

PHARMACIST CE:

A Review of Pathophysiology and Treatment of Polycystic Ovary Syndrome (PCOS)

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Polycystic ovary syndrome, or PCOS, is a condition characterized by hormonal imbalances in people of reproductive age with ovaries. This condition is characterized by irregular or extended menstruation, high levels of androgens, and/or cysts in the ovaries that prevent regular function. Specifically, the most salient clinical feature of PCOS is the impact on menstruation, including oligomenorrhea, amenorrhea, and menorrhagia.¹ Additionally, infertility is a hallmark characteristic of the condition, related to the presence of cysts or enlarged ovaries that may preclude proper ovulation. Other clinical characteristics of PCOS include skin disorders, including hirsutism, acne, and, in a smaller proportion of people, androgenic alopecia. Insulin resistance is present in many people with PCOS, which is also associated with metabolic syndrome and obesity. While PCOS has traditionally been described as a condition that impacts women, it is important to note that PCOS can impact cisgender women, transgender men, and nonbinary individuals. Therefore, we will use the phrase “individuals with PCOS” or “patients with PCOS” throughout the article. It is estimated that 6-20% of people of reproductive age are affected by PCOS.² PCOS is an endocrine disorder with androgenic, menstrual, fertility-related, and metabolic effects on the human body. While PCOS is a condition that impacts many people, pharmacists may lack adequate knowledge of how to support treatment decisions for patients with PCOS, given the wide range of clinical symptoms and treatment options. This review will assess available information regarding treatment of PCOS and compile it into one resource for pharmacists to use when caring for patients with PCOS.

CE FOR PHARMACISTS

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Learning Objectives

- Recognize the most common characteristics and presentation of PCOS.
- Describe the hormonal imbalances involved in the pathophysiology of PCOS.
- Define commonly used terms that relate to ovulatory and menstrual dysfunction in patients with PCOS.
- Compare and contrast the most common manifestations of hyperandrogenism, oligomenorrhea, metabolic disorders, and fertility challenges in PCOS.
- Identify preferred treatment options for PCOS in relation to hyperandrogenism, oligomenorrhea, metabolic changes, and fertility.

Pathophysiology

There are several hypotheses that may explain the pathophysiology leading to PCOS, including functional ovarian hyperandrogenism (FOH), the luteinizing hormone (LH) hypothesis, and the insulin theory. The FOH theory points to the ovary as the source of dysregulation, which is independent of cysts in the ovaries or an elevation in LH. In patients with PCOS, FOH occurs on a cellular level in the thecal cells of the ovary, where the activity level of certain oxidative enzymes is higher, resulting in the increased production of androgens in the ovary. Most of the time, hyperandrogenism is a result of ovary androgen production; however, in some cases, adrenal androgen production can also cause this to occur. Regardless of the source of hyperandrogenism, androgen excess is present in 60-80% of patients with PCOS. Additionally, elevated testosterone, LH, and LH-to-FSH (follicle stimulating hormone) ratio are present in many people with PCOS, which has led some researchers to hypothesize that an increased amount of circulating luteinizing hormone is responsible for PCOS.³ Hyperinsulinemia, resulting from insulin resistance, can

TABLE 1. Acronyms

BMI	Body mass index
COC	Combined oral contraceptive
FOH	Functional ovarian hyperandrogenism
FSH	Follicle stimulating hormone
GLP-1	Glucagon-like peptide 1
LH	Luteinizing hormone
OSA	Obstructive sleep apnea
PCOS	Polycystic ovary syndrome
T2DM	Type 2 diabetes mellitus

reduce the amount of sex hormone binding globulin and increase testosterone in circulation. Insulin along with excess LH work together to increase the production of androgens. Ultimately, ovarian follicle development is interrupted as result of hyperinsulinemia and hyperandrogenism, resulting in an anovulatory state.⁴ Based on the pathophysiology, there are 3 main diagnostic criteria: evidence of

