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Drug Therapy Updates: Rosiglitazone and Erythropoiesis Stimulating Agents

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Rosiglitazone (Avandia®, Avanadamet®, Avandaryl®)

A recent meta-analysis of 42 trials reported an increased risk of myocardial infarction and death from cardiovascular causes in patients receiving rosiglitazone compared to control groups.¹ Other studies^{2,3} have provided conflicting evidence concerning the increased risk of heart attack and heart-related deaths and the use of rosiglitazone in the treatment of type 2 diabetes mellitus. The FDA is aware of these reports and is in the process of reviewing the data from the 42 studies submitted by the makers of this drug, GlaxoSmithKline.

Currently, there are three commercial products containing rosiglitazone; Avandia® (rosiglitazone alone), Avanadamet® (rosiglitazone plus metformin), and Avandaryl® (rosiglitazone plus glimepiride). The current package insert of rosiglitazone does include cardiovascular events as part of the warning section. Both rosiglitazone and pioglitazone (Actos®), the only two thiazolidinedione agents available in the U.S., can also precipitate congestive heart failure due to fluid retention.

At this point it is not known whether the incidence of cardiovascular events is higher with rosiglitazone compared to pioglitazone, however the PROACTIVE study⁴ showed favorable results with the use of pioglitazone as compared to placebo.

An ongoing study⁵ (RECORD study) should help clarify the risks of cardiovascular events associated with rosiglitazone.

Until more information becomes available, we should carefully monitor the use of rosiglitazone and report any cases of cardiovascular events or other serious adverse events to the FDA (<http://www.fda.gov/medwatch/report/hcp.htm>).

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Epoetin alfa (Epogen®, Procrit®) and darbepoetin alfa (Aranesp®)

The FDA has recently approved changes in prescribing information concerning epoetin alfa (Epogen® Procrit®) and darbepoetin alfa (Aranesp®).¹ The new information, which is included in the Box Warning, indicates that erythropoiesis-stimulating agents (ESA) increased the risk for death and for serious cardiovascular events when administered to achieve a target hemoglobin level of more than 12 g/dL. They also recommend that antithrombotic prophylaxis should be strongly considered when ESA's are used to reduce allogeneic red blood cell transfusions after surgery.

Additional information that should be considered when using these agents is that a clinically significant increase in hematocrit may take between 2 to 6 weeks after administration. Also, iron supplementation will be needed in almost all patients to support erythropoiesis due to iron stores depletion.

As a guideline to reduce cardiovascular risks, the lowest possible dose of ESA's should be used, the hemoglobin concentration should not exceed 12 g/dL, and the rate of hemoglobin increase should not exceed 1g/dL in any two week period.

An additional controversy has surfaced concerning enhanced tumor growth in patients with certain types of cancers and the need to implement new guidelines that will promote prudent and evidence-based use of erythropoiesis-stimulating agents in cancer patients.²

REFERENCES

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