

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-178

CHEMISTRY REVIEW(S)

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

NDA 21-178

Chemistry Review # 1

Date Reviewed: 25-JUL-2000

Submission Type	Document Date	CDER Rec. Date	Filing Date	U.F. ID #
Original	30-SEP-1999	01-OCT-1999	29-NOV-1999	3809
Amendment	28-APR-2000	28-APR-2000		
Amendment	16-JUN-2000	16-JUN-2000		
Amendment	23-JUN-2000	26-JUN-2000		
Amendment	13-JUL-2000	14-JUL-2000		

Applicant: Bristol-Myers Squibb Pharmaceutical Research Institute
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Princeton, NJ 08543-4000

(609) 252-5228
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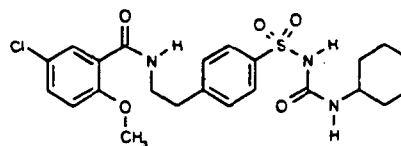
Drug Product Name Proprietary: Glucovance®
Nonproprietary/Established/USAN: Glyburide/Metformin Hydrochloride Fixed Combination Tablets
Chem. Type/ Ther. Class: 1 S

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

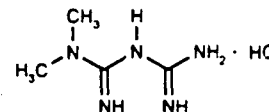
Dosage Form: Tablets **Strength(s):** 1.25-/250-, 2.5-/500- and 5-mg/500-mg
Route of Administration: Oral **Dispensed:** R

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

Glyburide
C₂₃H₂₈ClN₃O₅S
MW = 494.0
CAS 10238-21-8
1-[[p-[2-(5-Chloro-o-anisamido)-ethyl]phenyl]sulfonyl]-3-cyclohexylurea



Metformin Hydrochloride
C₄H₁₁N₅ · HCl
MW = 129.17 + 36.46 = 165.63
CAS 657-25-9 (base) 1115-70-4 (hydrochloride)
N,N-Dimethylimidodicarbonimidic diamine monohydrochloride or N,N-Dimethylbiguanide HCl



Conclusions & Recommendations: Satisfactory CMC information has been provided for the drug substances, Glyburide and Metformin hydrochloride, and drug product Glucovance® (metformin hydrochloride and glyburide) combination Tablets. From the Chemistry viewpoint the application is approvable pending satisfactory results of the inspection of the manufacturing facilities and an acceptable response to the minor deficiencies listed in the Draft Letter. See Draft Deficiencies and Comments.

Orig. NDA 21-178
cc: HFD-510/Division File
HFD-510/KochW/MisbinR/MooreS/SteigerwaltR/YsernX
HFD-820/GibbsJ

[/S/]

Xavier Ysern, PhD

R/D Init: by:

filename: /nda/21178_1.doc

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[/S/]
7/28/2000

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

NDA 21-178

Chemistry Review # 2

Date Reviewed: 28-JUL-2000

Submission Type	Document Date	CDER Rec. Date	Filing Date	U.F. ID #
Original	30-SEP-1999	01-OCT-1999	29-NOV-1999	3809
Amendment	26-JUL-2000	28-JUL-2000		
Amendment	28-JUN-2000	28-JUL-2000		

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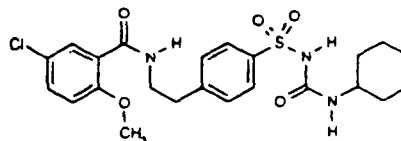
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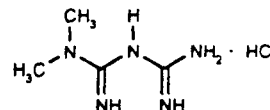
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Orig. NDA 21-178
cc: HFD-510/Division File
HFD-510/KochW/MisbinR/MooreS/SteigerwaltR/YsemX
HFD-820/GibbsJ

[/S/]
Xavier Ysem, PhD

R/D Init by:

AP

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