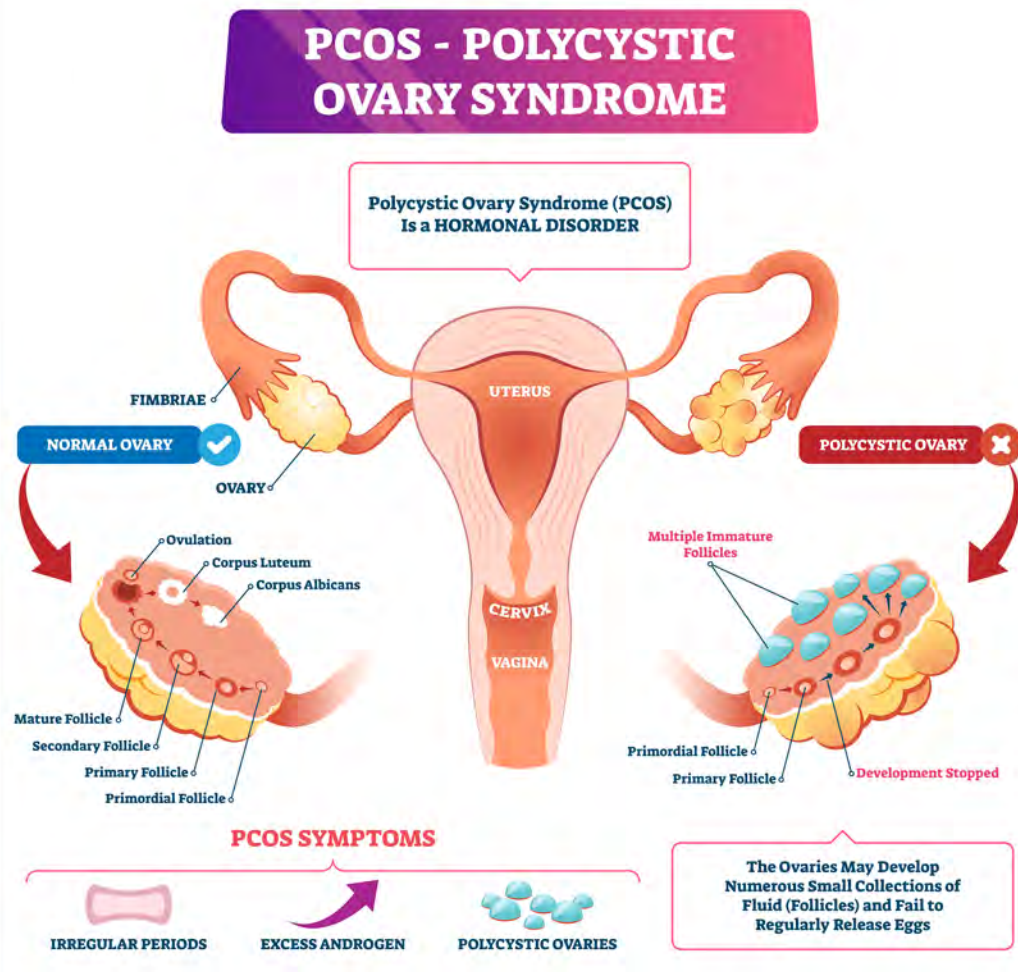
hyperandrogenism, ovulatory dysfunction, and polycystic ovaries. A diagnosis of PCOS is typically made when at least 2 of these are present and other related disorders are excluded. The pharmacotherapy treatment for this condition is centered around targeting the clinical manifestations that result from these hormonal imbalances.

Clinical Presentation

Metabolic

PCOS can present through a multitude of signs and symptoms, one of which is the presence of metabolic changes that could progress to metabolic syndrome. Metabolic syndrome is a cluster of characteristics that increases a patient's risk of developing cardiovascular disease, type 2 diabetes mellitus (T2DM), and stroke.⁵ Characteristics may include waist circumference of 102 cm or more in men or 88 cm in women, triglyceride levels of 150 mg/dL or greater, high density lipoprotein cholesterol levels less than 40 mg/dL in men or 50 mg/dL in women, blood pressure of 130/85 mm Hg or more, and fasting glucose of 100 mg/dL or more.⁵ Patients with PCOS are at a twofold increased risk of coronary heart disease or stroke compared to those without PCOS.⁶ In addition, they are also at a fourfold increased risk of developing T2DM. The number of women presenting with metabolic syndrome was significantly higher among those with PCOS compared to those without PCOS.⁶ Therefore, guidelines recommend that individuals with PCOS are screened for these metabolic changes.⁷ Metabolic differences are more prevalent in patients who are overweight and obese but have also been identified in nearly 40% of nonobese patients with PCOS.⁸ Obesity is not a diagnostic factor in PCOS but may affect the severity of metabolic and reproductive features of this disease state.⁹

A defining feature of metabolic syndrome in PCOS is insulin resistance, which can lead to T2DM. In patients who have T2DM without PCOS, this typically presents with impaired fasting glucose and is a result of insulin-mediated hepatic glucose production. In contrast, the hyperglycemia tends to be postprandial in PCOS due to impaired peripheral insulin-mediated glucose uptake. Therefore, this is more likely to present as impaired glucose tolerance rather than impaired fasting glucose.⁹ A



2018 study found that patients with PCOS had a 25% prevalence of impaired glucose tolerance while patients in the control group had 9.2% prevalence.¹⁰ Insulin resistance in individuals with PCOS predisposes them to long-term health conditions such as T2DM.¹¹ A meta-analysis found higher rates of diabetes mellitus in patients with PCOS.¹²

Given the metabolic changes that occur with PCOS, these individuals are also at an increased risk of cardiovascular disease. A 2020 meta-analysis found increased rates of hypertension and total cholesterol, no difference in low density lipoprotein and triglycerides, and decreased high density lipoprotein in those with PCOS compared to those without PCOS.¹² For non-fatal cardiovascular events, no difference was identified in coronary events, but a higher rate of cerebrovascular events was found in patients with PCOS. No difference was identified for fatal cardiovascular events.¹² The increased risk of cerebrovascular events, hypertension, and dyslipidemia in PCOS patients prompts screening and

identification for these concomitant disease states to ensure appropriate treatment.

