

HEALTH AND DRUG ALERTS

Rosiglitazone (Avandia) and macular edema

Reason for posting: Thiazolidinediones such as rosiglitazone are insulin sensitizers used in the treatment of type 2 diabetes and polycystic ovarian disease. Some patients taking these drugs experience peripheral edema.¹ Recent advisories² have noted that patients may also experience visual disturbances related to macular edema.

The condition: Macular edema occurs when the blood vessels leak plasma into the surrounding retina. Among people with type 2 diabetes, it can be found in 15% of those who use insulin and 4% of those who do not.³ Risk factors for macular edema and its symptoms are listed in Box 1.

Cases of rosiglitazone-related macular edema were first described in September 2005.⁴ The manufacturer of the drug, GlaxoSmithKline, announced subsequently that the effect had been reported in an undisclosed number of postmarketing cases worldwide.² Although limited clinical data on affected patients are available from GlaxoSmithKline or Health Canada, most of the patients affected were reported also to have fluid retention, peripheral edema or weight gain.² Key unreported case details included the patients' ages,

duration of diabetes, doses and duration of rosiglitazone use, concomitant medication use and occurrence, if any, of pre-existing diabetic retinopathy. Some patients improved after rosiglitazone use was discontinued.

Health Canada has received 9 reports of visual impairment in patients taking rosiglitazone. Of these, only one was clearly associated with macular edema: a 65-year-old woman who had taken an unspecified dosage for more than a year. Her symptoms, which also included hypertension and peripheral edema (but no retinopathy), resolved upon discontinuation of the drug (Barbara Raymond, Marketed Pharmaceuticals Division, Health Canada: personal communication, 2006).

The patients who appear to be at greatest risk of peripheral edema, fluid retention and weight gain, congestive heart failure and pulmonary edema related to rosiglitazone are those who use insulin or have New York Heart Association class II, III or IV cardiac status, left-ventricular dysfunction or renal insufficiency. These effects are dose-related. Although the exact cause of macular edema is unknown, thiazolidinediones are hypothesized to cause peripheral edema by affecting renal and intestinal ion transport, increasing plasma volume and sympathetic activation, and causing growth factor-related vascular permeability.⁴

What to do: Although rosiglitazone-

related macular edema is rare, patients using the drug should be advised to seek immediate medical attention if they begin to experience visual symptoms (Box 1). Consider discontinuing the medication if macular edema occurs. Asymptomatic macular edema is likely to be noted at a patient's yearly ophthalmologic screening for diabetic retinopathy. Individual patients' risk factors for macular edema, such as poor glycemic control and hypertension, should be optimized according to existing guidelines.³

Claire Kendall
Eric Wooltorton
CMAJ

REFERENCES

1. Wooltorton E. Rosiglitazone (Avandia) and pioglitazone (Actos) and heart failure. *CMAJ* 2002;166(2):219.
2. Health Canada. Association of Avandia and Avandamet with new onset and/or worsening of macular edema [Dear Healthcare Professional letter]. Available: www.hc-sc.gc.ca/dhp-mpps/medeff/advisories-avis/prof/avandia_avandamet_hpc-cps_e.html (accessed 2006 Jan 17).
3. Canadian Diabetes Association 2003 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. *Can J Diabetes* 2003;27 (Suppl 2):S1-152. Available: www.diabetes.ca/cpg2003 (accessed 2006 Jan 22).
4. Coluciello M. Vision loss due to macular edema induced by rosiglitazone treatment of diabetes mellitus. *Arch Ophthalmol* 2005;123:1273-5.

All Health and Drug Alerts are posted online ahead of print and are available at www.cmaj.ca. This article was posted on Feb. 8, 2006.

DOI:10.1503/cmaj.060074

Box 1: Macular edema

Risk factors

- Longstanding diabetes
- Insulin use
- Diabetic retinopathy
- Hypertension
- Poor glycemic control

Symptoms

- Blurred or distorted vision
- Decreased colour sensitivity
- Decreased dark adaptation

Canadian Adverse Reaction Newsletter Bulletin canadien des effets indésirables

To receive the Newsletter and health product Advisories free by email, join Health Canada's **MedEffect** mailing list.

Go to www.hc-sc.gc.ca/dhp-mpps/medeff/subscribe-abonnement/index_e.html.

Inscrivez-vous à la liste **MedEffet** de Santé Canada pour recevoir gratuitement par courriel le Bulletin et les Avis au sujet des produits de santé. Rendez-vous à l'adresse www.hc-sc.gc.ca/dhp-mpps/medeff/subscribe-abonnement/index_f.html.

**Report adverse reactions toll free to Health Canada
Signaler sans frais des effets indésirables à Santé Canada**

Tel./Tél. : 866 234-2345 • Fax/Télec. : 866 678-6789

Canada