CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 021071

CHEMISTRY REVIEW(S)
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

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<tr>
<th>Submission Type</th>
<th>Document Date</th>
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<td>02-APR-1999</td>
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Applicant:  SmithKline Beecham Pharmaceuticals
            1250 South Collegeville Road
            Mail Code UP4340, PO Box 5089
            Collegeville, PA 19426-0989

Drug Product Name: Proprietary:
                   Nonproprietary/Established/USAN:
                   Chem.Type/Ther.Class:

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
Route of Administration: Oral

Strength(s): 1.0-, 2.0-, 4.0- and 8.0-mg
Dispensed: N

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

\[
\text{C}_{12}\text{H}_{16}\text{N}_{2}\text{O}_{5}\text{S} \cdot \text{C}_{2}\text{H}_{4}\text{O}_{4}
\]

MW = 357.4 + 116.1 = 473.5

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

Patent Information: Patent #: Expiring date/Type of patent/Owner/
5,002,953/30-AUG-2008/drug, formulation and use/SmithKline 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/RSheigerwalt/JWeber/XYseym
    HFD-820/JGibbs

R/D Init by:

filename: nda21071_1.doc

Xavier Ysern, PhD

NDA 21-071  CMC Review # 1
DIVISION OF METABOLISM AND ENDOCRINE DRUG PRODUCTS - HFD-510
Review of Chemistry, Manufacturing and Controls

NDA 21-071

Submission Type: Original
24-NOV-1998
Amendment: 11-JAN-1999
02-APR-1999
12-APR-1999
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:
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.

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MW = 357.4 + 116.1 = 473.5
\( (\pm )-[4-[2-\text{Methyl}-2-(\text{pyridinylamino})\text{ethoxy}][\text{phenyl}][\text{methyl}]-2,4-\text{thiazolidinedione (Z)-2-butenedioate (1:1) } \)

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/XYsrem
HFD-820/JGibbs

R/D Init by: /S/ Xavier Ysrem, PhD

filename: /nda/21071_2.doc

NDA 21,071 Original Submission CMC Review # 2