In addition to T2DM and cardiovascular disease, patients with PCOS represent a population at higher risk for sleep disordered breathing and hepatic steatosis. Obstructive sleep apnea (OSA) as well as PCOS is commonly associated with hypertension, diabetes mellitus, and coronary artery disease.¹⁰ Patients with PCOS have a prevalence of OSA of 32% compared to 2% to 5% of adults with a uterus without PCOS.⁹ Hepatic steatosis—more specifically nonalcoholic fatty liver disease—has a prevalence of 25% in the general population, while in PCOS patients its prevalence is 67%.¹³

Ovulatory and Menstrual Dysfunction

PCOS is often diagnosed using 3 different diagnostic criteria, one of which is ovulatory dysfunction.¹⁴ Ovulatory dysfunction is commonly accompanied by menstrual dysfunction, including oligomenorrhea, amenorrhea, and menorrhagia. Oligomenorrhea refers to

a menstrual cycle that lasts more than 35 days in length, correlating to 10 or fewer cycles per year. However, some prefer to use a more rigorous definition of fewer than 8 cycles per year (cycle lasting more than 45 days). Amenorrhea, on the other hand, refers to the absence of monthly menstrual bleeding.¹⁵ Menorrhagia is defined as menstrual bleeding lasting longer than 7 days, often involving a very heavy flow.¹⁶

Menstrual dysfunction is a very common feature of PCOS, with 75% to 85% of patients experiencing menstrual dysfunction in some capacity.¹⁷ Despite menstrual dysfunction commonly occurring with ovulatory dysfunction, ovulatory dysfunction can present without menstrual dysfunction. It is important to note that when using ovulatory dysfunction as a diagnostic criterion for PCOS, it is not appropriate to assess until at least 1 year after menarche, or longer.¹⁸ Prior to this point in time, irregular menstrual cycles are a normal part of the transition in puberty.

With all of this in mind, it is important to recognize the relevant health implications of menstrual and ovulatory dysfunction in PCOS, including an increased risk of developing endometrial hyperplasia and carcinoma as well as fertility challenges.^{14,19} Endometrial hyperplasia is caused by unopposed and prolonged estrogen exposure on the endometrium, which is ultimately due to anovulation.²⁰ Thus, an increased malignancy risk is found in patients with PCOS. Additionally, ovulatory dysfunction may lead to anovulatory infertility, resulting in difficulties with conception.¹⁴ Infertility caused by PCOS accounts for 27% of all cases of infertility globally.⁷ This may even be the first sign that an individual has PCOS. For those who wish to conceive naturally, this may be viewed as a despairing consequence of the condition. Of note, reproductive challenges seem to be limited to difficulties in conception; once conception is achieved, individuals with PCOS have not been found to have any significant increased risk of miscarriages or early pregnancy loss.¹⁴ However, pregnant individuals with PCOS have been found to be at an increased risk of developing obstetric complications, including preeclampsia, gestational diabetes, and macrosomia.

Androgenic

An additional characteristic of PCOS includes hypersecretion of androgens, or hyperandrogenism.²¹ Physiologic manifestations of high testosterone levels commonly include hirsutism, acne, and occasionally male-patterned balding. Hirsutism can be measured using tools such as the Ferriman-Gallwey score. The Ferriman-Gallwey scoring tool ranks the degree of hair growth in nine body areas prone to hair growth upon androgen exposure. The ranking is on a scale of 0 to 4 in each area, where 0 represents no or minimal hair. A total sum of eight or more qualifies as generalized hirsutism among black and white women in the United States and United Kingdom.⁷ Of note, Ferriman-Gallwey scores must be considered within the context of patient ethnicity since hair growth differs across ethnic backgrounds and cut-off points can differ (≥ 9 to 10 in Mediterranean, Hispanic, and Middle Eastern Women; ≥ 6 in South American women; range for Asian women from ≥ 2 to for Han Chinese women to ≥ 7 for Southern Chinese women).²²

Psychological

One study found that patients with PCOS had a 26-38% and 20-39% increased incidence of depression and anxiety, respectively, when compared to two different sets of controls.²³ Additionally, this study found a 37-54% increased incidence of eating disorders in patients with PCOS compared to matched controls.²³ There is likely an array of contributing factors, but the psychological stress that comes with the physiological and societal impacts of PCOS, such as hirsutism, obesity, and infertility, is a major consideration. Therefore, screening for depression and anxiety among patients with PCOS should be strongly considered.

