INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: *OTC Norgestrel 0.075mg (Opill®)*
-August 2023-

Background:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) provided a drug review of Over-The-Counter (OTC) norgestrel 0.075mg tablets (Opill®) at the 2023 Summer meeting. The NPTC last reviewed contraception in 2016 and then, more specifically, long-acting reversible contraceptives in 2021. At present, the IHS National Core Formulary (NCF) includes the following contraceptives; (1) ethinyl estradiol/etonogestrel vaginal ring; (2) ethinyl estradiol/etonogestrel transdermal; (3) etonogestrel, implant; (4) intrauterine device, copper; (5) intrauterine device, levonorgestrel; (6) levonorgestrel (Plan B One-Step®); (7) medroxyprogesterone acetate, injection; (8) medroxyprogesterone, oral tablet; (9) oral contraceptive pill, extended cycle; (10) oral contraceptive pill, monophasic: 20mcg EE (low); (11) oral contraceptive pill, monophasic: 30-35mcg EE (medium); (12) oral contraceptive pill, progestin only; (13) oral contraceptive pill, triphasic and (14) ulipristal.[1]

Following review and analysis, the NPTC voted to (1) **ADD norgestrel 0.075mg tablets (Opill®)** to the NCF and (2) to **MODIFY language to the currently-named "Progestin-only pills, any product"** on the NCF **to now include "Progestin-only pills, any *prescription* product"**.

Discussion:

Unintended pregnancies make up nearly one-half of the 6.1 million annual pregnancies in the United States, creating a major public health issue effecting mothers, families, providers and society.[2] In pregnant adolescents aged 15-17 years, nearly three-quarters (72%) of pregnancies are unintended; furthermore, rates of unintended pregnancies are 5 times higher in patients living in poverty compared to those in higher socioeconomic living environments.[3] Barriers to accessing available and affordable contraception contribute greatly to unintended pregnancies. Common barriers include (but are not limited to) lack of transportation to healthcare visits; lack of health insurance; lack of time off from work or school; no relationship with a healthcare provider; and healthcare provider shortages. Major medical associations, including the American Medical Association and American College of Obstetricians and Gynecologists have long supported the OTC availability of a progestin-only oral contraceptive pill (POP) in part due to their acceptable safety profiles.[4-6]

Opill® (norgestrel 0.075mg tablets) is a progestin-only oral contraceptive pill (POP) which contains no estrogen. POPs are understood to alter cervical mucus and to suppress ovulation.[7] POPs are highly effective at preventing pregnancy with failure rates as low as 7-9% in the general population. Conversely, based on initial clinical trial data, the "perfect use" effectiveness rate (tablets administered same time, every day) for norgestrel is ~98%. Findings from the Opill ACCESS Use Study (required prior to OTC status approval) reported a Pearl Index (i.e., failure rate) of 4.4 (95% CI; 1.9-8.8) however clinical reviewers from the US Food and Drug Administration (FDA) indicated that failure rates with real-world use of Opill® would likely be closer to 7%.[8]

Norgestrel was originally approved in the US in 1973 under the brand name "Ovrette". It changed ownership several times in its five decades in the US market and notably in 2005, sales of Ovrette were temporarily discontinued. The FDA has clarified that Ovrette was not withdrawn for reasons of patient safety or effectiveness. Simply put, there were other similar, competing medications that made Ovrette unprofitable at that time.[9] In 2017, a supplemental new drug application was submitted to the FDA to change the brand name to Opill®, followed by an FDA "Prescription-to-Nonprescription" Switch request in June 2022. An FDA Public Advisory Committee voted unanimously (14-0) in May 2023 that the potential benefits and availability of an OTC norgestrel 0.075mg tablet outweighed the potential risks. Finally, on July 13, 2023, the FDA approved OTC Opill® with no age restrictions for use.[10]

The absence of estrogen in POPs improves its general safety profile by mitigating untoward medication events including cardiovascular and thromboembolic complications, relative to combination estrogen/progesterone contraceptives. Opill® is packaged in 28-day blister packs with no pill-free days or placebo tablets between monthly packs. As such, monthly menstrual cycles are not expected.[8] Commonly reported adverse events for Opill® include abnormal vaginal bleeding (21%), headache, dizziness, nausea, increased appetite, abdominal pain and cramps or bloating. Serious drug-drug interactions include those which induce hepatic enzymes (e.g., anti-epileptics, rifampin, St. John's Wort) but over 100 medications are listed with the potential to interact with Opill®.

Limitations for use (warnings and contraindications) include known or suspected pregnancy, known or suspected breast cancer, undiagnosed abnormal genital bleeding, concomitant use of other contraceptives (excluding barrier methods like condoms), hypersensitivity to norgestrel and excipients, benign or malignant liver tumors or active liver disease. Notably, Opill® is not indicated for use as an emergency contraceptive or for prevention of transmission of sexually transmitted diseases (STD) or the human immunodeficiency virus.[12]

Risks with the OTC availability of Opill® were also evaluated by the FDA and found to be qualitatively and quantitatively similar to those risks inherent to prescription norgestrel use. Possible unintended harms of OTC Opill® (via the absence of healthcare provider supervision) were profiled by FDA reviewers and included (1) the potential worsening of progestin-related cancers, (2) increased incidence of STDs, and (3) delayed medical evaluation of conditions manifesting as vaginal bleeding. Counterarguments to these potential scenarios are detailed in the FDA's Decisional Memorandum. The FDA ultimately determined that the benefit-to-risk ratio to the individual consumer remained favorable for Opill® availability.[8]

Findings:

The recent FDA re-evaluation, approval and availability of Opill® as a non-prescription product offers American Indian/Alaskan Native persons a safe and effective contraceptive tablet for those who may encounter barriers to accessing prescription contraceptives or otherwise have limited or no access to birth control or family planning methods.

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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