH) Agonists or Antagonists**, used in conjunction with **Gonadotropins** (FSH+/-LH) in controlled ovarian stimulation.
- C. **Human Chorionic Gonadotropin (hCG)** is prohibited at all times in males, but it is not prohibited in females. hCG is given as a single dose for ovulation induction, and also in luteal phase as 1-2 injections.
- D. **Metformin**.
- E. **Inositol** and related products.
- F. **Mitochondrial Replacement Therapy (MRT)** - in certain cases of infertility related to mitochondrial dysfunction, MRT as assisted reproductive treatment may be considered. MRT is a procedure that aims to restore normal cellular function at the embryonic level and does not have the potential to enhance sport performance; therefore, it is not considered a prohibited method.

Note that it is not necessary to try and fail alternatives before using the Prohibited Substance or Prohibited Method. The physician must explain why the treatment chosen was the most appropriate, e.g., based on experience, side-effect profiles or other medical justifications. This includes, where applicable, geographically specific medical practice and the ability to access medication.

5. Consequences to health if treatment is withheld

Significantly decreased quality of life if infertility is unresolved or if fertility is not preserved. If treatment is delayed, age-related underlying causes can exacerbate infertility.

6. Treatment monitoring

Fertility treatment is monitored individually by blood tests for hormone analyses and by ultrasound examinations.

7. TUE duration

The recommended duration of a TUE for female infertility is for the duration of treatment, which may be up to 12 months depending on the outcomes of the treatment.

References

1. Fertility problems: assessment and treatment Clinical Guideline (CG156). Published date: February 2013. Last updated September 2017. National Institute for Health Care Systems. Overview | Fertility problems: assessment and treatment | Guidance | NICE
2. European Society of Human Reproduction and Embryology - [ESHRE Guidelines, Consensus Documents and Recommendations](#)
3. ASRM Practice Guidance: Definition of infertility: a committee opinion (2023) | American Society for Reproductive Medicine | ASRM
4. DeStefano S, Davenport MH Egg freezing: expanding family-planning options for the elite female athlete British Journal of Sports Medicine Published Online First: 03 July 2025. doi: 10.1136/bjsports-2025-109697
5. Broekmans F J, O-232 Highlights of the updated ovarian stimulation guideline, *Human Reproduction*, Volume 40, Issue Supplement_1, June 2025, deaf097.232,