Treatment

Metabolic

American College of Obstetricians and Gynecologists Practice Bulletin Guideline recommendations relating to metabolic syndromes associated with PCOS are divided into level A and level B.¹ Level A recommendations are consistent and evidence based, while level B recommendations are based on limited or inconsistent evidence. The guidelines recommend increasing exercise combined

with dietary changes to reduce the risk of diabetes, and the use of insulin-sensitizing agents for improved glucose tolerance (Level A). They also recommend screening women with a PCOS diagnosis for impaired glucose tolerance and cardiovascular risk (Level B). Lifestyle management of PCOS includes dietary changes, physical activity, and behavioral strategies to reduce weight. These strategies decrease the risk of insulin resistance, therefore preventing progression to diabetes mellitus and reducing the risk of cardiovascular disease.

When lifestyle modifications alone are not beneficial, the addition of insulin-sensitizing agents may be considered. The most commonly used insulin-sensitizing agent is metformin, a member of the biguanide drug class. Metformin's mechanism of action is to inhibit hepatic glucose production, increase glucose uptake, and therefore increase insulin sensitivity. The 2018 International Evidence-Based Guideline for the Assessment and Management of PCOS recommends the use of metformin in addition to lifestyle changes for management of weight and metabolic outcomes.⁷ Side effects of metformin include nausea, vomiting, diarrhea, and abdominal bloating. Pharmacists can help patients with PCOS manage these symptoms through education and slow titration of the dosage.

Glucagon-like peptide 1 (GLP-1) receptor agonists have also shown benefit in patients with PCOS. A 2019 meta-analysis found patients who take GLP-1 receptor agonists to have improved insulin sensitivity, reduced body mass index (BMI), and decreased abdominal girth when compared to patients taking metformin. GLP-1 receptor agonists did not have an effect on triglycerides, total cholesterol, or blood pressure.²⁴ In addition, patients reported higher rates of nausea and headache when taking GLP-1 receptor agonists compared to metformin. This class of medications may be a good option in patients with PCOS who are obese and also have insulin resistance. However, data is still fairly limited in evaluating the effects of GLP-1 agonists in patients with PCOS.

Pioglitazone, which is a thiazolidinedione, may be beneficial in PCOS by reducing fasting serum glucose. This class of medications works by increasing peripheral glucose uptake

and regulating insulin action. When compared to metformin, pioglitazone as monotherapy resulted in increased BMI and increased triglycerides.¹¹ A 2021 meta-analysis found a combination of metformin and thiazolidinediones to be more efficacious to lower fasting glucose than metformin alone.¹³ Furthermore, they found gastrointestinal side effects and peripheral edema to be more frequent in thiazolidinediones compared to metformin. Notably, the use of metformin with thiazolidinediones was more efficacious than metformin alone to reduce triglycerides and total cholesterol.¹³ When selecting a drug to target insulin resistance, the impact on weight, glucose, and lipids should be considered.

Due to dyslipidemia being a strong predictor of cardiovascular risk, patients with PCOS may benefit from use of a statin. Statins, with atorvastatin being the primary medication studied, showed reduced insulin resistance and inflammatory markers in patients with PCOS compared to placebo.¹¹ A diagnosis of PCOS alone does not necessarily warrant statin treatment, as it is not currently known whether statin initiation in young individuals with PCOS prevents cardiovascular events in the long-term.

The clinical use of orlistat, a lipase inhibitor used for weight loss, remains controversial. Although it has been associated with improvements in lipid profiles, weight, BMI, and waist circumference, it comes with significant side effects, including diarrhea, abdominal pain, flatulence, and fatty stool. Bariatric surgery as a method to decrease metabolic abnormalities may be indicated in obese patients with a BMI of 40 kg/m² or more or BMI greater than 35 kg/m² with comorbidities.¹¹

Ovulatory and Menstrual Dysfunction

For the treatment of menstrual dysfunction in patients with PCOS who are not looking to become pregnant, combined oral contraceptives are recommended as first-line therapy.²⁰ Oral contraceptives work by helping to regulate the menstrual cycle and can also help to reduce the risk of endometrial hyperplasia in PCOS, thereby reducing the risk of endometrial cancer. For those who do not tolerate combined oral contraceptives, there are a few other

