CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

20-488

Trade Name: Magnesium Sulfate in 5% Dextrose Injection in Plastic Container, 10 mg/ml 20 mg/ml

Generic Name: magnesium sulfate in 5% dextrose

Sponsor: Abbott Laboratories

Approval Date: July 11, 1995

Indications: For use as an intravenous anticonvulsant for the prevention and control of seizures in severe toxemia of pregnancy.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-488

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	X
Other Action Letters	
Labeling	X
Summary Review	
Officer/Employee List	
Office Director Memo	
Cross Discipline Team Leader Review	
Medical Review(s)	X
Chemistry Review(s)	X
Environmental Assessment	
Pharmacology Review(s)	X
Statistical Review(s)	
Microbiology Review(s)	X
Clinical Pharmacology/Biopharmaceutics Review(s)	X
Other Reviews	
Risk Assessment and Risk Mitigation Review(s)	
Proprietary Name Review(s)	
Administrative/Correspondence Document(s)	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-488

APPROVAL LETTER

NDA 20-488

JUL 11 1995

Abbott Laboratories
Attention: Mr. Frederick A. Gustafson
Director, Regulatory Affairs
One Abbott Park Road
ABBOTT PARK ILL 60064

Dear Mr. Gustafson:

Please refer to your July 7, 1994, new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Magnesium Sulfate in 5% Dextrose Injection, 10 mg/mL and 20 mg/mL.

We acknowledge receipt of your amendments dated September 23 (2) and 27 and December 15, 1994, and January 11, March 31, May 22, and telefacsimiles dated July 5 and 6, 1995.

This new drug application provides for new strengths and a new solvent (dextrose) in plastic containers for use as an intravenous anticonvulsant for the prevention and control of seizures in severe toxemia of pregnancy.

We have completed the review of this application including the submitted draft labeling (July 5, 1995, package insert and September 23, 1995, container labels and overwraps) and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the draft labeling submitted July 5, 1995 with the revisions listed below. Accordingly, the application is approved. The revisions are as follows:

1. All references to the word [redacted] must be changed to the word "serum" in the package insert. b(4)

2. The "pharmacokinetic" subsection of the CLINICAL PHARMACOLOGY section of the package insert should be headed "Pharmacokinetics".

3. The "Special Populations" subheading within the "pharmacokinetic" subsection in the CLINICAL PHARMACOLOGY section should include only Renal Insufficiency, Hepatic Insufficiency, and Drug-Drug Interactions. [redacted] b(4)

4. In the PRECAUTIONS section, please remove reference to [redacted]

5. Within the PRECAUTIONS section, change the "Carcinogenesis, Mutagenesis, Impairment of Fertility" subsection to read "Studies with Magnesium Sulfate in

5% Dextrose Injection have not been performed to evaluate carcinogenic potential, mutagenic potential, or effects on fertility."

6. Within the PRECAUTIONS section, the subsection "Nursing Mothers" should read, "It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Magnesium Sulfate in 5% Dextrose Injection is administered to a nursing woman."

7. Also within the PRECAUTIONS section please omit the subsection ——— b(4)

These revisions are terms of the NDA approval. Marketing the product before making the revisions, exactly as requested, in the product's final printed labeling (FPL) may render the product misbranded and an unapproved new drug.

Please submit fifteen copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy weight paper or similar material. For administrative purposes this submission should be designated "FINAL PRINTED LABELING" for approved NDA 20-488. Approval of this labeling by FDA is not required before it is used.

Should additional information relating to the safety and effectiveness of the drug become available, further revision of that labeling may be required.

Please submit three copies of the introductory promotional material that you propose to use for these products. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional material and the package inserts directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising and Communications (HFD-240)
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of each strength product when available.

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any deficiencies that may occur.

Under section 736(a)(1)(B)(ii) of the Prescription Drug User Fee Act of 1992, this letter triggers the remaining 50% of the fee assessed for this application. You will receive an invoice for the amount due within the next month. Payment will be due within 30 days of the date of the invoice.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact:

Ms. Christina Kish
Consumer Safety Officer
(301) 443-3510

Sincerely yours,

9/18/95

Solomon Sobel, M.D.
Director
Division of Metabolism and
Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Original NDA
HFD-510
HF-2/Medwatch(+ draft labeling)
DISTRICT OFFICE
HFD-3/MLumpkin (+draft labeling)
HFD-5/THassall
HFD-85/+ draft labeling + exclusivity checklist
HFD-500/LRipper (+ draft labeling)
HFD-510/PPrice/DWu/DHertig
HFD-240/+ draft labeling
HFD-638/+ draft labeling
HFD-735/DBarash (+ draft labeling)
HFD-510/CKish/7.7.95/n20488.ap

Concurrences:PCorfman 7.10.95/DWu 7.10.95/YChiu 7.10.95/DHertig 7.11.95/EBarbenhen 7.11.95

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-488

LABELING

Labeling: EA Quiqes
NDA No: 20488 Rec'd. 8-7
Reviewed by: C Hurt 8/8/2

MAGNESIUM SULFATE IN 5% DEXTROSE INJECTION

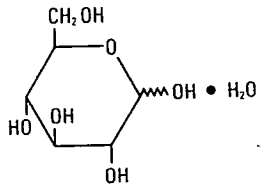
Flexible Plastic Container
For Intravenous Use Only

DESCRIPTION

Magnesium Sulfate in 5% Dextrose Injection is a sterile, nonpyrogenic solution of magnesium sulfate heptahydrate and dextrose in water for injection. Each 100 mL contains 1 or 2 g magnesium sulfate heptahydrate and dextrose, hydrous 5 g in water for injection. May contain sulfuric acid and/or sodium hydroxide for pH adjustment. The pH is 4.5 (3.5 to 6.5). It is available in 1% and 2% concentrations. See HOW SUPPLIED section for the content and characteristics of available dosage forms and sizes.

Magnesium Sulfate, USP heptahydrate is chemically designated $MgSO_4 \cdot 7H_2O$, colorless crystals or white powder freely soluble in water.

Dextrose, USP is chemically designated D-glucose, monohydrate ($C_6H_{12}O_6 \cdot H_2O$), a hexose sugar freely soluble in water. It has the following structural formula:



Molecular weight 198.17.

Water for Injection, USP is chemically designated H_2O.

The flexible plastic container is fabricated from a specially formulated polyvinylchloride. Water can permeate from inside the container into the overwrap but not in amounts sufficient to affect the solution significantly. Solutions in contact with the plastic container may leach out certain chemical components from the plastic in very small amounts; however, biological testing was supportive of the safety of the plastic container materials. Exposure to temperatures above 25°C/77°F during transport and storage will lead to minor losses in moisture content. Higher temperatures lead to greater losses. It is unlikely that these minor losses will lead to clinically significant changes within the expiration period.

CLINICAL PHARMACOLOGY

Magnesium (Mg^{++}) is an important cofactor for enzymatic reactions and plays an important role in neurochemical transmission and muscular excitability.

Magnesium prevents or controls convulsions by blocking neuromuscular transmission and decreasing the amount of acetylcholine liberated at the end plate by the motor nerve impulse. Magnesium is said to have a depressant effect on the central nervous system, but it does not adversely affect the mother, fetus or neonate when used as directed in eclampsia or pre-eclampsia. Normal serum magnesium levels range from 1.3 to 2.1 mEq/liter.

As serum magnesium rises above 4 mEq/liter, the deep tendon reflexes are first decreased and then disappear as the serum level approaches 10 mEq/liter. At this level respiratory paralysis may occur. Heart block also may occur at this or lower serum levels of magnesium.

Magnesium acts peripherally to produce vasodilation. With low doses only flushing and sweating occur, but larger doses cause lowering of blood pressure. The central and peripheral effects of magnesium poisoning are antagonized to some extent by intravenous administration of calcium.

With intravenous administration the onset of anticonvulsant action is immediate and lasts about 30 minutes. Following intramuscular administration the onset of action occurs in about one hour and persists for three to four hours. Effective anticonvulsant serum levels range from 2.5 to 7.5 mEq/liter.

Pharmacokinetics:

Absorption: Intravenously administered magnesium is immediately absorbed.

Distribution: Approximately 1-2% of total body magnesium is located in the extracellular fluid space. Magnesium is 30% bound to albumin.

Metabolism: Magnesium is not metabolized.

Excretion: Magnesium is excreted solely by the kidney at a rate proportional to the serum concentration and glomerular filtration.

Special Populations:

Renal Insufficiency: Magnesium is excreted solely by the kidney. In patients with severe renal insufficiency, the dose should be lower and frequent serum magnesium levels must be obtained (see Dosage and Administration).

Hepatic Insufficiency: Magnesium is excreted solely by the kidney. No dosing adjustments are necessary in hepatic insufficiency.

