



## Polycystic Ovary Syndrome

Polycystic Ovary Syndrome (PCOS) is a common endocrinopathic condition which affects between 5-10% of women during their reproductive years.<sup>1,2</sup> Standardized diagnostic criteria for PCOS have not been established; therefore, prevalence rates vary depending on which criteria clinicians have used. The cause of PCOS is not well understood. A prominent feature of PCOS is hyperinsulinemia secondary to insulin resistance which appears to correlate with excess androgen levels.<sup>1-3</sup> The symptomatic presentation of PCOS can be grouped into three categories: clinical, endocrine and metabolic. (Table 1) It is important to note that not all women with PCOS have polycystic ovaries and only 40-50% of these women are actually obese.<sup>1-4</sup>

**Table 1: Presentation of Polycystic Ovary Syndrome <sup>1</sup>**

Category	Clinical	Endocrine	Metabolic
<b>Presentation</b>	<ul style="list-style-type: none"> <li>✓ Menstrual abnormalities</li> <li>✓ Hirsutism</li> <li>✓ Acne</li> <li>✓ Alopecia</li> <li>✓ Anovulatory infertility</li> <li>✓ Recurrent miscarriages</li> </ul>	<ul style="list-style-type: none"> <li>✓ Elevated androgens</li> <li>✓ Elevated luteinizing hormone</li> <li>✓ Elevated estrogen levels</li> <li>✓ Elevated prolactin levels</li> </ul>	<ul style="list-style-type: none"> <li>✓ Insulin resistance</li> <li>✓ Obesity</li> <li>✓ Lipid abnormalities</li> <li>✓ Increased risk for impaired glucose tolerance</li> <li>✓ Increased risk for type 2 diabetes mellitus</li> </ul>

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### UNIQUE EMPLOYMENT OPPORTUNITY FOR PHARMACISTS!! DRUG INFORMATION CONSULTANT

The Saskatchewan Drug Information Service requires a full-time pharmacist for the health professional line. Duties include researching and responding to queries from pharmacists, physicians and other healthcare professionals, preparing newsletters, and supervising pharmacy students in the drug information office. No evenings or weekends. Applicants must have a practicing license for Saskatchewan. Good communication skills are essential. Prior experience in the drug information field would be an asset. For further information or to submit your resume please contact Karen Jensen, Manager, Saskatchewan Drug Information Service, College of Pharmacy and Nutrition, University of Saskatchewan, Saskatoon SK S7N 5C9, tel. (306) 966-6340/6349, e-mail [jensen@sask.usask.ca](mailto:jensen@sask.usask.ca) Application deadline is April 30, 2004.

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## Management of PCOS

Treatment of PCOS can vary from patient to patient depending on what their primary symptoms are. Response to therapy might take 3-9 months.<sup>4</sup> Obese women with PCOS should first undergo a weight reduction program to decrease hyperinsulinemia and its effects on hyperandrogenemia. Successful weight reduction may restore ovulation and improve hirsutism.<sup>3,4</sup> Appropriate treatment selection will reduce the risk of morbidities associated with PCOS such as coronary artery disease, cardiovascular disease, gestational diabetes, type 2 diabetes mellitus, endometrial cancer and ovarian cancer.<sup>3</sup>

A recent development in the treatment of PCOS involves the use of oral antihyperglycemic agents such as metformin and thiazolidenediones, with metformin being the most extensively studied.<sup>3,5</sup> Growing evidence has shown metformin improves insulin sensitivity and ovarian function.<sup>5,6</sup> This in turn leads to decreased insulin resistance and free testosterone resulting in increased pregnancy rates, decreased body mass index, improved menstrual cycle regulation and decreased hirsutism in women with PCOS.<sup>3,6</sup> Limited data suggests metformin 500 mg three times daily is effective in managing PCOS.<sup>3,6</sup> In one study, metformin used in combination with clomiphene citrate increased ovulation rates in up to 90% of women however this has yet to be duplicated by other studies.<sup>1,7</sup>

Various agents including oral contraceptives, anti-androgens, cyproterone acetate, clomiphene citrate, gonadotropins, gonadotropin releasing hormone (GnRH) agonists and glucocorticoids have been used in PCOS however their place in therapy is yet to be established by further study. Suggested agents and dosing regimens for the treatment of PCOS are outlined in Table 2.

Surgery is only used in the management of PCOS after treatment failure with clomiphene citrate, gonadotropins, and GnRH agonists.<sup>3</sup> Ovulation can be induced by laparoscopic ovarian drilling however women undergoing this procedure are at risk of ovarian adhesions.<sup>3</sup>

## Pharmacist's role in the management of PCOS<sup>1,3</sup>

Pharmacists are in an ideal position to educate patients about the disease itself, and also about the treatment options available for the symptoms of PCOS. Pharmacists should be able to discuss the long-term complications of PCOS and advise women on appropriate prevention strategies. Patients can be counseled on the importance of exercise and healthy eating to reduce weight, improve lipid profiles, prevent hypertension and decrease the risk of type 2 diabetes. Women with PCOS should get their cholesterol, triglycerides, blood sugar, and insulin checked annually and should monitor their blood pressure. Patients with type 2 diabetes mellitus or impaired glucose tolerance should be reminded to monitor their blood glucose levels. The importance for endometrial and ovarian cancer screening should also be stressed.