TABLE 2. Clinical Guidelines for PCOS

<i>Organization</i>	<i>Year Published</i>	<i>Title</i>
American College of Obstetricians and Gynecologists ¹	2018	Polycystic Ovary Syndrome: ACOG Practice Bulletin, Number 194
American Society for Reproductive Medicine ⁷	2018	Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome
The Endocrine Society ²¹	2013	Diagnosis and Treatment of Polycystic Ovary Syndrome: An Endocrine Society Clinical Practice Guideline

options to be considered, including non-oral combined hormonal contraceptives or progestin-only contraceptives.¹⁴ Based on use in the general population, it is plausible to consider use of a contraceptive patch or vaginal ring in those who are unable to tolerate oral contraceptives.²⁵ Before selecting a patch, it is important to note that its effectiveness for pregnancy prevention may be decreased in patients who weigh more than 198 pounds.²⁶ Progestin-only contraceptives may be considered in patients where estrogen is contraindicated.²⁵ Options for progestin-only contraceptives include long-acting injectables like depot medroxyprogesterone, an etonogestrel-containing implant, or an intrauterine device. Progestin-only options prevent pregnancy and reduce risk of endometrial hyperplasia, but there is less data supporting their usefulness and effectiveness specifically in individuals with PCOS compared to combined oral contraceptives.

For any of the previously listed treatment options, it is important to first screen whether a patient has any contraindications to using hormonal contraception. Then, careful evaluation of the side effects and how these may impact other clinical features associated with PCOS should be considered.²⁵ For example, the depot medroxyprogesterone acetate (DMPA) injection is known to cause weight gain and insulin resistance, and the etonogestrel-containing implant is associated with more irregular bleeding. Through shared decision-making, the provider and patient can work to find the most suitable regimen.

For patients who wish to conceive children naturally, treatment of the subfertility/infertility caused by PCOS may be pursued. This may be done by ovulation

induction through lifestyle modification and various possible pharmacological and non-pharmacological methods. Obesity is a common concomitant condition in patients with PCOS and can independently impact fertility. For patients with obesity and PCOS, the first intervention to be made in treating infertility is body weight reduction through lifestyle modifications in diet and exercise. Weight loss can aid in regulating ovulation and thus increasing the likelihood of conception.^{1,7,21}

Pharmacologic options for ovulation induction include letrozole, clomiphene citrate, and clomiphene citrate plus metformin. Letrozole is an aromatase inhibitor, which promotes the secretion of FSH and has the resulting effect of facilitating the process of ovulation. Clomiphene citrate is a selective estrogen receptor modulator, which is used to stimulate final maturation of follicles and increases the probability of ovulation. Metformin works in conjunction with clomiphene citrate to further promote ovulation.

While clomiphene citrate has traditionally been used first-line, recent randomized controlled trials and meta-analyses actually suggest that letrozole is more effective for ovulation induction and live birth rates.²⁷ In a Cochrane Review, among 2954 patients in 13 studies, live birth rates were significantly higher among those who used letrozole compared to clomiphene citrate with or without adjuncts (OR 1.68, 95% CI 1.42 to 1.99).²⁷ Clomiphene citrate may still be used first line over letrozole if cost is a concern as clomiphene is less expensive. Combination of clomiphene citrate plus metformin can be considered if patients do not have success

TABLE 3. Summary of medications used for PCOS

<i>Drug</i>	<i>Considerations when initiating and monitoring treatment</i>	<i>Weight Loss</i>	<i>Insulin Resistance</i>	<i>Endometrial Protection</i>	<i>Menstrual Dysfunction</i>	<i>Infertility</i>	<i>Hirsutism/Acne</i>
Metformin	May cause gastrointestinal side effects; start at low dose and titrate slowly		✓			✓	
Pioglitazone	May increase weight due to peripheral edema		✓				
GLP-1 agonist	May cause gastrointestinal side effects; start at low dose and titrate slowly	✓	✓				
Orlistat	May help with weight loss but associated with many side effects	✓					
Combined oral contraceptive	Consider selecting COC containing drospirenone or norgestimate when being used for hirsutism/acne. Use caution or avoid COC with higher levels of ethinyl estradiol (35 mcg) due to increased risk for thromboembolism.			✓	✓		✓
Non-oral combined contraceptive (patch, ring)	Avoid patch in patients who weigh more than 198 lbs due to decreased efficacy.			✓	✓		
Progestin-only contraceptives	May be considered but less studied for purposes of menstrual cycle regulation in patients with PCOS.			✓	✓		
Letrozole	Important to educate patient on timing of initiation in relation to menses or progestin-induced bleed					✓	
Clomiphene citrate	Important to educate patient on timing of initiation in relation to menses or progestin-induced bleed					✓	
Spironolactone	Teratogenic; some form of contraception recommended in patients at risk of pregnancy						✓
Eflornithine	Hair removal techniques should be continued, and cream can be applied after at least 5 minutes after hair removal						✓

with clomiphene citrate alone. Of note, pharmacists can play an essential role in providing education to patients about how to take these oral medications for ovulation induction. The timing of dosing these medications is important in relation to the patient's menses or progestin-induced bleed. Additionally, intercourse should be timed for when it is expected that ovulation will occur, which can be estimated based on when the medication was taken.