Drug-Drug Interactions: Drug induced renal losses of magnesium occur with the following drugs or drug classes:

Aminoglycosides	Amphotericin B
Cyclosporine	Diuretics
Digitalis	Cisplatin
Alcohol	

INDICATIONS AND USAGE

Magnesium Sulfate in 5% Dextrose Injection is indicated for use as an intravenous anticonvulsant for the prevention and control of seizures (convulsions) in severe toxemia of pregnancy. When used judiciously it effectively prevents and controls the convulsions of eclampsia without producing deleterious depression of the central nervous system of the mother or infant. However, other effective drugs are available for this purpose.

CONTRAINDICATIONS

Intravenous magnesium should not be given to mothers with toxemia of pregnancy during the two hours preceding delivery.

WARNINGS

Intravenous use in eclampsia should be reserved for immediate control of life-threatening convulsions.

Parenteral use in the presence of renal insufficiency may lead to magnesium intoxication.

PRECAUTIONS

Because magnesium is removed from the body solely by the kidneys, the drug should be used with caution in patients with renal impairment. Urine output should be maintained at a level of 100 mL every four hours. Monitoring serum magnesium levels and the patient's clinical status is essential to avoid the consequences of overdosage in toxemia. Clinical indications of a safe dosage regimen include the presence of the patellar reflex (knee jerk) and

absence of respiratory depression (approximately 16 breaths or more/minute). Serum magnesium levels usually sufficient to control convulsions range from 3 to 6 mg/100 mL (2.5 to 5 mEq/liter). The strength of the deep tendon reflexes begins to diminish when serum magnesium levels exceed 4 mEq/liter. Reflexes may be absent at 10 mEq magnesium/liter, where respiratory paralysis is a potential hazard. An injectable calcium salt should be immediately available to counteract the potential hazards of magnesium intoxication in eclampsia.

Magnesium Sulfate in 5% Dextrose Injection should be administered slowly to avoid producing hypermagnesemia.

Carcinogenesis, Mutagenesis, Impairment of Fertility:
Studies with Magnesium Sulfate in 5% Dextrose Injection have not been performed to evaluate carcinogenic potential, mutagenic potential or effects on fertility.

Pregnancy Category A. Studies in pregnant women have not shown that magnesium sulfate injection increases the risk of fetal abnormalities if administered during all trimesters of pregnancy. If this drug is used during pregnancy, the possibility of fetal harm appears remote. However, because studies cannot rule out the possibility of harm, magnesium sulfate solution should be used during pregnancy only if clearly needed.

When administered by continuous intravenous infusion (especially for more than 24 hours preceding delivery) to control convulsions in toxemic mothers, the newborn may show signs of magnesium toxicity, including neuromuscular or respiratory depression. See OVERDOSAGE.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Magnesium Sulfate in 5% Dextrose Injection is administered to a nursing woman.

ADVERSE REACTIONS

The adverse effects of parenterally administered magnesium usually are the result of magnesium intoxication. These include flushing, sweating, hypotension, depressed reflexes, flaccid paralysis, hypothermia, circulatory collapse, cardiac and central nervous system depression proceeding to respiratory paralysis. Hypocalcemia with signs of tetany secondary to magnesium sulfate therapy for eclampsia has been reported.

OVERDOSAGE

Magnesium intoxication is manifested by a sharp drop in blood pressure and respiratory paralysis. Disappearance of the patellar reflex is a useful clinical sign to detect the onset of magnesium intoxication. In the event of overdosage artificial ventilation must be provided until a calcium salt can be injected intravenously to antagonize the effects of magnesium.

In adults intravenous administration of 5 to 10 mEq of 10% calcium gluconate will usually reverse respiratory depression or heart block due to magnesium intoxication. In extreme cases, peritoneal or hemodialysis may be required.

Hypermagnesemia in the newborn may require resuscitation and assisted ventilation via endotracheal intubation or intermittent positive pressure ventilation as well as intravenous calcium.

DOSAGE AND ADMINISTRATION

Magnesium Sulfate in 5% Dextrose Injection is intended for intravenous use only. For the management of pre-eclampsia or eclampsia, intravenous infusions of dilute solutions of magnesium (1% to 8%) are often given in combination with intramuscular injections of 50% Magnesium Sulfate Injection, USP. Therefore, in the clinical conditions cited below, both forms of therapy are noted, as appropriate.

In Eclampsia

In severe pre-eclampsia or eclampsia, the total initial dose is 10 to 14 g of magnesium sulfate. To initiate therapy, 4 g of Magnesium Sulfate in 5% Dextrose Injection may be administered intravenously. The rate of I.V. infusion should generally not exceed 150 mg/minute, or 7.5 mL of a 2% concentration (or its equivalent) per minute, except in severe eclampsia with seizures. Simultaneously, 4 to 5 g (32.5 to 40.6 mEq) of magnesium sulfate may be administered intramuscularly into each buttock using undiluted 50% Magnesium Sulfate Injection, USP. After the initial I.V. dose, some clinicians administer 1-2 g/hour by constant I.V. infusion.

Subsequent intramuscular doses of 4 to 5 g of magnesium sulfate may be injected into alternate buttocks every four hours, depending on the continuing presence of the patellar reflex, adequate respiratory function, and absence of signs of magnesium toxicity. Therapy should continue until paroxysms cease.

A serum magnesium level of 6 mg/100 mL is considered optimal for control of seizures. A total daily (24 hr) dose of 30 to 40 g magnesium sulfate should not be exceeded. In the presence of severe renal insufficiency, frequent serum magnesium concentrations must be obtained, and the maximum recommended dosage of magnesium sulfate is 20 g per 48 hours.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Do not administer unless solution is clear. Discard unused portion.

HOW SUPPLIED

Magnesium Sulfate in 5% Dextrose Injection is supplied in single-dose flexible plastic containers as follows:

List No.	Size Container	Total Magnesium Sulfate*	Total Magnesium Ion	Magnesium Sulfate* Concentration	Magnesium Ion Concentration	Osmolarity (calc.)
6727	100 mL	1 g	8.1 mEq	1% (10 mg/mL)	8.1 mEq/100 mL	333 mOsmol/Liter
6727	1000 mL	10 g	81.1 mEq	1% (10 mg/mL)	8.1 mEq/100 mL	333 mOsmol/Liter
6728	500 mL	10 g	81.1 mEq	2% (20 mg/mL)	16.2 mEq/100 mL	415 mOsmol/Liter
6728	1000 mL	20 g	162.3 mEq	2% (20 mg/mL)	16.2 mEq/100 mL	415 mOsmol/Liter

*As the heptahydrate.

WARNING: DO NOT USE FLEXIBLE CONTAINER IN SERIES CONNECTIONS.

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. Protect from freezing. It is recommended that the product be stored at room temperature (25°C/77°F); however, brief exposure up to 40°C does not adversely affect the product.

Caution: Federal (USA) law prohibits dispensing without prescription.

06-9244-R1-Rev. July, 1995

Printed in USA

ABBOTT LABORATORIES, NORTH CHICAGO, IL 60064, USA

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-488

MEDICAL REVIEW(S)

ORIGINAL JUN 1995

Memo to the File
July 10, 1995
Re: NDA 20-488

On July 7, 1995, the division of Biopharmaceutics completed it's review of NDA 20-488. In the review, a request was made for the reviewing medical officer to comment on the amount of dextrose to be used with this drug. On July 7, 1995, Dr. Corfman was notified of this request. He noted that the amount of Dextrose used was standard practice, and therefore nothing to be concerned about.

7/10/95

Christina Kish, CSO

cc:
Original NDA
HFD-510
HFD-510/CKish/PPrice/PCorfman

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-488

CHEMISTRY REVIEW(S)

ORIGINAL JUN 27 1995

DIVISION OF METABOLISM AND ENDOCRINE DRUG PRODUCTS - HFD-510

Review of Chemistry, Manufacturing, and Controls

NDA #: 20-488 **Date Reviewed:** 6/27/95

Review #: 1 **Reviewer:** Duu-Gong Wu

Submission Type	Document Date	CDER Date	Assigned Date
Original	7/12/94	7/12/94	7/13/94 (User Fee: 7/11/95)
Amendment	9/23/94		
Amendment	1/11/95		
Amendment	3/3/95		
Amendment	5/22/95		

Name & Address Of Applicant: Abbott Laboratories
One Abbott Park Road
Illinois 60064

Drug Product Name

Proprietary:

Established: Magnesium Sulfate in 5% Dextrose Injection

Code Name/#:

Chem. Type/Ther. Class: SVP & LVP

ANDA Suitability Petition/DESI/Patent Status: N/A

Pharmacol. Category/Indication: Anticonvulsant

Dosage Form: Injection

Strengths: 10 mg/mL (100 mL and 1000 mL in 5% dextrose in PVC container)
20 mg/mL (500 mL and 1000 mL in 5% dextrose in PVC container)

Route Of Administration: Intravenous

Dispensed: __X__ Rx _____ OTC

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

$MgSO_4.7H_2O$, Mol. Wt. 120.38

Supporting Documents:

NDA 20-309 (magnesium sulfate in water for injection), NDA 16-366, NDA 16-367, DMF — (Abbott Laboratories, Type — , DMF 1218 (Abbott Laboratories, Type I)

b(4)

Related Documents (if applicable):

Consults: Microbiology

Remarks:

Magnesium sulfate, which is a grandfathered drug, has been used as an intravenous anticonvulsant for the prevention and control of seizures in severe toxemia of pregnancy. Magnesium sulfate injection and in 5% dextrose are currently marketed by Abbott Laboratories in glass containers and magnesium sulfate in water for injection in PVC plastic container was recently approved (NDA 20-309, Magnesium sulfate in water for injection). Abbott Laboratories is filing this NDA to formulate the magneisium sulfate in 5% dextrose to be packaged in PVC plastic containers. According to 21 CFR 310.509, a NDA is required for any

parenteral drug packaged in a plastic container.