Table 2: Treatment Options for PCOS 1,3,4,8-12

TREATMENT	THERAPEUTIC USE(S)	DOSES
<b>WHEN PREGNANCY IS DESIRED</b>		
Metformin	<ul style="list-style-type: none"> <li>✓ Improve insulin sensitivity</li> <li>✓ Decrease insulin resistance</li> <li>✓ Reduce weight</li> <li>✓ Improve ovulation</li> <li>✓ Induce fertility</li> <li>✓ Reduce elevated testosterone levels</li> </ul>	1500-2000mg/day
Rosiglitazone	<ul style="list-style-type: none"> <li>✓ Improve insulin sensitivity</li> </ul>	4mg/day (limited data available)
Clomiphene citrate	<ul style="list-style-type: none"> <li>✓ <b>FIRST LINE FOR INDUCING OVULATION</b></li> <li>✓ Induce fertility</li> </ul>	Initially: 50 mg od x 5 days during the follicular phase. Dose can be increased to 100 mg and then to 150 mg if ovulation does not occur. Lowest effective dose should be used and if 150 mg is ineffective, try another therapy
GnRH agonists: leuprolide acetate, goserelin acetate, and nafarelin acetate	<ul style="list-style-type: none"> <li>✓ Induce ovulation</li> </ul>	Doses not established
Human menopausal gonadotropin (hMG) and Human chorionic gonadotropin (hCG)	<ul style="list-style-type: none"> <li>✓ Induce ovulation in clomiphene resistant women</li> </ul>	Initial dose of hMG (75 IU of FSH) is given IM daily for 14 days. Increase dose by 37.5 IU every 7 days until follicular ripening is complete. hCG is administered after leading follicle is obtained to achieve ovulation.
Glucocorticoids	<ul style="list-style-type: none"> <li>✓ Adjunctive therapy for induction of ovulation</li> </ul>	Initially: 0.5 mg dexamethasone + 50 mg clomiphene on day 5 of menstrual cycle. Dose of clomiphene can be increased to 150 mg a day
<b>WHEN PREGNANCY IS NOT DESIRED</b>		
Combination oral contraceptives (COC)	<ul style="list-style-type: none"> <li>✓ Regulates menstrual cycle</li> <li>✓ Reduce acne</li> <li>✓ Reduce hirsutism</li> </ul>	COC with low androgenic potential i.e. Marvelon®, Cyclen®, Tri-Cyclen®
Cyproterone acetate	<ul style="list-style-type: none"> <li>✓ Reduce acne</li> <li>✓ Reduce hirsutism</li> </ul>	Diane-35® (ethinyl estradiol/cyproterone acetate) or cyproterone acetate 25-50mg/day on days 1-10 of menstrual cycle
Medroxyprogesterone (MPA)	<ul style="list-style-type: none"> <li>✓ Regulates menstrual cycle</li> </ul>	10mg PO daily x 12-14 days/month
Anti-androgens	<ul style="list-style-type: none"> <li>✓ Reduce hirsutism</li> <li>✓ Reduce alopecia</li> </ul>	Spironolactone: 100-200 mg daily in divided doses for 6-12 months Finasteride: 5 mg od x 12 months Flutamide: 250mg BID x 3 months (used when other therapies are ineffective)

**Disclaimer:** The doses mentioned are **suggested doses** based on limited available evidence. Use your professional judgment when interpreting and applying the above information.

# **SASKATCHEWAN REGIONAL ADVERSE REACTION CENTRE**

WORKING TO IMPROVE THE SAFETY OF MARKETED HEALTH PRODUCTS

## **WHY REPORT?**

Adverse reaction reports improve health product safety by generating early warning signals for new and unexpected effects.

The Health Canada database is monitored to ensure:

- Benefits of health products marketed in Canada continue to outweigh the risks
- Healthcare professionals and the Canadian public are kept informed about significant adverse reactions
- Labeling and product information is continuously updated

## **WHAT TO REPORT?**

All **suspected** reactions that are:

- Serious** reactions
- Unexpected** reactions (not consistent with product labeling)
- Reactions to **new drugs** (marketed within the last 5 years) regardless of nature or severity

Suspected products include:

- Prescription drugs
- Non-prescription drugs (OTCs)
- Biological products
- Radiopharmaceutical products
- Natural Health Products (including complementary and herbal products)

Proof that a health product has caused a reaction is not a requirement for reporting.

## **HOW TO REPORT?**

For reporting forms or to report suspected adverse reactions contact:

### **Saskatchewan Regional Adverse Reaction Centre**

c/o Saskatchewan Drug Information Service

College of Pharmacy and Nutrition

University of Saskatchewan

110 Science Place

Saskatoon SK S7N 5C9

Tel: Toll Free 1-866-234-2345

Fax: Toll Free 1-866-678-6789

*Expect the unexpected – recognize and report all suspected adverse reactions.*

## References

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