

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-202

CHEMISTRY REVIEW(S)

SEP 28 2000

DIVISION OF METABOLISM AND ENDOCRINE DRUG PRODUCTS - HFD-510

Review of Chemistry, Manufacturing and Controls

NDA 21-202 Chemistry Review # 3 Date Reviewed: 27-SEP-2000

Submission Type Document Date CDER Rec. Date Filing Date U.F. ID #
Original 12-NOV-1999 12-NOV-1999 12-JAN-2000 3831

Applicant: Bristol-Myers Squibb Pharmaceutical Research Institute
P.O Box 4000 Phone: (609) 252-5228
Princeton, NJ 08543-4000 Fax: (609) 252-6000

Drug Product Name Proprietary: Glucophage XR
Nonproprietary/Established/USAN: Metformin HCl Extended Release Tablets
Chem.Type/ Ther.Class: 3 S

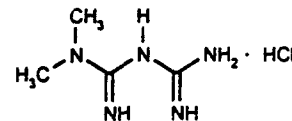
Pharmacological Category/indication: Hypoglycemic Agent. Adjunct to diet to improve glycemic control in patients with NIDDM whose hyperglycemia cannot be managed by diet alone.

Dosage Form: Tablets Strength(s): 500-mg
Route of Administration: Oral Dispensed: R

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

Metformin Hydrochloride

C4H11N5 · HCl
MW = 129.17 + 36.46 = 165.63
CAS 657-25-9 (free base) 1115-70-4 (hydrochloride)



N,N-Dimethylimidodicarbonimidic diamine monohydrochloride or N,N-Dimethylbiguanide HCl

Conclusions & Recommendations: Satisfactory CMC information has been provided to assure the quality of Glucophage XR (metformin hydrochloride) Modified Release Tablets. All the facilities involved in the manufacture, testing and packaging of both drug substance and drug product have been found acceptable by the Office of Compliance (EER Summary Report dated 27-SEP-2000, attached). From the Chemistry viewpoint the application can be approved.

[/S/]
Xavier Ysern, PhD

Orig. NDA 21-202
cc: HFD-510/Division File
HFD-510/SMalozowski/SMoore/JEI-Hagel/JWeber/XYsern
HFD-820/JGibbs

R/D Init by:

Handwritten initials and date: AP, /S/, 1.9/27/00

filename: /nda/21202_3.doc

WITHHOLD 4 PAGE(S)

WITHHOLD 7 PAGE (S)

APR 25 2000

DIVISION OF METABOLISM AND ENDOCRINE DRUG PRODUCTS - HFD-510

Review of Chemistry, Manufacturing and Controls

NDA 21-202 Chemistry Review # 1 Date Reviewed: 20-APR-2000

Submission Type Original Document Date 12-NOV-1999 CDER Rec. Date 12-NOV-1999 Filing Date 12-JAN-2000 U.F. ID # 3831

Applicant: Bristol-Myers Squibb Pharmaceutical Research Institute P.O Box 4000 Princeton, NJ 08543-4000 Phone: (609) 252-5228 Fax: (609) 252-6000

Drug Product Name Proprietary: Glucophage XR Nonproprietary/Established/USAN: Metformin HCl Extended Release Tablets Chem.Type/ Ther.Class: 3 S

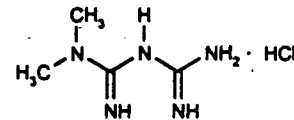
Pharmacological Category/indication: Hypoglycemic Agent. Adjunct to diet to improve glycemic control in patients with NIDDM whose hyperglycemia cannot be managed by diet alone.

Dosage Form: Tablets Strength(s): 500-mg Route of Administration: Oral Dispensed: R

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

Metformin Hydrochloride

C4H11N5 · HCl MW = 129.17 + 36.46 = 165.63 CAS 657-25-9 (free base) 1115-70-4 (hydrochloride)



N,N-Dimethylimidodicarbonimidic diamine monohydrochloride or N,N-Dimethylbiguanide HCl

Conclusions & Recommendations: Satisfactory CMC information has been provided to assure the quality of Glucophage XR (metformin hydrochloride) Modified Release Tablets. From the Chemistry viewpoint the application is approvable pending satisfactory results of the inspection of the manufacturing.

[/S/] Xavier Ysern, PhD

Orig. NDA 21-202 cc: HFD-510/Division File HFD-510/SMalozowski/SMoore/RSteigerwalt/JWeber/XYsern HFD-820/JGibbs

R/D Init by:

BEST POSSIBLE COPY

filename: /nda/21202_1.doc

AE [/S/ 4/24/2000]

WITHHOLD 23 PAGE (S)