The four dosage strengths of different concentration and volume include 10 mg/mL mangesium sulfate either in 100 mL or 1,000 mL 5% dextrose in PVC bags and 20 mg/mL mangesium sulfate either in 500 mL or 1,000 mL 5% dextrose in PVC containers. The 100, 500, and 1,000 mL PVC containers are currently approved in more than ____ NDAs in HFD-160, HFD-530, and HFD-630, and most recently for NDA 20-309 in this division. The safety and efficacy of the PVC material from which the finished container is fabricated have been well established in preclinical and clinical studies. Abbott has referred **NDA 20-309, NDA 16-367** for data and Abbott's **DMF** ____ for : ____, and manufacturing procedure. The amendment of **9/23/94** provides for additional information including Debarment statement and patent information. The amendments of **12/15/94** and **1/11/95** provide information requested by the reviewer during the review of NDA 20-309/s001. The information is for the same 500 and 1,000 mL PVC containers used in this NDA. The amendment dated **1/11/95** provides for stability data (12 month) for the 500 mL and 1000 mL doage form of the production batch size to support the requested expiration dating. The : ____

b(4)

____

b(4)

____

Conclusions & Recommendations:
Adequate information has been provided. The microbiology consult review also recommended approval of this submission and an acceptable FUR dated 6/23/95 has been received. From chemistry standpoint, the NDA now can be approved. Issue approval letter

Org. NDA 20-488
HFD-510
HFD-510/D.G.Wu/
HFD-510/C. Kish
HFD-510/Y. Chiu

Duu-Gong Wu, Ph.D.
Review Chemist

R/D Init by:
Filename: 20309.ND1

6/27/95

15 Page(s) Withheld

X Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-488

PHARMACOLOGY REVIEW(S)

NDA 20-488

31 January 1995

Abbott Hospital Products Division
One Abbott Park Road
Abbott Park, Illinois 60064-3500

JAN 31 1995

Submission: dtd 7 July 1994; Rec'd 12 Jul 94

ORIGINAL

REVIEW AND EVALUATION OF PHARMACOLOGY AND TOXICOLOGY DATA
Original Summary

Magnesium Sulfate 10 mg/ml and 20 mg/ml in 5% Dextrose Injection in Flexible Plastic Containers

Anticonvulsant

Indicated Use: As an intravenous anticonvulsant for the prevention and control of seizures (convulsions) in severe toxemia of pregnancy.

Related: NDA 20-309 - Magnesium sulfate

Comments:

Magnesium Sulfate has been used as an intravenous anticonvulsant for the prevention and control of seizures in severe toxemia of pregnancy prior to 1938, and thus its indication is "grandfathered".

This application for magnesium sulfate is being filed separately from NDA 20-309 (Magnesium Sulfate 40 mg/ml and 80 mg/ml in Water for Injection in Flexible Plastic Containers) at FDA's request because it is formulated in 5% dextrose rather than water, however, the active ingredient and indications for use are the same. Reportedly, the proposed PVC container is currently approved in more than [redacted] NDAs and is also used for the magnesium sulfate product submitted under NDA 20-309. It is reported that the safety and efficacy of the PVC material from which the finished container is fabricated have been well established in preclinical and clinical studies included in NDAs 16-366 and 16-367 in HFD-160. b(4)

Labeling: Reference to ": [redacted] should be removed from the Precautions section of the labeling. b(4)
Sections should be changed to read as follows:

Carcinogenesis, Mutagenesis, Impairment of Fertility: Studies with Magnesium Sulfate in 5% Dextrose Injection have not been performed to evaluate carcinogenic potential, mutagenic potential or effects on fertility.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Magnesium Sulfate in 5% Dextrose Injection is administered to a nursing woman.

[redacted] Omit b(4)

Recommendation:

Magnesium sulfate is currently marketed by Abbott Laboratories in glass containers in the same formulation, concentrations and volumes as proposed in this application for the flexible polyvinylchloride (PVC) container. Thus, if Chemistry can assure a pure product, Pharmacology recommends approval of NDA 20-488 for Magnesium Sulfate in plastic containers with the above labeling changes.

cc: Original NDA 20-488; HFD-345
HFD-510 NDA 20-488;
HFD-510 AJordan; HFD-510 DHertig

D. Hertig
David H. Hertig
Pharmacologist

A Jordan
1/31

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-488

MICROBIOLOGY REVIEW(S)

JAN 12 1995

Consultative Review to HFD-510
DIVISION OF MEDICAL IMAGING, SURGICAL,
and DENTAL DRUG PRODUCTS; HFD-160

Microbiologist's Review #1
11 January 1995

ORIGINAL

A. 1. NDA 20-488
APPLICANT: Abbott Laboratories
Hospital Products Division
One Abbott Park Road
Abbott Park, Illinois 60064-3500

2. PRODUCT NAMES: Magnesium Sulfate 10 mg/mL and 20 mg/mL in 5% Dextrose Injection in Flexible Plastic Containers

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
Sterile, nonpyrogenic solution in flexible polyvinylchloride container for intravenous administration. A concentration of 10 mg/mL in 100 mL (1 g total dose) or 1000 mL (10 g total dose) containers and a concentration of 20 mg/mL in 500 mL (10 g total dose) or 1000 mL (20 g total dose) are covered.

4. METHODS OF STERILIZATION:
The drug product is [redacted] sterilized. b(4)

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The drug is an anticonvulsant for the prevention and control of seizures (convulsions) in severe toxemia of pregnancy.

B. 1. DATE OF INITIAL SUBMISSION: 13 July 1994

2. DATE OF AMENDMENT: (none)

3. RELATED DOCUMENTS: Table 1. Documents referenced in NDA 20-488.

Document	Subject
NDA 20-309	Magnesium Sulfate 40 mg/mL and 80 mg/mL in Water for Injection in Plastic Containers
NDA 16-366	Safety of PVC Container
NDA 16-367	Safety of PVC Container
DMF [redacted]	[redacted] b(4)
DMF 1218	Abbott Labs, North Chicago facility
DMF 1561	Abbott Labs, Rocky Mount, NC facility

4. ASSIGNED FOR REVIEW: 12 December 1994

C. REMARKS: The application provides for packaging of the drug product in plastic, rather than glass containers. Administration and additive ports on the container are [redacted] prior to being attached to the bag. The active drug substance dissolved in Water for Injection, in similar packaging, has been previously approved. Since release criteria for this product have been reviewed previously, and are assumed not to have changed, they are not reviewed here. b(4)

D. CONCLUSIONS: The submission is recommended for approval on the basis of sterility assurance.

Paul Stinavage, Ph.D.

PHC 1/12/95

cc: Original NDA 20-488
HFD-160/Stinavage/Consult File
HFD-510/Div File/L. Stockbridge
Drafted by: P. Stinavage, 1/11/95
R/D initialed by P. Cooney, 1/12/95

7 Page(s) Withheld

X Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-488

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

ORIGINAL

JUL 7 1995

NDA 20-488
Magnesium Sulfate
10 and 20 mg/mL in 5% dextrose Injection
in Flexible Plastic Containers

SUBMISSION DATE: July 07, 1994

Abbott Laboratories
Abbott Park, IL

REVIEWER: Hae-Young Ahn, Ph.D.

TYPE OF SUBMISSION: Original

Code: 3S

SYNOPSIS: The sponsor has submitted an original NDA 20-488 for an injectable magnesium sulfate solution (10 and 20 mg/mL) in 5% dextrose. This NDA is for changing container from glass to a PVC flexible container. Currently this same product is on the market without an NDA and is being marketed in glass containers. For NDA 20-488, a request to waive the submission of evidence demonstrating in vivo bioavailability is granted under 21 CFR 320.22(e) (i.e., for good cause).

The sponsor faxed a revised package insert to the Agency on July 05, 1995 and the revised package insert contains the pharmacokinetic section which is formated based on the Division of Biopharmaceutics' recommendation.