Second-line treatments for anovulatory infertility are low-dose follicle-stimulating hormone stimulation and the non-pharmacological procedures of ovarian electrocautery.¹ Low-dose FSH stimulation may be indicated in patients who fail first-line treatments; however, it is not

preferred due to the possible need to turn to in-vitro fertilization, a very costly process with mediocre success rates, later on in the treatment. Ovarian electrocautery is not fully understood and has the risk of physical injury, but some evidence points towards its effectiveness in decreasing testosterone levels and in patients who are resistant to clomiphene citrate.

Androgenic

Use of combined oral contraceptives can be used to target cutaneous symptoms such as hirsutism and acne. Oral contraceptives are a first-line recommendation for patients who are not planning to become pregnant and desire management of aforementioned PCOS symptoms. When selecting a COC,

special consideration should be taken in the progestin component. Progestins with no androgenic activity (drospirenone) or low androgenic activity (norgestimate) may be preferred given the pathophysiology of acne and hirsutism in patients with PCOS. If the response to COC is inadequate, use of an antiandrogen such as spironolactone can be initiated as monotherapy or in combination with a COC. If used as monotherapy, it is important to note that spironolactone is teratogenic and other methods to prevent pregnancy should be recommended. Before initiating a COC, patients should be screened for risk factors that may increase their risk of venous thromboembolism.²⁸

Non-pharmacologic options such as waxing, electrolysis, or shaving could

also be considered to manage hirsutism. Plucking, or epilation, should be avoided as it can cause scarring and tissue damage, especially to those with more pigmented skin. While many methods are advertised as “permanent,” these follicles may experience regrowth due to continued stimulation via the patient’s androgens. Suppression of androgens through pharmacologic means may be helpful in these situations. Finally, topical agents such as eflornithine cream can be used to facilitate more rapid and sustained hair loss in combination with laser hair removal. Eflornithine is a hair growth inhibitor and will not remove existing hair if used as monotherapy.²²

Psychological

There are currently no specific recommendations regarding pharmacotherapy for treatment of mental health disorders specifically in patients with PCOS. Patients with PCOS should be screened for depression, anxiety, and other mental health conditions as necessary and then treated according to guidelines for the general population.²⁹

Role of the Pharmacist

Pharmacists are the most accessible healthcare providers in the community setting. As such, patients commonly ask pharmacists for assistance in treating a wide array of symptoms and ailments. When pharmacists are approached by a patient complaining of excessive hair growth, oily skin, balding, acne, or menstrual abnormalities, for example, pharmacists can make an impact by assisting patients in the next steps for managing these symptoms. This could include referring to physicians for further workup, recommending non-pharmacologic options to treat their symptoms, or recommending appropriate prescription treatment to their provider.

Pharmacists are important practitioners in ensuring patients are adequately educated about the correct use and expected outcomes of pharmacotherapy for PCOS. Pharmacists are well trained to elicit information from patients to guide their counseling through the use of frameworks like the Three Prime Question approach developed by the Indian Health Service.³⁰ First, pharmacists can identify individuals with PCOS during medication consultation by using the first prime question: “What

are you using this medication for?” It is important for pharmacists to recognize that certain medications, such as metformin or pioglitazone, may be prescribed for PCOS, not for diabetes mellitus. When conducting patient education, including key components—such as time to benefit, realistic goal setting, and establishing expectations—is crucial for pharmacists, to help ensure optimized treatment for patients with PCOS. Pharmacists can help to recognize potential gaps in treatment, as there are many different clinical features of PCOS and subsequent long-term consequences. Pharmacists should then be able to recommend treatment for specific manifestations of PCOS, like hyperandrogenism, metabolic changes, oligomenorrhea, or infertility. Lastly, community pharmacists are uniquely positioned in the community to monitor for efficacy, safety, and tolerability of pharmacotherapy when patients pick up refills of medications. A list of the most recent guidelines can be found in table 2, and a summary of which treatment options can be used for which clinical manifestations can be found in Table 3.

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References

1. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Gynecology. ACOG Practice Bulletin No. 194: Polycystic ovary syndrome [published correction appears in *Obstet Gynecol*. 2020 Sep;136(3):638]. *Obstet Gynecol*. 2018;131(6):e157-e171. doi:10.1097/AOG.0000000000002656
2. Witchel SF, Oberfield SE, Peña AS. Polycystic ovary syndrome: pathophysiology, presentation, and treatment with emphasis on adolescent girls. *J Endocr*

