

# Valproate for Bipolar Disorder Carries PCOS Risk

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EXPERT ANALYSIS FROM A  
PSYCHOPHARMACOLOGY UPDATE

LOS ANGELES – It's reasonable to consider the anticonvulsant valproate as a last option for women with bipolar disorder, given the drug's associations with the risk of developing isolated features of polycystic ovary syndrome, according to Dr. Harold Carlson.

"I don't have any problem with that," he said, when an audience member suggested it and also noted the drug's teratogenicity.

Women under age 25, and particularly adolescents in their midteens, are most at risk for valproate-induced PCOS, usually within the first year of treatment, said Dr. Carlson, professor of endocrinology at Stony Brook (N.Y.) University.

In one study, 9 of 86 women with bipolar disorder (10.5%) treated with valproate developed PCOS; 2 of 144 women with bipolar disorder (1.4%) developed PCOS when treated with other

When valproate cannot be switched out for a mood stabilizer, prescribing birth control pills at the start of therapy might be a smart move, Dr. Carlson said at the meeting, sponsored by the American Academy of Child and Adolescent Psychiatry. That appeared to help prevent PCOS in valproate-treated women in one study (*Seizure* 2003;12:323-9).

Baseline pelvic ultrasounds might seem like a good idea, too, but they're

"not worth doing," he said. The reason is that 10%-15% of healthy women have cysts on their ovaries without having PCOS, and ovarian cysts aren't always present in PCOS.

When women are started on the drug, ask them "every time you see them about their menstrual function. Look at them and see if they are getting acne and hirsutism. Ask them about it. Provide some counseling on diet and exercise to

avoid the excessive weight gain, which only makes it worse," Dr. Carlson said.

Should PCOS develop, Metformin is the first-line symptom treatment. Clomiphene can induce ovulation if pregnancy is the goal. Endocrinology, urology, or gynecology referrals also are in order to help with symptoms, he said.

Dr. Carlson said he is a consultant to Eli Lilly & Co., and has received research funding from GlaxoSmithKline. ■



**Ask patients on valproate about their menstrual function. Look to see if they are getting acne and hirsutism.**

DR. CARLSON

mood stabilizers (*Biol. Psychiatry* 2006;59:1078-86).

Valproate seems to pose a particular risk for the condition driven by something more than the weight gain caused by the drug.

After all, "the folks [who] gain all that weight on olanzapine don't get PCOS," Dr. Carlson noted.

Valproate appears to act directly on the ovaries, altering their hormone production. Cultured ovarian cells produce more testosterone in its presence. The excess testosterone shuts off menstruation, and causes acne and hirsutism. Obesity, insulin resistance, and dyslipidemia are problems in PCOS, as well.

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## Easy to use<sup>1</sup>

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## Important Safety Information for Lantus<sup>®</sup>

### Contraindications

Lantus<sup>®</sup> is contraindicated in patients hypersensitive to insulin glargine or one of its excipients.

### Warnings and precautions

Monitor blood glucose in all patients treated with insulin. Insulin regimens should be modified cautiously and only under medical supervision. Changes in insulin strength, manufacturer, type, or method of administration may result in the need for a change in insulin dose or an adjustment in concomitant oral antidiabetic treatment.

Do not dilute or mix Lantus<sup>®</sup> with any other insulin or solution. If mixed or diluted, the solution may become cloudy, and the onset of action/time to peak effect may be altered in an unpredictable manner. Do not administer Lantus<sup>®</sup> via an insulin pump or intravenously because severe hypoglycemia can occur. Insulin devices and needles must not be shared between patients.

Hypoglycemia is the most common adverse reaction of insulin therapy, including Lantus<sup>®</sup>, and may be life-threatening.

Severe life-threatening, generalized allergy, including anaphylaxis, can occur.

A reduction in the Lantus<sup>®</sup> dose may be required in patients with renal or hepatic impairment.

### Drug interactions

Certain drugs may affect glucose metabolism, requiring insulin dose adjustment and close monitoring of blood glucose. The signs of hypoglycemia may be reduced in patients taking anti-adrenergic drugs (e.g., beta-blockers, clonidine, guanethidine, and reserpine).

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Important Limitations of Use: Lantus<sup>®</sup> is not recommended for the treatment of diabetic ketoacidosis. Use intravenous short-acting insulin instead.

Lantus<sup>®</sup> SoloSTAR<sup>®</sup> is a disposable prefilled insulin pen.

**Please see brief summary of full prescribing information for Lantus<sup>®</sup> on the next page.**

References: 1. Data on file, sanofi-aventis U.S. LLC. 2. Lantus Prescribing Information. September 2009.