COMMENT to the Medical Officer: The reviewing medical officer should assess if exposure to 10 - 20 g of dextrose is a safety concern to treated patients.

LABELING COMMENTS:
1. The pharmacokinetic part in the CLINICAL PHARMACOLOGY section of the package insert should be created with the heading, "Pharmacokinetics".

2. Under the pharmacokinetic part of the CLINICAL PHARMACOLOGY section, it is recommended that Special Population section include only Renal Insufficiency, Hepatic Insufficieny and Drug-Drug Interactions. It is recommended that

b(4)

RECOMMENDATION:
The Division of Biopharmaceutics has reviewed NDA 20-488 which was submitted on July 07, 1994 and it grants the sponsor's request for a waiver of the need to submit in vivo bioavailability data. The Division of Biopharmaceutics also finds the revised package insert acceptable, provided the labeling comments are incorporated as appropriate.

Please convey the Recommendation and Labeling Comments to the sponsor.

7/07/95

Hae-Young Ahn, Ph.D.
Reviewer, Division of Biopharmaceutics

RD/FT initiated by J. Hunt 7/7/95

cc: NDA 20-488, HFD-510 (Price and Kish), HFD-340 (Vish), HFD-426 (Fleischer), HFD-427 (Ahn, Chen.M), Chron, Drug, Review, FOI (HFD-19)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-488

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

EXCLUSIVITY SUMMARY FOR NDA # 20-488 SUPPL # _____

Trade Name Magnesium Sulfate in 5% Dextrose Inj Generic Name _____

Applicant Name Abbott HFD # 510

Approval Date If Known _____

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following question about the submission.

a) Is it an original NDA?

YES /✓/ NO /___/

b) Is it an effectiveness supplement?

YES /___/ NO /✓/

If yes, what type? (SE1, SE2, etc.) _____

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES /___/ NO /✓/

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

_____

_____

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

_____

_____

Form OGD-011347 Revised 7-90

cc: Original NDA Division File HFD-85 Mary Ann ~~Ward~~ Holovac

CSO Kish

d) Did the applicant request exclusivity?

YES /___/ NO /___/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

_____

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule, previously been approved by FDA for the same use?

YES /✓/ NO /___/

If yes, NDA # 20-309 Drug Name Magnesium Sulfate

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /___/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# _____ _____

NDA# _____ _____

NDA# _____ _____

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# _____ _____

NDA# _____ _____

NDA# _____ _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. IF "YES" GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /___/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /___/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

_____

_____

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /___/ NO /___/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion?

YES /___/ NO /___/

If yes, explain: _____

_____

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /___/

If yes, explain: _____

_____

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

_____

_____

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

_____ _____

_____ _____

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

_____ _____

_____ _____

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

_____ _____

_____ _____

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1	
IND # _____ YES /___/	NO /___/ Explain: _____
	_____
Investigation #2	
IND # _____ YES /___/	NO /___/ Explain: _____
	_____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1	
YES /___/ Explain _____	NO /___/ Explain _____
_____	_____
_____	_____
Investigation #2	
YES /___/ Explain _____	NO /___/ Explain _____
_____	_____
_____	_____

DF

NDA 20-488

SEP 22 1995

Abbott Laboratories
Attention: Ms. Jill Sackett
200 Abbott Park Road, D-389 AP30
ABBOTT PARK ILL 60064-3537

Dear Ms. Sackett:

We acknowledge the receipt of your August 4, 1995, submission containing final printed labeling in response to our July 11, 1995, letter approving your new drug application for Magnesium Sulfate in 5% Dextrose Injection.

We have reviewed the labeling that you have submitted in accordance with our July 11, 1995, letter, and we find it acceptable. This labeling will be retained in our files.

Sincerely yours,

9/21/95

Solomon Sobel, M.D.
Director
Division of Metabolism and
Endocrine Drug Products (HFD-510)

cc:
Original NDA
HFD-510
HFD-510/PPrice/DWu/DHertig
HF-2/medwatch (w/labeling)
DISTRICT OFFICE (w/labeling)
HFD-85/(w/labeling)
HFD-240/SSherman (w/labeling)
HFD-500/(w/labeling)
HFD-613/(w/labeling)
HFD-510/CKish/9.1,21.95/n20488.ar

concurrences:EGAlliers 9.20.95

ACKNOWLEDGE AND RETAIN (AR)

ABBOTT

ORIGINAL

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

FA

August 4, 1995

CENTER FOR DRUG EVALUATION AND RESEARCH
DIVISION OF METABOLISM AND ENDOCRINE
DRUG PRODUCTS, HFD #510
Attn: DOCUMENT CONTROL ROOM #14B-19
5600 Fishers Lane
Rockville, Maryland 20857

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
AUG 0 7 1995
HFD-510

ATTENTION: Solomon Sobel, M.D.
Director

RE: **FINAL PRINTED LABELING for Approved NDA 20-488**
Magnesium Sulfate (10 mg/mL and 20 mg/mL) in 5% Dextrose Injection

Abbott Laboratories hereby responds to an approval letter received from the Agency dated July 11, 1995, that requested final printed labeling (FPL) for the above referenced products. Fifteen copies of the requested FPL are enclosed with this correspondence.

Sincerely,

ABBOTT LABORATORIES

Jill N. Sackett
Manager, Regulatory Affairs
Hospital Products Division
Phone: (708) 937-4085
Fax: (708) 938-7867
8-95fda.jxn

REVIEWS COMPLETED

CSO ACTION:

☑ LETTER ☒ N.A.I.

CSO INITIALS DATE

9/22/96

Changes made as required w/ approval letter dated July 11, 1995. 9/9/96

Abbott called and request for made 9/9/96

b(4)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG FOR HUMAN USE OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314)

Form Approved: OMB No. 0910-0001
Expiration Date; March 31, 1990.
See OMB Statement on Page 3.

FOR FDA USE ONLY	
DATE RECEIVED	DATE FILED
DIVISION ASSIGNED	NDA/ANDA NO. ASS.

NOTE: No application may be filed unless a completed application form has been received *(21 CFR Part 314)*.

NAME OF APPLICANT
Abbott Laboratories

DATE OF SUBMISSION
August 4, 1995

ADDRESS *(Number, Street, City, State and Zip Code)*
200 Abbott Park Road, D-389 AP30
Abbott Park, Illinois 60064-3537

TELEPHONE NO. *(Include Area Code)*
(708) 937-3213

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER (If previously issued)
20-488

DRUG PRODUCT

ESTABLISHED NAME *(e.g., USP/USAN)*
Magnesium Sulfate 10mg/mL &q 20mg/mL in 5% Dextrose Injection in Flexible Plastic Containers

PROPRIETARY NAME *(If any)*

CODE NAME *(If any)*

CHEMICAL NAME $MgSO_4\ 7H_2O \quad (C_6H_{12}O_6\ H_2O)$

DOSAGE FORM	ROUTE OF ADMINISTRATION	STRENGTH(S)
Flexible Plastic Container	I.V.	10 & 20mg/mL

PROPOSED INDICATIONS FOR USE

I.V. anticonvulsant for the prevention and control of seizures (convulsions) in severe toxemia of pregnancy.

LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS *(21 CFR Part 312)*, NEW DRUG OR ANTIBIOTIC APPLICATIONS *(21 CFR Part 314)*, AND DRUG MASTER FILES *(21CFR 314.420)* REFERRED TO IN THIS APPLICATION:

INFORMATION ON APPLICATION

TYPE OF APPLICATION *(Check one)*

☒ THIS SUBMISSION IS A FULL APPLICATION *(21 CFR 314.50)* ☐ THIS SUBMISSION IS AN ABBREVIATED APPLICATION (ANDA) (21 CFR 314.55)

IF AN ANDA, IDENTIFY THE APPROVED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

NAME OF DRUG

HOLDER OF APPROVED APPLICATION

STATUS OF APPLICATION *(Check one)*

☐ PRESUBMISSION
☐ ORIGINAL APPLICATION
☒ AN AMENDMENT TO A PENDING APPLICATION
☐ RESUBMISSION
☐ SUPPLEMENTAL APPLICATION

PROPOSED MARKETING STATUS *(Check one)*

☒ APPLICATION FOR A PRESCRIPTION DRUG PRODUCT *(Rx)*
☐ APPLICATION FOR AN OVER - THE - COUNTER PRODUCT *(OTC)*

CONTENTS OF APPLICATION

This application contains the following items: *(Check all that apply)*

	1. Index
	2. Summary (21 CFR 314.50 (c))
	3. Chemistry, manufacturing, and control section (21 CFR 314.50 (d) (1))
	4. a. Samples (21 CFR 314.50 (e) (1)) (Submit only upon FDA's request)
	b. Methods Validation Package (21 CFR 314.50 (e) (2) (i))
▨	c. Labeling (21 CFR 314.50 (e) (2) (ii))
	i. draft labeling *(4 copies)*
X	ii. final printed labeling (12 copies)
	5. Nonclinical pharmacology and toxicology section (21 CFR 314.50 (d) (2))
	6. Human pharmacokinetics and bioavailability section (21 CFR 314.50 (d) (3))
	7. Microbiology section (21 CFR 314.50 (d) (4))
	8. Clinical data section (21 CFR 314.50 (d) (5))
	9. Safety update report (21 CFR 314.50 (d) (5) (vi) (b))
	10. Statistical section (21 CFR 314.50 (d) (6))
	11. Case report tabulations (21 CFR 314.50 (f) (1))
	12. Case reports forms (21 CFR 314.50 (f) (1))
	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b) (2) or (j) (2) (A))
	15. OTHER *(Specify)*