- Soc*. 2019;3(8):1545-1573. doi:10.1210/js.2019-00078
3. Hunter MH, Sterrett JJ. Polycystic ovary syndrome: it's not just infertility. *Am Fam Physician*. 2000;62(5):1079-1090.
4. Dumitrescu R, Mehedintu C, Briceag I, Purcarea VL, Hudita D. The polycystic ovary syndrome: an update on metabolic and hormonal mechanisms. *J Med Life*. 2015;8(2):142-145.
5. Karoli R, Fatima J, Chandra A, Gupta U, Islam FU, Singh G. Prevalence of hepatic steatosis in women with polycystic ovary syndrome. *J Hum Reprod Sci*. 2013;6(1):9-14. doi:10.4103/0974-1208.112370
6. Lim SS, Kakoly NS, Tan JWJ, et al. Metabolic syndrome in polycystic ovary syndrome: a systematic review, meta-analysis and meta-regression. *Obes Rev*. 2019;20(2):339-352. doi:10.1111/obr.12762
7. Teede HJ, Misso ML, Costello MF, et al. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Hum Reprod*. 2018;33(9):1602-1618. doi:10.1093/humrep/dey256
8. Romualdi D, Versace V, Lanzone A. What is new in the landscape of insulin-sensitizing agents for polycystic ovary syndrome treatment. *Ther Adv Reprod Health*. 2020;14:2633494120908709. doi:10.1177/2633494120908709
9. Torchen LC. Cardiometabolic risk in PCOS: more than a reproductive disorder. *Curr Diab Rep*. 2017;17(12):137. doi:10.1007/s11892-017-0956-2
10. Cooney LG, Dokras A. Beyond fertility: polycystic ovary syndrome and long-term health. *Fertil Steril*. 2018;110(5):794-809. doi:10.1016/j.fertnstert.2018.08.021
11. Abdalla MA, Deshmukh H, Atkin S, Sathyapalan T. A review of therapeutic options for managing the metabolic aspects of polycystic ovary syndrome. *Ther Adv Endocrinol Metab*. 2020;11:2042018820938305. doi:10.1177/2042018820938305
12. Wekker V, van Dammen L, Koning A, et al. Long-term cardiometabolic disease risk in women with PCOS: a systematic review and meta-analysis. *Hum Reprod Update*. 2020;26(6):942-960. doi:10.1093/humupd/dmaa029
13. Zhao H, Xing C, Zhang J, He B. Comparative efficacy of oral insulin sensitizers metformin, thiazolidinediones, inositol, and berberine in improving endocrine and metabolic profiles in women with PCOS: a network meta-analysis. *Reprod Health*. 2021;18(1):171. doi:10.1186/s12978-021-01207-7
14. Azziz R. Polycystic ovary syndrome. *Obstet Gynecol*. 2018;132(2):321-336. doi:10.1097/AOG.0000000000002698
15. McCartney CR, Marshall JC. Polycystic ovary syndrome. *N Engl J Med*. 2016;375(1):54-64. doi:10.1056/NEJMc1514916
16. Heavy menstrual bleeding. CDC.gov. Published December 20, 2017. Accessed June 18, 2022. <https://www.cdc.gov/ncbddd/blooddisorders/women/menorrhagia.html#:~:text=Menorrhagia%20is%20menstrual%20bleeding%20that,larger%2C%20that%20is%20heavy%20bleeding>
17. Azziz R, Carmina E, Dewailly D, et al. The androgen excess and PCOS society criteria for the polycystic ovary syndrome: the complete task force report. *Fertil Steril*. 2009;91(2):456-88. doi:10.1016/j.fertnstert.2008.06.035
18. Neven ACH, Laven J, Teede HJ, Boyle JA. A summary on polycystic ovary syndrome: diagnostic

criteria, prevalence, clinical manifestations, and management according to the latest international guidelines. *Semin Reprod Med.* 2018;36(1):5-12. doi: 10.1055/s-0038-1668085

19. Bednarska S, Siejka A. The pathogenesis and treatment of polycystic ovary syndrome: what's new? *Adv Clin Exp Med.* 2017;26(2):359-367. doi: 10.17219/acem/59380

20. Jin P, Xie Y. Treatment strategies for women with polycystic ovary syndrome. *Gynecol Endocrinol.* 2018;34(4):272-277. doi: 10.1080/09513590.2017.1395841

21. Legro RS, Arslanian SA, Ehrmann DA, et al. Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2013;98(12):4565-4592. doi: 10.1210/jc.2013-2350

22. Martin KA, Anderson RR, Chang RJ, et al. Evaluation and treatment of hirsutism in premenopausal women: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* 2018;103(4):1233-1257. doi:10.1210/jc.2018-00241

23. Berni TR, Morgan CL, Berni ER, Rees DA. Polycystic ovary syndrome is associated with adverse mental health and neurodevelopmental outcomes. *J Clin Endocrinol Metab.* 2018;103(6):2116-2125. doi:10.1210/jc.2017-02667

24. Han Y, Li Y, He B. GLP-1 receptor agonists versus metformin in PCOS: a systematic review and meta-analysis. *Reprod Biomed Online.* 2019;39(2):332-342. doi:10.1016/j.rbmo.2019.04.017

