

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 021071

CHEMISTRY REVIEW(S)

Wolber

APR - 9 1999

DIVISION OF METABOLISM AND ENDOCRINE DRUG PRODUCTS - HFD-510
Review of Chemistry, Manufacturing and Controls

NDA 21-071	Chemistry Review # 1	Date Reviewed: 06-APR-1999		
Submission Type	Document Date	CDER Rec. Date	Filing Date	U.F. ID #
Original	24-NOV-1998	27-NOV-1998	24-JAN-1999	3590
Amendment	11-JAN-1999			
Amendment	02-APR-1999			

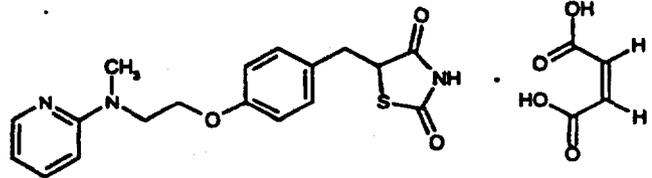
Applicant:	SmithKline Beecham Pharmaceuticals 1250 South Collegeville Road Mail Code UP4340, PO Box 5089 Collegeville, PA 19426-0989	G. Clare Kahn, PhD Group Director/ Regulatory Affairs Phone: (610) 917-7250 Fax: (610) 917-4815
-------------------	---	---

Drug Product Name	Proprietary:	Avandia™
	Nonproprietary/Established/USAN:	Rosiglitazone Maleate
	Chem.Type/ Ther.Class:	1 S

Pharmacological Category/Indication: Hypoglycemic Agent. Adjunct to diet to improve glycemic control in patients with NIDDM whose hyperglycemia cannot be managed by diet alone.

Dosage Form: Tablets	Strength(s): 1.0-, 2.0-, 4.0- and 8.0-mg
Route of Administration: Oral	Dispensed: R

Chemical Name, Structural Formula, Molecular Formula, Molecular Weight:



$C_{18}H_{19}N_3O_5S \cdot C_4H_4O_4$
 MW = 357.4 + 116.1 = 473.5
 (±)-5-[[4-[2-Methyl-2-(pyridinylamino)ethoxy]phenyl]methyl]-2,4-thiazolidinedione (Z)-2-butenedioate (1:1)

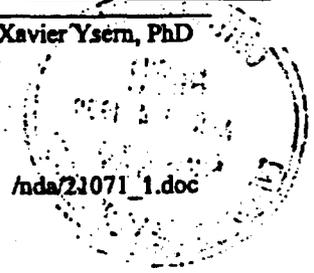
Patent Information: Patent #/ Expiring date/ Type of patent/ Owner/
 5,002,953/ 30-AUG-2008/ drug, formulation and use/ Beecham Group/
 5,741,803/ 21-APR-2015/ drug, formulation and use/ SmithKline Beecham/

Conclusions & Recommendations: Satisfactory CMC information has been provided to judge the quality of the drug substance, Rosiglitazone Maleate, and the drug product, Avandia (Rosiglitazone Maleate) Tablets. The application is approvable from the Chemistry viewpoint pending satisfactory responses to the minor deficiencies. Minor deficiencies are listed in the draft deficiency letter. Issue information request letter.

Orig. NDA 21-071
 cc: HFD-510/Division File
 HFD-510/SMalozowski/SMoore/RSteigerwalt/JWeber/XYsem
 HFD-820/JGibbs

/S/ [Redacted]

Xavier Ysem, PhD



R/D Init by:
 AE [Redacted] /S/
 [Redacted] /S/
 1/9/99

filename: /nda/21071_1.doc

MAY 25 1999

DIVISION OF METABOLISM AND ENDOCRINE DRUG PRODUCTS - HFD-510
Review of Chemistry, Manufacturing and Controls

NDA 21-071

Chemistry Review # 2

Date Reviewed: 25-MAY-1999

Submission Type	Document Date	CDER Rec. Date	Filing Date	U.F. ID # 3590
Original	24-NOV-1998	27-NOV-1998	24-JAN-1999	
Amendment	11-JAN-1999			
Amendment	02-APR-1999			
Amendment	12-APR-1999			
Amendment	05-MAY-1999			

Applicant: SmithKline Beecham Pharmaceuticals
1250 South Collegeville Road
Mail Code UP4340, PO Box 5089
Collegeville, PA 19426-0989

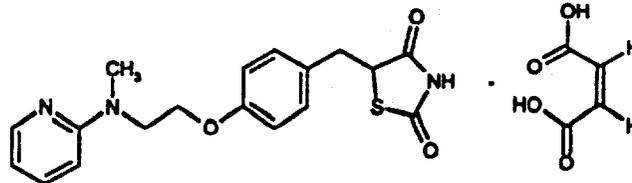
G. Clare Kahn, PhD
Group Director/ Regulatory Affairs
Phone: (610) 917-7250
Fax: (610) 917-4815

Drug Product Name	Proprietary:	Avandia™
	Nonproprietary/Established/USAN:	Rosiglitazone Maleate
	Chem. Type/ Ther. Class:	1 S

Pharmacological Category/indication: Hypoglycemic Agent. Adjunct to diet to improve glycemic control in patients with NIDDM whose hyperglycemia cannot be managed by diet alone.

Dosage Form: Tablets	Strength(s):	1.0-, 2.0-, 4.0- and 8.0-mg
Route of Administration: Oral	Dispensed:	R

Chemical Name, Structural Formula, Molecular Formula, Molecular Weight:



$C_{13}H_{19}N_3O_3S \cdot C_4H_4O_4$

MW = 357.4 + 116.1 = 473.5

(±)-5[[4-[2-Methyl-2-(pyridinylamino)ethoxy]phenyl]methyl]-2,4-thiazolidinedione (Z)-2-butenedioate (1:1)

Patent Information: Patent #/ Expiring date/ Type of patent/ Owner/
5,002,953/ 30-AUG-2008/ drug, formulation and use/ Beecham Group/
5,741,803/ 21-APR-2015/ drug, formulation and use/ SmithKline Beecham/

Conclusions & Recommendations: All minor deficiencies have been addressed adequately. Satisfactory CMC information has been provided to judge the quality of the drug substance, Rosiglitazone Maleate, and the drug product, Avandia (Rosiglitazone Maleate) Tablets. The application is approvable from the Chemistry viewpoint.

Orig. NDA 21-071
cc: HFD-510/Division File
HFD-510/SMalozowski/SMoore/RSteigerwalt/JWeber/XYsern
HFD-820/JGibbs

/S/

Xavier Ysern, PhD

R/D Init by: /S/

AP /S/

/S/

5/25/99

filename: /nda/21071_2.doc