



TITLE: Rosiglitazone and Pioglitazone for Patients with Type 2 Diabetes: Safety

DATE: 30 August 2010

RESEARCH QUESTION:

What is the comparative safety of rosiglitazone and pioglitazone for patients with type 2 diabetes?

METHODS:

A limited literature search was conducted on key health technology assessment resources, including PubMed, the Cochrane Library (Issue 8, 2010), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI (Health Devices Gold), EuroScan, international health technology agencies, and a focused Internet search. The search was limited to English language articles published between January 1, 2005 and August 16, 2010. No filters were applied to limit the retrieval by study type. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

RESULTS:

HTIS reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, and non-randomized studies.

One health technology assessment, four systematic reviews, and 17 non-randomized studies were identified regarding the comparative safety of rosiglitazone and pioglitazone for patients with type 2 diabetes. Additional articles of potential interest can be found in the appendix.

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OVERALL SUMMARY OF FINDINGS:

Overall, the majority of studies stated that rosiglitazone was associated with an increased risk of cardiovascular events and all-cause mortality.^{1,2,7,9-12,15,19} and pioglitazone was associated with a decreased risk of cardiovascular events and all-cause mortality.^{1,8-10, 14,19} Both rosiglitazone and pioglitazone appear to have no association with the incidence of first stroke.²⁰ Patients receiving either drug appear to be at an increased risk for bone fracture.^{4,21,22} Table 1 provides details of the major outcomes reported in the included studies.

Table 1: Outcomes Reported for Rosiglitazone and Pioglitazone

Reported outcomes	Number of Studies
<i>Cardiovascular</i>	
Rosiglitazone is associated with an increased risk of cardiovascular events and/or all-cause mortality	1 HTA, ¹ 1 SR, ² and 7 NRS ^{7,9,12-15,19}
Pioglitazone is associated with a decreased risk of cardiovascular events and/or all-cause mortality	1 HTA ¹ and 5 NRS ^{8-10,14,19}
No significant difference observed in cardiac outcomes/risk between the two drugs	3 NRS ^{6,11,16}
Insufficient data to make a comparative conclusion regarding cardiovascular risk between the two drugs	1 SR ³
Rosiglitazone has a higher risk of edema than pioglitazone	1 SR ⁵
Both drugs appear to have similar side effect profiles	1 SR ³
Neither drug is associated with an increased risk of AMI	1 NRS ⁸
<i>Cerebrovascular</i>	
Neither drug is associated with a decrease in incidence of first stroke	1 NRS ²⁰
<i>Fracture Risk</i>	
Both drugs increase fracture risk in men and women	1 SR, ⁴ and 2 NRS ^{21,22}
Both drugs were used more frequently by patients with fracture than controls	1 NRS ¹⁷

AMI = acute myocardial infarction; HTA = health technology assessment; NRS = non-randomized study; SR = systematic review

REFERENCES SUMMARIZED:

Health technology assessments

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Systematic reviews and meta-analyses

Cardiovascular

2. Selvin E, Bolen S, Yeh HC, Wiley C, Wilson LM, Marinopoulos SS, et al. Cardiovascular outcomes in trials of oral diabetes medications: a systematic review. *Arch Intern Med* [Internet]. 2008 [cited 2010 Aug 27] ;168(19):2070-80. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2765722/?tool=pubmed> [PubMed: PM18955635](#)
Structured Abstract available:
<http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=12008106508>
3. Norris SL, Carson S, Roberts C. Comparative effectiveness of pioglitazone and rosiglitazone in type 2 diabetes, prediabetes, and the metabolic syndrome: a meta-analysis. *Curr Diabetes Rev*. 2007 May;3(2):127-40. [PubMed: PM18220664](#)

Fracture risk

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Edema

5. Berlie HD, Kalus JS, Jaber LA. Thiazolidinediones and the risk of edema: a meta-analysis. *Diabetes Res Clin Pract*. 2007 May;76(2):279-89. [PubMed: PM17055103](#)

Randomized controlled trials

No literature identified.

Non-randomized studies

Cardiovascular

6. Bilik D, McEwen LN, Brown MB, Selby JV, Karter AJ, Marrero DG, et al. Thiazolidinediones, cardiovascular disease and cardiovascular mortality: translating research into action for diabetes (TRIAD). *Pharmacoepidemiol Drug Saf*. 2010 Jul;19(7):715-21. [PubMed: PM20583206](#)

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11. Pantalone KM, Kattan MW, Yu C, Wells BJ, Arrigain S, Jain A, et al. The risk of developing coronary artery disease or congestive heart failure, and overall mortality, in type 2 diabetic patients receiving rosiglitazone, pioglitazone, metformin, or sulfonylureas: a retrospective analysis. *Acta Diabetol*. 2009 Jun;46(2):145-54. [PubMed: PM19194648](#)
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Cerebrovascular

20. Azoulay L, Schneider-Lindner V, Dell'aniello S, Filion KB, Suissa S. Thiazolidinediones and the risk of incident strokes in patients with type 2 diabetes: a nested case-control study. *Pharmacoepidemiol Drug Saf.* 2010 Apr;19(4):343-50. [PubMed: PM19998318](#)

Fracture risk

21. Aubert RE, Herrera V, Chen W, Haffner SM, Pendergrass M. Rosiglitazone and pioglitazone increase fracture risk in women and men with type 2 diabetes. *Diabetes Obes Metab.* 2010 Aug;12(8):716-21. [PubMed: PM20590749](#)
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APPENDIX – FURTHER INFORMATION:

Systematic reviews – non-comparative

23. Second-line therapy for patients with diabetes inadequately controlled on Metformin: a systematic review and cost-effectiveness analysis. Optimal Therapy Report [Internet]. 2010 Aug [cited 2010 Aug 27];4(2):i-224. Available from: http://www.cadth.ca/media/pdf/C1110_SR_Report_final_e.pdf
Note: see Outcomes related to safety, page 22
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Non-randomized studies - retrospective

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Review articles

Cardiovascular

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Additional safety information

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