I agree to update this application with new safety information about the drug that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit these safety update reports as follows: (1) 4 months after the initial submission, (2) following receipt of an approvable letter and (3) at other times as requested by FDA. If this application is approved, I agree to comply with all laws and regulations that apply to approved applications, including the following:

1. Good manufacturing practice regulations in 21 CFR 210 and 211.
2. Labeling regulations in 21 CFR 201.
3. In the case of a prescription drug product, prescription drug advertising regulations in 21 CFR 202.
4. Regulations on making changes in application in 21 CFR 314.70, 314.71, and 314.72.
5. Regulations on reports in 21 CFR 314.80 and 314.81.
6. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the controlled substances Act I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

NAME OF RESPONSIBLE OFFICIAL OR AGENT	SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	DATE
Jill Sackett	Jill Sackett	08/02/95

ADDRESS *(Street, City, State, Zip Code)*	TELEPHONE NO. *(Include Area Code)*
200 Abbott Park Rd, D-389 AP30 Abbott Park, Illinois 60064-3537	(708) 937-4085

(WARNING: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec.1001.)

ABBOTT

ORIGINAL

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

July 6, 1995

CENTER FOR DRUG EVALUATION AND RESEARCH
DIVISION OF METABOLISM AND ENDOCRINE
DRUG PRODUCTS, HFD #510
Attn: DOCUMENT CONTROL ROOM #14B-19
5600 Fishers Lane
Rockville, Maryland 20857

ATTENTION: Solomon Sobel, M.D.
Director

Re: NDA 20-488 Magnesium Sulfate (10 mg/mL and 20 mg/mL) in 5% Dextrose Injection

Abbott Laboratories hereby submits a **Safety Update** to the above-referenced New Drug Application as requested by Ms. Christina Kish of the Division.

As stated in the subject application, there were no clinical studies associated with the subject NDA. The clinical information contained in this submission was included by reference to the clinical data included in Abbott Laboratories' approved NDA 20-309 Magnesium Sulfate Solution (40 mg/mL and 80 mg/mL) in Water for Injection in Flexible Containers. The studies included in NDA 20-309 are complete and there is no new safety information to report.

We trust that this information is complete.

Sincerely,

ABBOTT LABORATORIES

Frederick A. Gustafson
Director, Regulatory Affairs
Hospital Products Division
Phone: (708) 937-3213
Fax: (708) 938-7867

DTG/dg
G:\dtg\7-95fda.dtg

REVIEWS COMPLETED

CSO ACTION:

☐ LETTER ☐ N.A.I.

CSO INITIALS DATE

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG FOR HUMAN USE OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314)

Form Approved: OMB No. 0910-0001
Expiration Date; March 31, 1990.
See OMB Statement on Page 3.

FOR FDA USE ONLY	
DATE RECEIVED	DATE FILED
DIVISION ASSIGNED	NDA/ANDA NO. ASS.

NOTE: No application may be filed unless a completed application form has been received *(21 CFR Part 314).*

NAME OF APPLICANT
Abbott Laboratories

DATE OF SUBMISSION
July 6, 1995

TELEPHONE NO. *(Include Area Code)*
(708) 937-3213

ADDRESS *(Number, Street, City, State and Zip Code)*
200 Abbott Park Road, D-389 AP30
Abbott Park, Illinois 60064-3537

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER (If previously issued)
20-488

DRUG PRODUCT

ESTABLISHED NAME (e.g., USP/USAN)
Magnesium Sulfate 10mg/mL &q 20mg/mL in 5% Dextrose Injection in Flexible Plastic Containers

PROPRIETARY NAME *(If any)*

CODE NAME *(If any)*

CHEMICAL NAME $MgSO_4\ 7H_2O \quad (C_6H_{12}O_6\ H_2O)$

DOSAGE FORM	ROUTE OF ADMINISTRATION	STRENGTH(S)
Flexible Plastic Container	I.V.	10 & 20mg/mL

PROPOSED INDICATIONS FOR USE

I.V. anticonvulsant for the prevention and control of seizures (convulsions) in severe toxemia of pregnancy.

LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS *(21 CFR Part 312)*, NEW DRUG OR ANTIBIOTIC APPLICATIONS *(21 CFR Part 314)*, AND DRUG MASTER FILES *(21CFR 314.420)* REFERRED TO IN THIS APPLICATION:

INFORMATION ON APPLICATION

TYPE OF APPLICATION *(Check one)*

X ☐ THIS SUBMISSION IS A FULL APPLICATION *(21 CFR 314.50)* ☐ THIS SUBMISSION IS AN ABBREVIATED APPLICATION (ANDA) (21 CFR 314.55)

IF AN ANDA, IDENTIFY THE APPROVED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

NAME OF DRUG	HOLDER OF APPROVED APPLICATION

STATUS OF APPLICATION *(Check one)*

☐ PRESUBMISSION ☐ ORIGINAL APPLICATION
X ☐ AN AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ SUPPLEMENTAL APPLICATION

PROPOSED MARKETING STATUS *(Check one)*

X ☐ APPLICATION FOR A PRESCRIPTION DRUG PRODUCT *(Rx)* ☐ APPLICATION FOR AN OVER - THE - COUNTER PRODUCT *(OTC)*

CONTENTS OF APPLICATION

This application contains the following items: *(Check all that apply)*

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	i. draft labeling *(4 copies)*
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	7. Microbiology section (21 CFR 314.50 (d) (4))
	8. Clinical data section (21 CFR 314.50 (d) (5))
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	10. Statistical section (21 CFR 314.50 (d) (6))
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	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b) (2) or (j) (2) (A))
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I agree to update this application with new safety information about the drug that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit these safety update reports as follows: (1) 4 months after the initial submission, (2) following receipt of an approvable letter and (3) at other times as requested by FDA. If this application is approved, I agree to comply with all laws and regulations that apply to approved applications, including the following:

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2. Labeling regulations in 21 CFR 201.
3. In the case of a prescription drug product, prescription drug advertising regulations in 21 CFR 202.
4. Regulations on making changes in application in 21 CFR 314.70, 314.71, and 314.72.
5. Regulations on reports in 21 CFR 314.80 and 314.81.
6. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the controlled substances Act I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

NAME OF RESPONSIBLE OFFICIAL OR AGENT	SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	DATE
Jill Sackett	Jill Sackett/ns	07/06/95

ADDRESS *(Street, City, State, Zip Code)*	TELEPHONE NO. *(Include Area Code)*
200 Abbott Park Rd, D-389 AP30 Abbott Park, Illinois 60064-3537	(708) 937-4085

(WARNING: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec.1001.)

ABBOTT

ORIGINAL

NEW CORRESP

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

May 22, 1995

CENTER FOR DRUG EVALUATION AND RESEARCH
DIVISION OF METABOLISM AND ENDOCRINE
DRUG PRODUCTS, HFD #510
Attn: DOCUMENT CONTROL ROOM #14B-19
5600 Fishers Lane
Rockville, Maryland 20857

ATTENTION: Solomon Sobel, M.D.
Director

RE: NDA 20-488 Magnesium Sulfate (10 mg/mL amd 20 mg/mL) in 5% Dextrose Injection b(4)

Abbott Laboratories wishes to _____

_____

_____

MAY 30 1995
EVALUATION AND

Sincerely,

ABBOTT LABORATORIES

Frederick A. Gustafson

Frederick A. Gustafson
Director, Regulatory Affairs
Hospital Products Division
Phone: (708) 937-3213
Fax: (708) 938-7867

5-95fda.jxn

REVIEWS COMPLETED

CSO ACTION:

☒ LETTER ☐ N.A.I.

CSO INITIALS 7/11/95 DATE

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG FOR HUMAN USE OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314)

Form Approved: OMB No. 0910-0001
Expiration Date; March 31, 1990.
See OMB Statement on Page 3.

FOR FDA USE ONLY

DATE RECEIVED	DATE FILED
DIVISION ASSIGNED	NDA/ANDA NO. ASS.

NOTE: No application may be filed unless a completed application form has been received *(21 CFR Part 314)*.

