UROLOGICAL SOCIETY OF AUSTRALIA AND NEW ZEALAND

Position Statement

Clomiphene use for male infertility, oligospermia and hypogonadism

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Subject:	Patient Care	**Distribution:**		External	
Authorised by:	Board of Directors	**Approved Date:**	3 Aug 2019	**Review Date:**	Aug 2022

Purpose and Scope

This statement was developed in response to a request from the Department of Health and Human Services (Vic) to the Royal Australasian College of Surgeons (RACS) requesting input into a review on the policy requiring specialists to apply for separate warrants to prescribe clomiphene for male infertility, oligospermia and hypogonadism.

Statement

Clomiphene citrate (commercially available as Clomid® in Australia) is a selective estrogen receptor modulator (SERM) that has been used since the 1960s to facilitate ovulation induction. While clomiphene use has not been formally approved by the Food and Drug Administration (FDA) or European Medicines Agency (EMA) for administration in men, it has been used off-label for many years, to raise luteinizing hormone (LH), follicle stimulating hormone (FSH) and testosterone levels in men with secondary or idiopathic hypogonadism particularly in the setting of male infertility or men who wish to preserve future fertility, and to raise sperm counts in men with a history of infertility or steroid use. Clomiphene binds competitively to the estrogen receptors on the hypothalamus and pituitary gland and thus stimulates the release of LH and FSH, which in turn drives both the steroidogenic and spermatogenic functions of the testes, potentially increasing spermatogenesis and testosterone production.

Published literature has shown that clomiphene use can improve semen parameters, sperm retrieval rate and potentially higher pregnancy rate. However, it may not be effective in patients with an elevated FSH level or in patients lacking a post-treatment FSH surge.

Compared to conventional testosterone replacement therapy for male hypogonadism, clomiphene does not suppress endogenous gonadotropin secretion that is universally seen with (practically) all forms of exogenous testosterone therapy; as a result, clomiphene, unlike exogenous testosterone therapy, should not have a negative effect on spermatogenesis and consequently it does not impact the size of the testes. Due to its mechanism of action of increasing gonadotropin levels, clomiphene is also less effective in raising testosterone levels in men who already have elevated LH levels prior to the initiation of treatment.

The recommended dose of clomiphene is to start at a low dose of 25 to 50 mg every other day and increase to 50 mg daily to optimize clinical outcome. Clomiphene is generally well tolerated with common side effects such as gastrointestinal distress, dizziness, mood swing and gynecomastia.

While clinical studies showed that clomiphene is safe and well tolerated to effectively augment and/or normalise low testosterone and improve male fertility in a carefully selected group of men, caution must be advised in their off-label use. The prescription of clomiphene should be conducted by an experienced andrologist (urologist and endocrinologist) after a careful discussion on various treatment alternatives, the expected benefits and risk profile, as well as the need for regular monitoring.

It is advisable that biochemical proven hypogonadal men with fertility issue should return to (and receive) standard testosterone therapy once his fertility has been addressed.

Longer term and larger multi-centre clinical trials need to be undertaken to establish the long-term efficacy and safety of clomiphene in men.

Roles and responsibilities

- The USANZ Board of Directors is the approval authority for Position Statements and other Policies that relate to patient care.
- The Andrology Speciality Advisory Group (SAG) is responsible for the development and review of position statements and policies that relate to andrology medical matters and for making recommendations to the Board of Directors.

Superseded documents

- None

Revision history

Version	Date	Notes	By
draft	July 2019	Drafted by Eric Chung, Andrology SAG Leader.	Andrology SAG
1.0	3 Aug 2019	Approved.	Board of Directors

Review date

This position statement will be reviewed every 3 years by the Speciality Advisory Group and the Board of Directors. The next review date is August 2012.

Contact

USANZ President
Email: president@usanz.org.au