

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20802

CHEMISTRY REVIEW(S)

DIVISION OF ANTI-INFLAMMATORY, ANALGESIC AND OPHTHALMIC DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA #: 20-802

REVIEW # 1

DATE REVIEWED: 4/24/97

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
SUBMISSION	1/14/97	1/15/97	1/24/97

AMENDMENT

NAME & ADDRESS OF APPLICANT:

Bristol-Myers Products
1350 Liberty Avenue
Hillside, NJ 07207-6050

DRUG PRODUCT NAME

Proprietary: Excedrin® Extra Strength Tablets Caplets and Geltabs
Established: Acetaminophen (250 mg), aspirin (250 mg) & caffeine (65 mg)

Code Name/#:

Chem.Type/Ther.Class:

PHARMACOL. CATEGORY: Antiinflammatory

DOSAGE FORM: Tablets, Caplets and Geltabs

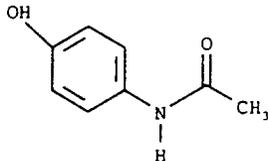
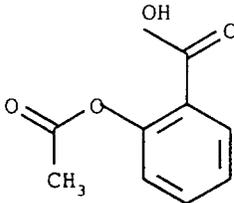
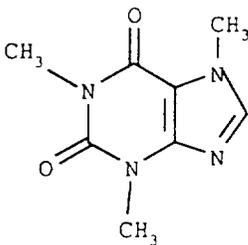
STRENGTHS: Acetaminophen (250 mg), aspirin (250 mg) & caffeine (65 mg)

ROUTE OF ADMINISTRATION: oral

DISPENSED: Rx OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA AND WEIGHT:

Attribute	Acetaminophen	Aspirin	Caffeine
Chemical Name:	N-(4-hydroxy-phenyl)-acetamide	2-(Acetoxy)benzoic acid	1,3,7-Trimethylxanthine
Molecular Weight	151.17	180.16	194.19
Molecular Formula	C ₈ H ₉ NO ₂	C ₉ H ₈ O ₄	C ₈ H ₁₀ N ₄ O ₂

Structural Formula			
CAS #	130-90-2	50-78-2	58-08-2
Physical Description	Large monoclinic prisms. V. slightly sol. in cold water. Sol. in methanol, ethanol, acetone and ethyl acetate. UV max 250 nm	Needle like crystals. Sparingly sol. in water with decomp. Decomp. in moist air. Sol. in alcohols, chlorof. and ether. UV max 229 nm.	Very sol. in water. Less sol. in alcohols, chlorof. and ether.

SUPPORTING DOCUMENTS:

IND #

RELATED DOCUMENTS

USP and Merck Index.

REMARKS:

There is no approved NDA for this product. Therefore, this NDA is submitted for a new indication for products that have been on the OTC market for many years. No changes have been made in the NDA with regard to CMC procedures used for the manufacture of the OTC products.

CONCLUSIONS & RECOMMENDATIONS:

The information provided in the CMC section is satisfactory, but some deficiencies need to be addressed. It is recommended that the NDA be approvable, pending satisfactory resolution of these deficiencies..

Hasmukh B. Patel
Hasmukh Patel Ph. D., Team Leader

7-7-97
Date

Vispi P. Bhavnagri
Vispi P. Bhavnagri Ph. D., Review Chemist

5/29/97 Revised 7-7-97
Date

CC:

NDA # 20-802.
HFD-550/Division File
HFD-550/V.Bhavnagri
HFD-550/H.Patel
HFD-550/S.Cook

HFD-550/W.Chambers
HFD-550/D.Bashaw
HFD-550/C.Fang
HFD-550/W.Coulter
HFD-830/C.Chen

APPROVABLE

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DIVISION OF ANTI-INFLAMMATORY, ANALGESIC AND OPHTHALMIC DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA #: 20-802

REVIEW # 2

DATE REVIEWED: 11/26/97

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
SUBMISSION	10/10/97	10/10/97	10/23/97

AMENDMENT BC 11/18/97

11/19/97

NAME & ADDRESS OF APPLICANT: 11/17

11/20/97

Bristol-Myers Products
1350 Liberty Avenue
Hillside, NJ 07207-6050

DRUG PRODUCT NAME

Proprietary: Excedrin® Extra Strength Tablets Caplets and Geltabs

Established: Acetaminophen (250 mg), aspirin (250 mg) & caffeine (65 mg)

Code Name/#:

Chem.Type/Ther.Class:

PHARMACOL. CATEGORY: Antiinflammatory

DOSAGE FORM: Tablets, Caplets and Geltabs

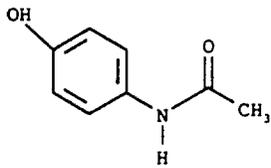
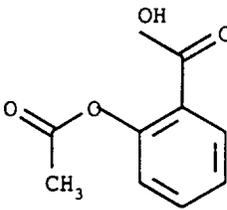
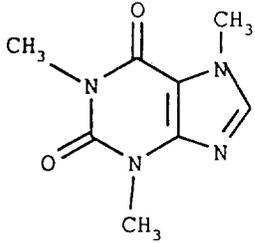
STRENGTHS: Acetaminophen (250 mg), aspirin (250 mg) & caffeine (65 mg)

ROUTE OF ADMINISTRATION: oral

DISPENSED: ___ Rx X OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA AND WEIGHT:

Attribute	Acetaminophen	Aspirin	Caffeine
Chemical Name:	N-(4-hydroxy-phenyl)-acetamide	2-(Acetoxy)benzoic acid	1,3,7-Trimethylxanthine
Molecular Weight	151.17	180.16	194.19
Molecular Formula	C ₈ H ₉ NO ₂	C ₉ H ₈ O ₄	C ₈ H ₁₀ N ₄ O ₂

Structural Formula			
CAS #	130-90-2	50-78-2	58-08-2
Physical Description	Large monoclinic prisms. V. slightly sol. in cold water. Sol. in methanol, ethanol, acetone and ethyl acetate. UV max 250 nm	Needle like crystals. Sparingly sol. in water with decomp. Decomp. in moist air. Sol. in alcohols, chlorof. and ether. UV max 229 nm.	Very sol. in water. Less sol. in alcohols, chlorof. and ether.

SUPPORTING DOCUMENTS:

None

RELATED DOCUMENTS

USP and Merck Index.

REMARKS:

All the deficiencies have been addressed satisfactorily (see attachment). The EER was also found to be satisfactory (see attachments). The company wanted to give the product a new name for treating the signs and symptoms of Migraine. The Nomenclature and Labeling Committee has no objection to the company using the name "Excedrin Migraine"(see attachment).

CONCLUSIONS & RECOMMENDATIONS:

All the CMC issues have been addressed satisfactorily. It is recommended that the NDA be approved.

Signature of H. Patel
Hasmukh Patel Ph. D., Team Leader

Dec. 5, 1997
Date

Signature of V. P. Bhavnagri
Vispi P. Bhavnagri Ph. D., Review Chemist

12/5/97
Date

CC:

NDA # 20-802

HFD-550/Division File

HFD-550/V. Bhavnagri

HFD-550/H. Patel

HFD-550/S. Cook

HFD-550/J. Hyde

HFD-550/D. Bashaw

HFD-550/C. Fang

HFD-550/W. Coulter

HFD-830/C. Chen

APPROVE

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