



### Patients with Fractures in ADOPT

	Rosiglitazone		Metformin		Glyburide	
<b>MALE PATIENTS</b>	811 Males 2766.7 PY		864 Males 2957.6 PY		836 Males 2612.8 PY	
	n (%)	Rate/100 PY	n (%)	Rate/100 PY	n (%)	Rate/100 PY
	Experienced a fracture	32 (3.95)	1.16	29 (3.36)	0.98	28 (3.35)
<b>FEMALE PATIENTS</b>	645 Females 2187.2 PY		590 Females 1948.0 PY		605 Females 1630.8 PY	
	n (%)	Rate/100 PY	n (%)	Rate/100 PY	n (%)	Rate/100 PY
	Experienced a fracture *	60 (9.30)	2.74	30 (5.09)	1.54	21 (3.47)
Lower limb **	36 (5.58)	1.65	18 (3.05)	0.92	8 (1.32)	0.49
Hip	2 (0.31)	0.09	2 (0.34)	0.10	0	0
Foot	22 (3.41)	1.01	7 (1.19)	0.36	4 (0.66)	0.25
Upper limb ***	22 (3.41)	1.01	10 (1.70)	0.51	9 (1.49)	0.55
Hand	8 (1.24)	0.37	4 (0.68)	0.21	1 (0.17)	0.06
Humerus	5 (0.78)	0.23	0	0	0	0
Spine	1 (0.16)	0.05	1 (0.17)	0.05	1 (0.17)	0.06
Other	5 (0.78)	0.23	4 (0.68)	0.21	4 (0.66)	0.25

Rate/100 PY = Patients with Events per 100 Patient Years, n = number of patients

\* Some patients experienced fractures in more than one category.

\*\* Other sites of fracture included: ankle, femur, fibula, lower limb (general), patella, and tibia.

\*\*\* Other sites of fracture included: clavicle, forearm, radius, upper limb (general), and wrist.

At GSK's request, an independent safety committee reviewed an interim analysis of fractures in another large ongoing, long-term, controlled rosiglitazone clinical trial. The primary purpose of that study is to investigate cardiovascular endpoints in patients with type 2 diabetes mellitus. The results of the preliminary analysis were reported to GSK as being consistent with the observations from ADOPT. The independent safety committee also recommended that the study continue without modification. Final results of this study are anticipated to be available in 2009.

Presently, our understanding of the clinical significance of the findings from these two long-term trials is incomplete, and the mechanism(s) for the observed increase in fractures is uncertain. Further evaluation of these observations is ongoing. GlaxoSmithKline believes the risk of fracture should be considered in the care of patients, especially female patients, with type 2 diabetes mellitus who are currently being treated with rosiglitazone, or when initiation of rosiglitazone treatment is being considered. In these patients, as with all patients with type 2 diabetes mellitus, attention should be given to assessing and maintaining bone health according to current standards of care.

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Should you have any questions or require additional information, please contact your local GlaxoSmithKline information line (1-888-825-5249).

Sincerely,



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GlaxoSmithKline

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