NAME OF APPLICANT
Abbott Laboratories

DATE OF SUBMISSION
May 22, 1995

ADDRESS *(Number, Street, City, State and Zip Code)*
One Abbott Park Road
Abbott Park, Illinois 60064

TELEPHONE NO. *(Include Area Code)*
(708) 937-3213

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER (If previously issued)
20-488

DRUG PRODUCT

ESTABLISHED NAME *(e.g., USP/USAN)*
Magnesium Sulfate 10mg/mL & 20mg/mL in 5% Dextrose Injection in Flexible Plastic Containers

PROPRIETARY NAME *(If any)*
$MgSO_4\ 7H_2O \quad (C_6H_{12}O_6\ H_2O)$

CODE NAME *(If any)*

CHEMICAL NAME

DOSAGE FORM	ROUTE OF ADMINISTRATION	STRENGTH(S)
Flexible Plastic Container	I.V.	10 & 20mg/mL

PROPOSED INDICATIONS FOR USE

I.V. anticonvulsant for the prevention and control of seizures (convulsions) in severe toxemia of pregnancy.

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IF AN ANDA, IDENTIFY THE APPROVED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

NAME OF DRUG	HOLDER OF APPROVED APPLICATION

STATUS OF APPLICATION *(Check one)*

☐ PRESUBMISSION ☐ ORIGINAL APPLICATION ☒ AN AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION ☐ SUPPLEMENTAL APPLICATION

PROPOSED MARKETING STATUS *(Check one)*

☒ APPLICATION FOR A PRESCRIPTION DRUG PRODUCT *(Rx)* ☐ APPLICATION FOR AN OVER - THE - COUNTER PRODUCT *(OTC)*

CONTENTS OF APPLICATION

This application contains the following items: *(Check all that apply)*

	1. Index
	2. Summary (21 CFR 314.50 (c))
	3. Chemistry, manufacturing, and control section (21 CFR 314.50 (d) (1))
	4. a. Samples (21 CFR 314.50 (e) (1)) (Submit only upon FDA's request)
	b. Methods Validation Package (21 CFR 314.50 (e) (2) (i))
▨	c. Labeling (21 CFR 314.50 (e) (2) (ii))
	i. draft labeling *(4 copies)*
	ii. final printed labeling (12 copies)
	5. Nonclinical pharmacology and toxicology section (21 CFR 314.50 (d) (2))
	6. Human pharmacokinetics and bioavailability section (21 CFR 314.50 (d) (3))
	7. Microbiology section (21 CFR 314.50 (d) (4))
	8. Clinical data section (21 CFR 314.50 (d) (5))
	9. Safety update report (21 CFR 314.50 (d) (5) (vi) (b))
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	11. Case report tabulations (21 CFR 314.50 (f) (1))
	12. Case reports forms (21 CFR 314.50 (f) (1))
	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b) (2) or (j) (2) (A))
X	15. OTHER *(Specify)*

I agree to update this application with new safety information about the drug that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit these safety update reports as follows: (1) 4 months after the initial submission, (2) following receipt of an approvable letter and (3) at other times as requested by FDA. If this application is approved, I agree to comply with all laws and regulations that apply to approved applications, including the following:

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2. Labeling regulations in 21 CFR 201.
3. In the case of a prescription drug product, prescription drug advertising regulations in 21 CFR 202.
4. Regulations on making changes in application in 21 CFR 314.70, 314.71, and 314.72.
5. Regulations on reports in 21 CFR 314.80 and 314.81.
6. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the controlled substances Act I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

NAME OF RESPONSIBLE OFFICIAL OR AGENT	SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	DATE
Frederick A. Gustafson	Frederick A. Gustafson/mo	05/22/95

ADDRESS *(Street, City, State, Zip Code)*	TELEPHONE NO. *(Include Area Code)*
One Abbott Park Rd Abbott Park, Illinois 60064	(708) 937-3213

(WARNING: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec.1001.)

4 Page(s) Withheld

X Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

ABBOTT

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

January 11, 1995

ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH
DIVISION OF METABOLISM AND ENDOCRINE
DRUG PRODUCTS, HFD #510
Attn: DOCUMENT CONTROL ROOM #14B-19
5600 Fishers Lane
Rockville, Maryland 20857

ATTENTION: Solomon Sobel, M.D.
Director

GENERAL CORRESPONDENCE

RE: NDA 20-488 **Magnesium Sulfate 10 mg/mL and 20 mg/mL in 5% Dextrose Injection in Flexible Plastic Containers**

Abbott Laboratories hereby submits additional information as requested in a telephone conversation held on December 16, 1994, between Dr. Duu-Gong Wu of the Agency and Ms. Jill Sackett of Abbott Laboratories regarding NDA 20-488:

List Number	Concentration	Dosage Form	Manufacturing Facility
6727	10 mg/mL in D5W (10 g total dose)	1000 mL Flexible Plastic Container	Rocky Mount, NC
6727	10 mg/mL in D5W (1 g total dose)	100 mL Flexible Plastic Container	North Chicago, IL
6728	20 mg/mL in D5W (10 g total dose)	500 mL Flexible Plastic Container	Rocky Mount, NC
6728	20 mg/mL in D5W (20 g total dose)	1000 mL Flexible Plastic Container	Rocky Mount, NC

Dr. Wu's requests and our responses follow:

Request 1: NDA 20-309, which covers similar magnesium sulfate parenteral solutions, was recently reviewed and approved at the Agency. NDA 20-309 featured 50 mL and 100 mL size flexible plastic containers in ——— overwraps, for which only 18 months expiry dating was approved. This NDA similarly features 100 mL size flexible plastic containers in ——— overwraps for which —— months shelf life is being requested, *as well as* 500 mL and 1000 mL size flexible plastic containers in ——— overwraps, for which ——— shelf life is being requested. Full term stability data for these

b(4)

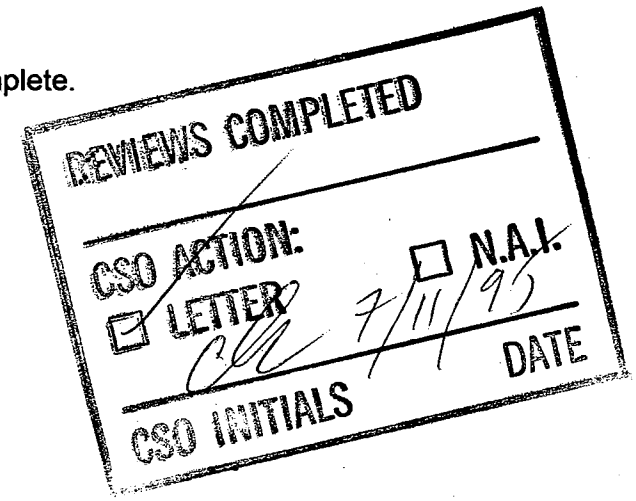
Request 1: (continued) larger sizes were not yet available at the time of the original submission. Provide any additional available stability data to support the requested shelf life of ——— for the 500 mL and 1000 mL sizes. b(4)

Response: Stability data are now available through 12 months, 30°C These data are appended in Exhibit I, and further serve to support the requested expiry dating.

500 mL and 1000 mL flexible plastic containers in —— overwraps are currently utilized in a wide variety of NDA-approved Abbott products. In contrast to 50 mL and 100 mL size plastic containers, the solution-to-surface area ratio in 500 mL and 1000 mL plastic containers is much larger, thus making the effects of moisture vapor loss over time much less significant. Appended in Exhibit II are marketed product stability data for NDA 16-366, 0.9% Sodium Chloride Injection, and NDA 18-090, 0.45% Sodium Chloride Injection, which are also packaged in 500 mL and 1000 mL flexible plastic containers in —— overwraps. These data have already been submitted to the Agency in recent Annual Reports. These sodium chloride products have an approved expiry dating of 24 months. In general, the appended stability data readily support a ——— expiry dating for these package configurations. b(4)

We also wish to take this opportunity to refer to our correspondence dated December 15, 1994. In that correspondence, we acknowledged Dr. Wu's telephone request for a reference to a *previously approved* NDA wherein sterilization data and packaging information for the same package configurations had already been reviewed. We referenced ANDA 74-468, for which approval was imminent, but not yet received. We are pleased to state that approval of ANDA 74-468 has now been received; a copy of the approval letter is provided in Exhibit III.

We trust that this information is complete.



Sincerely,

ABBOTT LABORATORIES

Frederick A. Gustafson /lp

Frederick A. Gustafson
Director, Regulatory Affairs
Hospital Products Division
Phone: (708) 937-3213
Fax: (708) 938-7867
1-95fda.jxn

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG FOR HUMAN USE OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314)

Form Approved: OMB No. 0910-0001
Expiration Date; March 31, 1990.
See OMB Statement on Page 3.

FOR FDA USE ONLY	
DATE RECEIVED	DATE FILED
DIVISION ASSIGNED	NDA/ANDA NO. ASS.

NOTE: No application may be filed unless a completed application form has been received *(21 CFR Part 314)*.

