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## ➔ DIRECT-TO-CONSUMER ADVERTISEMENTS FOR *GLUCOPHAGE XR*

The pharmaceutical industry is increasingly advertising drugs directly to patients in newspapers, magazines and on television. To help prescribers deal with questions arising from these ads, the Medical Letter is starting a new department, Direct-To-Consumer Advertisements, that will appear occasionally in our newsletter and more frequently on our website, [www.medletter.com](http://www.medletter.com). The arrow symbol in the margin will identify articles on this subject. Appropriate suggestions for new topics for this department are welcome at our website or by e-mail to [dtc@themedicalletter.org](mailto:dtc@themedicalletter.org).

**NEW ADS** — Full-page newspaper advertisements addressed to patients with type 2 diabetes are promoting the convenience of "NEW *once-a-day Glucophage XR* (metformin HCl extended-release tablets)," and offering a coupon for a free 30-day supply in the month of March. Immediate-release *Glucophage* is usually taken b.i.d. Metformin is also available in combination with glyburide as *Glucovance* (Medical Letter 2000; 42:105). Metformin went off patent in September, 2000, and one or more immediate-release generics will probably be available soon.

**PROBLEMS WITH METFORMIN** — Metformin is a biguanide that decreases production and increases uptake of glucose. In many patients it is as effective as a sulfonylurea without causing hypoglycemia or weight gain, but rarely it can cause lactic acidosis, particularly in patients with renal impairment or congestive heart failure. Even a temporary reduction in renal function, such as occurs after pyelography or angiography, can cause lactic acidosis in patients taking metformin. Alcohol also increases the risk of lactic acidosis. Metformin frequently causes abdominal discomfort and diarrhea, and can cause a metallic taste, nausea, vomiting and anorexia. The drug can also decrease absorption of vitamin B<sub>12</sub> and folic acid, causing a deficiency of these vitamins.

**WHAT'S DIFFERENT** — Without food, the extent of absorption is about the same with either product. Food decreases absorption of metformin from *Glucophage* and increases it from *Glucophage XR*. The extended-release formulation (*Glucophage XR*) reaches peak plasma concentrations in 4 to 8 hours, compared to about 2 to 4 hours with *Glucophage*. According to the manufacturer, patients taking *Glucophage* twice daily can be switched to *Glucophage XR* at the same total dosage taken once daily. *Glucophage* is available as 500-, 850- and 1000-mg tablets; *Glucophage XR* is only available as 500-mg tablets. The manufacturer recommends taking the immediate-release product twice daily with meals, and extended-release tablets once daily with the evening meal. The cost of 30 days' treatment with

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*Glucophage* 1500 mg, about \$67, decreases to about \$59 when the patient switches to *Glucophage XR*, according to AWP listings in *Drug Topics Red Book Update*, March 2001. In one comparative study, available only as an abstract, effectiveness was about the same and the incidence of adverse effects was slightly higher with the extended-release formulation (K Fujio-ka et al, *Diabetes* 2000; 49 suppl 1:A107).

**CONCLUSION** — Whether the effectiveness and adverse effects of metformin are any different with *Glucophage XR* remains to be established. Patients who are doing well with immediate-release metformin should probably stay on it. Much less expensive generic formulations will probably be available soon.

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