25. Yildiz B. Approach to the patient: contraception in women with polycystic ovary syndrome. *J Clin Endocrinol Metab.* 2015;100(3):794-802. doi: 10.1210/jc.2014-3196

26. Xulane. Package Insert. Mylan Pharmaceuticals Inc; 2016.

27. Franik S, Eltrop SM, Kremer JA, Kiesel L, Farquhar C. Aromatase inhibitors (letrozole) for subfertile women with polycystic ovary syndrome. *Cochrane Database Syst Rev.* 2018;5(5):CD010287. doi:10.1002/14651858.CD010287.pub3

28. Somani N, Turvey D. Hirsutism: an evidence-based treatment update. *Am J Clin Dermatol.* 2014;15(3):247-266. doi: 10.1007/s40257-014-0078-4

29. Çoban ÖG, Tulacı ÖD, Adanır AS, Önder A. Psychiatric disorders, self-esteem, and quality of life in adolescents with polycystic ovary syndrome. *J Pediatr Adolesc Gynecol.* 2019;32(6):600-604. doi: 10.1016/j.jpog.2019.07.008

30. Lam N, Muravez SN, Boyce RW. A comparison of the Indian Health Service counseling technique with traditional, lecture-style counseling. *J Am Pharm Assoc (2003).* 2015;55:503-510. doi: 10.1331/JAPhA.2015.14093 following period

Assessment Questions

- Which of the following are common conditions or characteristics that people with PCOS present with?
 - Irregular menstruation
 - Cysts in the ovaries
 - Changes in fertility
 - Excess hair growth
 - All of the above
- Which of the following is found in excess in a majority of people with PCOS?
 - Serotonin
 - Androgens
 - Angiotensin
 - Histamine
- Menstrual dysfunction in PCOS may present as oligomenorrhea, often defined as a menstrual cycle lasting longer than ____ days in length.
 - 15
 - 25
 - 30
 - 35
- Which of the following is first-line therapy in the treatment of menstrual dysfunction in patients with PCOS?
 - Progestin-only contraceptives
 - Metformin
 - Clomiphene citrate
 - Combined oral contraceptive
- Which of the following metabolic conditions are people with PCOS at an increased risk of developing?
 - Type 2 Diabetes
 - Cardiovascular Disease
 - Arthritis
 - Chronic Kidney Disease
 - Both A and B
- What is the best option for insulin resistance in a patient with PCOS, obesity, and history of pancreatitis?
 - Pioglitazone
 - Metformin
 - Liraglutide
 - Insulin
- Which of the following is the most commonly used scoring system used to analyze hirsutism in patients with PCOS?
 - Ferriman-Gallwey tool
 - Rotterdam criteria
 - PCOSQ scale
 - Stein-Leventhal
- Which of the following would be the best option for inducing ovulation in patients with PCOS?
 - Metformin alone
 - Clomiphene citrate plus letrozole
 - Clomiphene citrate plus metformin
 - Letrozole plus metformin
- Did the activity meet the stated learning objectives? (if you answer no, please email sarahs@pswi.org to explain)
 - Yes
 - No
- On a scale of 1 – 10 (1-no impact; 10-strong impact), please rate how this program will impact the medication therapy management outcomes or safety

of your patients.

- On a scale of 1 – 10 (1-did not enhance; 10-greatly enhanced), please rate how this program enhanced your competence in the clinical areas covered.
- On a scale of 1 – 10 (1-did not help; 10-great help), please rate how this program helped to build your management and leadership skills.
- How useful was the educational material?
 - Very useful
 - Somewhat useful
 - Not useful
- How effective were the learning methods used for this activity?
 - Very effective
 - Somewhat effective
 - Not effective
- Learning assessment questions were appropriate.
 - Yes
 - No
- Were the authors free from bias?
 - Yes
 - No
- If you answered “no” to question 15, please comment (email info@pswi.org).
- Please indicate the amount of time it took you to read the article and complete the assessment questions.

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Quiz Answer Form

circle one answer per question

- | | |
|--------------|-----------|
| 1) a b c d e | 10) _____ |
| 2) a b c d | 11) _____ |
| 3) a b c d | 12) _____ |
| 4) a b c d | 13) a b c |
| 5) a b c d e | 14) a b c |
| 6) a b c d | 15) a b |
| 7) a b c d | 16) a b |
| 8) a b c d | 17) _____ |
| 9) a b | 18) _____ |

September/October 2022
A Review of Pathophysiology and Treatment of Polycystic Ovary Syndrome (PCOS)
 ACPE Universal Activity Number:
 0175-0000-22-152-H01-P
Target Audience: Pharmacists
Activity Type: Knowledge-based
Release Date: September 1, 2022
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