NAME OF APPLICANT
Abbott Laboratories

DATE OF SUBMISSION
January 11, 1995

ADDRESS *(Number, Street, City, State and Zip Code)*
One Abbott Park Road
Abbott Park, Illinois 60064

TELEPHONE NO. *(Include Area Code)*
(708) 937-3213

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER (If previously issued)
20-488

DRUG PRODUCT

ESTABLISHED NAME *(e.g., USP/USAN)*
Magnesium Sulfate 10mg/mL & 20mg/mL in 5% Dextrose Injection in Flexible Plastic Containers

PROPRIETARY NAME *(If any)*
$MgSO_4\ 7H_2O \quad (C_6H_{12}O_6\ H_2O)$

CODE NAME *(If any)*

CHEMICAL NAME

DOSAGE FORM	ROUTE OF ADMINISTRATION	STRENGTH(S)
Flexible Plastic Container	I.V.	10 & 20mg/mL

PROPOSED INDICATIONS FOR USE

I.V. anticonvulsant for the prevention and control of seizures (convulsions) in severe toxemia of pregnancy.

LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS *(21 CFR Part 312)*, NEW DRUG OR ANTIBIOTIC APPLICATIONS *(21 CFR Part 314)*, AND DRUG MASTER FILES *(21CFR 314.420)* REFERRED TO IN THIS APPLICATION:

NDA 20-309
NDA 16-366
NDA 16-367
DMF —— Abbott Laboratories) b(4)
DMF 1218 (Abbott Laboratories)
DMF 1561 (Abbott Laboratories)

INFORMATION ON APPLICATION

TYPE OF APPLICATION *(Check one)*

☒ THIS SUBMISSION IS A FULL APPLICATION *(21 CFR 314.50)* ☐ THIS SUBMISSION IS AN ABBREVIATED APPLICATION (ANDA) (21 CFR 314.55)

IF AN ANDA, IDENTIFY THE APPROVED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

NAME OF DRUG	HOLDER OF APPROVED APPLICATION

STATUS OF APPLICATION *(Check one)*

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I agree to update this application with new safety information about the drug that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit these safety update reports as follows: (1) 4 months after the initial submission, (2) following receipt of an approvable letter and (3) at other times as requested by FDA. If this application is approved, I agree to comply with all laws and regulations that apply to approved applications, including the following:

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NAME OF RESPONSIBLE OFFICIAL OR AGENT	SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	DATE
Frederick A. Gustafson	Frederick A. Gustafson	01/11/95

ADDRESS *(Street, City, State, Zip Code)*	TELEPHONE NO. *(Include Area Code)*
One Abbott Park Rd Abbott Park, Illinois 60064	(708) 937-3213

(WARNING: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec.1001.)

2

ABBOTT

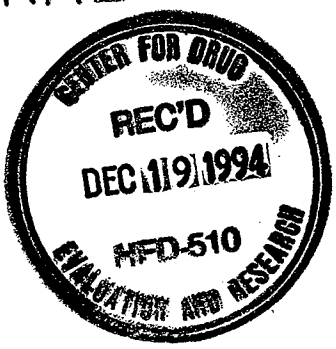
Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

BC

December 15, 1994

CENTER FOR DRUG EVALUATION AND RESEARCH
DIVISION OF METABOLISM AND ENDOCRINE
DRUG PRODUCTS, HFD #510
Attn: DOCUMENT CONTROL ROOM #14B-19
5600 Fishers Lane
Rockville, Maryland 20857

ORIGINAL



ATTENTION: Solomon Sobel, M.D.
Director

GENERAL CORRESPONDENCE

RE: NDA 20-488 Magnesium Sulfate 10 mg/mL and 20 mg/mL in 5% Dextrose Injection in Flexible Plastic Containers

Abbott Laboratories hereby submits additional information as requested in a telephone conversation held today between Dr. Duu-Gong Wu of the Agency and Ms. Jill Sackett of Abbott Laboratories regarding NDA 20-488:

List Number	Concentration	Dosage Form	Manufacturing Facility
6727	10 mg/mL in D5W (10 g total dose)	1000 mL Flexible Plastic Container	Rocky Mount, NC
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6728	20 mg/mL in D5W (20 g total dose)	1000 mL Flexible Plastic Container	Rocky Mount, NC

Dr. Wu requested reference to a *previously approved* New Drug Application wherein sterilization data and packaging information for package configurations identical to the 500 mL and 1000 mL sizes called out in the above *pending* NDA had been reviewed.

These package configurations are used in numerous FDA approved Abbott products and have been marketed since the early 1980's. NDA 16-367, filed with the Division of Medical Imaging, Surgical and Dental Drug Products, is one of many older NDAs in which these package configurations have been reviewed and approved. However, the *most recent* sterilization data and packaging information for these configurations may be found in ANDA 74-468 for Cimetidine Hydrochloride Injection in 0.9% Sodium Chloride, recently filed with the Office of Generic Drugs. We understand that a full review of this ANDA has been completed and that approval is imminent. Pertinent sections may be located as follows:

For the 500 mL Size Flexible Plastic Container:

Engineering Validation	Volume 2	Page 2-53
Microbiological Validation Production Sterilizer Master Solution Concept Production Sterilizer Microbial Solution Validation	Volume 2	Page 2-146
Sterilization Closure Validation Inactivation Kinetic Comparison	Volume 2	Page 2-169
Maintenance of Sterility	Volume 2	Page 2-354
Packaging Information	Volume 9	Pages 9-81 through 9-151

For the 1000 mL Size Flexible Plastic Container:

Engineering Validation	Volume 2	Page 2-53
Microbiological Validation Production Sterilizer Master Solution Concept Production Sterilizer Microbial Solution Validation	Volume 2	Page 2-302
Sterilization Closure Validation Inactivation Kinetic Comparison	Volume 2	Page 2-326
Maintenance of Sterility	Volume 2	Page 2-354
Packaging Information	Volume 9	Pages 9-81 through 9-151

Please contact us if we can be of additional assistance.

Sincerely,

ABBOTT LABORATORIES

Frederick A. Gustafson

Frederick A. Gustafson
Director, Regulatory Affairs
Hospital Products Division
Phone: (708) 937-3213
Fax: (708) 938-7867

12-94fda.jxn

REVIEWS COMPLETED
CSO ACTION:
LETTER
M.A.I.
7/11/95
DATE
INITIALS

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG FOR HUMAN USE OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314)

Form Approved: OMB No. 0910-0001
Expiration Date; March 31, 1990.
See OMB Statement on Page 3.

FOR FDA USE ONLY	
DATE RECEIVED	DATE FILED
DIVISION ASSIGNED	NDA/ANDA NO. ASS.

NOTE: No application may be filed unless a completed application form has been received *(21 CFR Part 314).*

NAME OF APPLICANT Abbott Laboratories	DATE OF SUBMISSION December 15, 1994
ADDRESS *(Number, Street, City, State and Zip Code)* One Abbott Park Road Abbott Park, Illinois 60064	TELEPHONE NO. *(Include Area Code)* (708) 937-3213
	NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER (If previously issued) 20-488

DRUG PRODUCT

ESTABLISHED NAME (e.g., USP/USAN)	PROPRIETARY NAME *(If any)*
Magnesium Sulfate 10mg/mL & 20mg/mL in 5% Dextrose Injection in Flexible Plastic Containers	$MgSO_4$ $7H_2O$ $(C_6H_{12}O_6$ $H_2O)$

CODE NAME *(If any)*	CHEMICAL NAME

DOSAGE FORM	ROUTE OF ADMINISTRATION	STRENGTH(S)
Flexible Plastic Container	I.V.	10 & 20mg/mL

PROPOSED INDICATIONS FOR USE

I.V. anticonvulsant for the prevention and control of seizures (convulsions) in severe toxemia of pregnancy.

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NDA 16-366
NDA 16-367
DMF ——— Abbott Laboratories)
DMF 1218 (Abbott Laboratories)
DMF 1561 (Abbott Laboratories)

b(4)

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NAME OF RESPONSIBLE OFFICIAL OR AGENT	SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	DATE
Frederick A. Gustafson	Frederick A Gustafson, Jr	12/15/94

ADDRESS *(Street, City, State, Zip Code)*	TELEPHONE NO. *(Include Area Code)*
One Abbott Park Rd Abbott Park, Illinois 60064	(708) 937-3213

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FORM FDA 356h (10/89)

ABBOTT

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

C

Voted Approvable 10/17/94

September 23, 1994

CENTER FOR DRUG EVALUATION AND RESEARCH
DIVISION OF METABOLISM AND ENDOCRINE
DRUG PRODUCTS, HFD #510
Attn: DOCUMENT CONTROL ROOM #14B-03
5600 Fishers Lane
Rockville, Maryland 20857

ORIGINAL

See Pharm Review dtd 31 Jan 95 DH

ATTENTION: Christina Kish
Consumer Safety Officer

GENERAL CORRESPONDENCE

RE: NDA 20-488 Magnesium Sulfate 10 mg/mL and 20 mg/mL in 5% Dextrose Injection in Flexible Plastic Containers

Abbott Laboratories hereby supplies additional copies of specified sections of the above referenced NDA as requested on September 21, 1994, by Ms. Christina Kish of the Agency. The following sections, and their location in the NDA, are as follows:

Section	Location	Comments
Cover Letter to Agency	Preface (no page number)	Provided for reference.
Table of Contents	1-5 through 1-7	
NDA Summary	1-8 through 1-34	
Labeling	1-13 through 1-36	Included as part of NDA Summary
Medical/Statistical	3-398 through 3-416	
~~Integrated Summary of Safety~~	3-417	
✓ Debarment Statement	Amendment (no page number)	Supplied as Minor Amendment dated September 23, 1994.
✓ Patent Information	Amendment (no page number)	Supplied as Minor Amendment dated September 23, 1994.

