Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: *Polycystic Ovarian Syndrome*
-February 2017-

Background:
Polycystic Ovarian Syndrome (PCOS) is a metabolic disorder affecting between 5 and 10 percent of women of childbearing age[1]. Ovulatory dysfunction, hyperandrogenism and polycystic ovaries are hallmark symptoms of PCOS. Additionally, many women affected also exhibit cutaneous manifestations (acne), hyperinsulinemia, infertility, hirsutism, dyslipidemia, obstructive sleep apnea, depression and anxiety[2-5]. The National Pharmacy & Therapeutics Committee (NPTC) reviewed available therapies for PCOS. As a result of the clinical review and NPTC discussion, **oral medroxyprogesterone was added** to the National Core Formulary (NCF).

Discussion:
Determining an appropriate treatment plan for PCOS ultimately depends on the patient's goal. Patients who present with androgenic symptoms such as acne, hirsutism, and amenorrhea or oligomenorrhea may benefit from combined hormonal contraceptives (CHCs). The CHCs are considered first-line agents for PCOS management in patients not intending to conceive[2]. Combined hormonal contraceptives offer menstrual cycle regulation and endometrial protection as well as benefits against clinical and biochemical hyperandrogenism. No single formulation is recommended over another, however regimens with lower estrogen/progestin doses may confer benefit over other regimens. Estrogen increases the risk of thromboembolism (VTE), especially in overweight women. Patients at risk for adverse effect due to estrogen (e.g., history of VTE, hypertension, smokers) should have "progestin-only" alternatives considered. Metformin may be used as second-line therapy (after CHCs) for menstrual cycle regulation. Cosmetic procedures such as blended electrolysis and photoepilation are sometimes effective for mild to moderate hirsutism. More severe cases of hirsutism may respond to spironolactone, but should be used cautiously due to adverse effects[2, 6].

Many women with PCOS develop insulin resistance particularly those who are inactive and/or obese, which can lead to Type 2 diabetes over time. Additionally, because of the increased likelihood of metabolic disorders, women with PCOS should be screened, treated, or appropriately referred if certain comorbidities (i.e., Type 2 diabetes, impaired glucose tolerance, hypertension, dyslipidemia, obesity, mood disorders, obstructive sleep apnea) are present. Weight loss using exercise and a calorie-restricted diet is recommended to reduce cardiovascular risks for obese women with PCOS, as well as those with Type 2 diabetes or impaired glucose tolerance (IGT). Metformin is recommended for PCOS patients diagnosed with IGT or Type 2 diabetes who are inadequately managed by diet and exercise. Metformin has been demonstrated to have no effect on cutaneous manifestations such as acne and has not been shown to improve pregnancy outcomes[2, 4].

The 2013 Endocrine Society guidelines for PCOS recommend clomiphene or a comparable estrogen modulator (e.g., letrozole) as first-line therapy for ovulation induction in women

experiencing infertility[2]. A recent meta-analysis involving nine randomized controlled trials comparing letrozole and clomiphene (with or without adjuncts in 1 or both arms) followed by timed intercourse found the birth rate higher in the letrozole group (OR 1.64; 95% CI: 1.32 - 2.04, n=1783, I^2=3%)[7]. The American College of Gynecology considers exogenous gonadotropins as a second-line therapy for ovulation induction[8,9].

Key points:

- CHCs are first-line agents for PCOS management to address both menstrual abnormalities and hyperandrogenism (acne/hirsutism). Progestin-only contraceptives or metformin may be considered as second-line therapies
- Weight loss is recommended as a first-line therapy for obese women with PCOS
- Clomiphene or a comparable estrogen modulator (e.g., letrozole) is recommended as first-line for ovulatory dysfunction resulting in infertility
- Metformin is recommended for women with PCOS diagnosed with Type 2 diabetes or OGT who fail diet and exercise
- Antiandrogens (spironolactone, finasteride, etc.) are suggested only in managing severe hirsutism or when CHCs are contraindicated

Findings:

Polycystic Ovary Syndrome is a common condition in women, often accompanied by a multitude of metabolic comorbidities and infertility. Review of medications on the NCF show there are sufficient pharmacotherapies to adequately address patients with PCOS and associated complications. Medroxyprogesterone is currently on the NCF as injection only to provide extended duration contraception**. The NPTC added the oral formulation of medroxyprogesterone** to offer providers an option for managing secondary physiologic amenorrhea and other conditions for which the injection may not be suitable.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the NPTC website.

References:

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