CENTER FOR DRUG EVALUATION AND RESEARCH RECD OCT 3 1994 HFD-510

REVIEWS COMPLETED
CSO ACTION: ☐ LETTER ☐ N.A.L.
CSO INITIALS 7/11/95 DATE

Sincerely,

ABBOTT LABORATORIES
Frederick A. Gustafson
Director, Regulatory Affairs
Hospital Products Division
Phone: (708) 937-3213
Fax: (708) 938-7867
9-94fda.jxn

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG FOR HUMAN USE OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314)

Form Approved: OMB No. 0910-0001
Expiration Date; March 31, 1990.
See OMB Statement on Page 3.

FOR FDA USE ONLY	
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NAME OF APPLICANT
Abbott Laboratories

DATE OF SUBMISSION
September 23, 1994

ADDRESS *(Number, Street, City, State and Zip Code)*
One Abbott Park Road
Abbott Park, Illinois 60064

TELEPHONE NO. *(Include Area Code)*
(708) 937-3213

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER (If previously issued)
20-488

DRUG PRODUCT

ESTABLISHED NAME *(e.g. USP/USAN)*
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ROUTE OF ADMINISTRATION
I.V.

STRENGTH(S)
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PROPOSED INDICATIONS FOR USE

I.V. anticonvulsant for the prevention and control of seizures (convulsions) in severe toxemia of pregnancy.

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NDA 16-366
NDA 16-367
DMF [redacted] (Abbott Laboratories) b(4)
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INFORMATION ON APPLICATION

TYPE OF APPLICATION *(Check one)*

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IF AN ANDA, IDENTIFY THE APPROVED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

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	9. Safety update report (21 CFR 314.50 (d) (5) (vi) (b))
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	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b) (2) or (j) (2) (A))
X	15. OTHER *(Specify)*

Additional Information

I agree to update this application with new safety information about the drug that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit these safety update reports as follows: (1) 4 months after the initial submission, (2) following receipt of an approvable letter and (3) at other times as requested by FDA. If this application is approved, I agree to comply with all laws and regulations that apply to approved applications, including the following:

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2. Labeling regulations in 21 CFR 201.
3. In the case of a prescription drug product, prescription drug advertising regulations in 21 CFR 202.
4. Regulations on making changes in application in 21 CFR 314.70, 314.71, and 314.72.
5. Regulations on reports in 21 CFR 314.80 and 314.81.
6. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the controlled substances Act I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

NAME OF RESPONSIBLE OFFICIAL OR AGENT	SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	DATE
Frederick A. Gustafson	Frederick A. Gustafson	09/23/94

ADDRESS *(Street, City, State, Zip Code)*	TELEPHONE NO. *(Include Area Code)*
One Abbott Park Rd Abbott Park, Illinois 60064	(708) 937-3213

(WARNING: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)

ABBOTT

Hospital Products Division
Abbott Laboratories
D-389, Bldg. AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-3537

ORIGINAL

September 23, 1994

CENTER FOR DRUG EVALUATION AND RESEARCH
DIVISION OF METABOLISM AND ENDOCRINE
DRUG PRODUCTS, HFD #510
Attn: DOCUMENT CONTROL ROOM #14B-03
5600 Fishers Lane
Rockville, Maryland 20857

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
SEP 26 1994
HFD-510

10/6/94
Noted
NAI

ATTENTION: Solomon Sobel, M.D.
Director

MINOR AMENDMENT

RE: NDA 20-488 Magnesium Sulfate 10 mg/mL and 20 mg/mL in 5% Dextrose Injection in Flexible Plastic Containers

Abbott Laboratories hereby amends the above referenced NDA with a signed certification statement as required under the Generic Drug Enforcement Act of 1992, Section 306(k) (1) of the act (21 USC 335a(k) (1)), and patent and exclusivity information.

Sincerely,

ABBOTT LABORATORIES

Frederick A. Gustafson

Frederick A. Gustafson
Director, Regulatory Affairs
Hospital Products Division
Phone: (708) 937-3213
Fax: (708) 938-7867
9-94fda.jxn

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☒ N.A.I.
10/12/94
CSO INITIALS DATE

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG FOR HUMAN USE OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314)

Form Approved: OMB No. 0910-0001
Expiration Date; March 31, 1990.
See OMB Statement on Page 3.

FOR FDA USE ONLY	
DATE RECEIVED	DATE FILED
DIVISION ASSIGNED	NDA/ANDA NO. ASS.

NOTE: No application may be filed unless a completed application form has been received *(21 CFR Part 314).*

NAME OF APPLICANT
Abbott Laboratories

DATE OF SUBMISSION
September 23, 1994

ADDRESS *(Number, Street, City, State and Zip Code)*
One Abbott Park Road
Abbott Park, Illinois 60064

TELEPHONE NO. *(Include Area Code)*
(708) 937-3213

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER (If previously issued)
20-488

DRUG PRODUCT

ESTABLISHED NAME *(e.g., USP/USAN)*
Magnesium Sulfate 10mg/mL & 20mg/mL in 5% Dextrose Injection in Flexible Plastic Containers

PROPRIETARY NAME *(If any)*
$MgSO_4$ $7H_2O$ $(C_6H_{12}O_6$ $H_2O)$

CODE NAME *(If any)*

CHEMICAL NAME

DOSAGE FORM	ROUTE OF ADMINISTRATION	STRENGTH(S)
Flexible Plastic Container	I.V.	10 & 20mg/mL

PROPOSED INDICATIONS FOR USE

I.V. anticonvulsant for the prevention and control of seizures (convulsions) in severe toxemia of pregnancy.

LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS *(21 CFR Part 312)*, NEW DRUG OR ANTIBIOTIC APPLICATIONS *(21 CFR Part 314)*, AND DRUG MASTER FILES *(21CFR 314.420)* REFERRED TO IN THIS APPLICATION:

NDA 20-309
NDA 16-366
NDA 16-367
DMF —— (Abbott Laboratories) b(4)
DMF 1218 (Abbott Laboratories)
DMF 1561 (Abbott Laboratories)

INFORMATION ON APPLICATION

TYPE OF APPLICATION *(Check one)*

☒ THIS SUBMISSION IS A FULL APPLICATION *(21 CFR 314.50)* ☐ THIS SUBMISSION IS AN ABBREVIATED APPLICATION (ANDA) (21 CFR 314.55)

IF AN ANDA, IDENTIFY THE APPROVED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

NAME OF DRUG

HOLDER OF APPROVED APPLICATION

STATUS OF APPLICATION *(Check one)*

☐ PRESUBMISSION ☒ ORIGINAL APPLICATION ☐ AN AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION ☐ SUPPLEMENTAL APPLICATION

PROPOSED MARKETING STATUS *(Check one)*

☒ APPLICATION FOR A PRESCRIPTION DRUG PRODUCT *(Rx)* ☐ APPLICATION FOR AN OVER - THE - COUNTER PRODUCT *(OTC)*

CONTENTS OF APPLICATION

This application contains the following items: *(Check all that apply)*

	1. Index
	2. Summary (21 CFR 314.50 (c))
	3. Chemistry, manufacturing, and control section (21 CFR 314.50 (d) (1))
	4. a. Samples (21 CFR 314.50 (e) (1)) (Submit only upon FDA's request)
	b. Methods Validation Package (21 CFR 314.50 (e) (2) (i))
▨	c. Labeling (21 CFR 314.50 (e) (2) (ii))
	i. draft labeling *(4 copies)*
	ii. final printed labeling (12 copies)
	5. Nonclinical pharmacology and toxicology section (21 CFR 314.50 (d) (2))
	6. Human pharmacokinetics and bioavailability section (21 CFR 314.50 (d) (3))
	7. Microbiology section (21 CFR 314.50 (d) (4))
	8. Clinical data section (21 CFR 314.50 (d) (5))
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Frederick A. Gustafson	Frederick A. Gustafson, JR	09/23/94

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FORM FDA 356h (10/89)