CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

88-441

Generic Name: Bethanechol Chloride Tablets, 25mg

Sponsor: Sidmak Laboratories, Inc.

Approval Date: May 29, 1984

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

88-441

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Reviews / Information Included in this ANDA Review.

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

88-441

APPROVAL LETTER

MAY 29 1984

NDA 88-441

Sidmak Laboratories, Inc.
Attention: Satish P. Patel, Ph.D.
17 West Street, P.O. Box 371
East Hanover, NJ 07936

Gentlemen:

Reference is made to your abbreviated new drug application dated July 25, 1983, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Bethanechol Chloride Tablets, 25 mg.

Reference is also made to your letter of May 14, 1984 amending this application.

We have completed the review of this abbreviated new drug application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved.

Any significant change in the conditions outlined in this abbreviated new drug application requires an approved supplemental application before the change may be made, except for changes made in conformance with other provisions of Section 314.8 of the new drug regulations.

This Administration should be advised of any change in the marketing status of this drug.

For Initial Campaigns: We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your immediate advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Advertising and Labeling (HFN-240). Also, please do not use Form FD-2253 for this submission.

For Subsequent Campaigns: We call your attention to Regulation 21 CFR 310.300 (b)(3) which requires that material for any subsequent advertising or promotional campaigns, at the time of their initial use, be submitted to our Division of Drug Advertising and Labeling (HFN-240) with a completed Form FD-2253. A copy of Form FD-2253 is enclosed for your convenience.

The enclosures summarize the conditions relating to the approval of this application.

Sincerely yours,

Marvin Seife 5/29/84

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drugs and Biologics

Enclosures:
Conditions of Approval of a New Drug Application
Records & Reports Requirements
Form FD 2253

cc: NWK-DO
HFN-230
HFN-10
HFN-313
HFN-83 5/24/84
TPoux/JMeyer/VWalton
R/D INITIAL JMeyer/MSeife
mm:5/24/84 (3009A)
Approved

V. Walton 5/24/84

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

88-441

FINAL PRINTED LABELING

BETHANECHOL CHLORIDE TABLETS, USP

MAY 29 1984

APPROVED

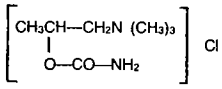
DESCRIPTION:

Bethanechol chloride, an ester of a choline-like compound, is 2-[(aminocarbonyl)oxy]-N,N,N-trimethyl-1-propanaminium chloride. Bethanechol chloride is a white hygroscopic, crystalline powder having an amine-like odor and is freely soluble in water.

The structural formula is:

$C_7H_{17}C1N_2O_2$

Molecular Weight: 196.68



Bethanechol chloride, a cholinergic agent, is available as 10mg. and 25mg. tablets intended for oral use.

CLINICAL PHARMACOLOGY:

Bethanechol chloride acts principally by producing the effects of stimulation of the parasympathetic nervous system. It increases the tone of the detrusor urinae muscle, usually producing a contraction sufficiently strong to initiate micturition and empty the bladder. It stimulates gastric motility, increases gastric tone, and often restores impaired rhythmic peristalsis.

Stimulation of the parasympathetic nervous system releases acetylcholine at the nerve endings. When spontaneous stimulation is reduced and therapeutic intervention is required, acetylcholine can be given, but is rapidly hydrolyzed by cholinesterase, and its effects are transient. Bethanechol chloride is not destroyed by cholinesterase and its effects are more prolonged than those of acetylcholine.

It has predominant muscarinic action and only feeble nicotinic action. Doses that stimulate micturition and defecation and increase peristalsis do not ordinarily stimulate ganglia or voluntary muscles. Therapeutic test doses in normal human subjects have little effect on heart rate, blood pressure, or peripheral circulation.

INDICATIONS AND USAGE:

Bethanechol chloride is indicated for the treatment of acute postoperative and postpartum nonobstructive (functional) urinary retention, and neurogenic atony of the urinary bladder with retention.

CONTRINDICATIONS:

Bethanechol chloride is contraindicated in the presence of mechanical obstruction of the gastrointestinal or urinary tracts, or in conditions where the integrity of the gastrointestinal or bladder wall is questionable. Also, it is contraindicated in spastic gastrointestinal disturbances, peptic ulcer, acute inflammatory conditions of the gastrointestinal tract, or peritonitis, or in marked vagotonia.

Bethanechol chloride is also contraindicated in latent or active asthma, hyperthyroidism, coronary occlusion, bradycardia, vasomotor instability, hypotension, coronary artery disease, epilepsy, and parkinsonism.

WARNINGS:

Asthmatic attacks may be precipitated, especially in susceptible individuals. Substernal pressure or pain may occur; however, it is uncertain whether this is due to bronchoconstriction, or spasm of the esophagus. Myocardial hypoxia must be considered if a marked fall in blood pressure occurs.

Transient syncope with cardiac arrest, transient complete heart block , dyspnea, and orthostatic hypotension may be associated with large doses. Patients with hypertension may react to the drug with a precipitous fall in blood pressure. Short periods of atrial fibrillation have been observed in hyperthyroid individuals following the administration of cholinergic drugs. Involuntary defecation and urinary urgency may occur after large doses.

PRECAUTION:

General: In urinary retention, if the sphincter fails to relax as bethanechol contracts the bladder, urine may be forced up the ureter into the kidney pelvis. If there is bacteriuria, this may cause a reflux infection.

Drug Interactions:

Special care and consideration are required when bethanechol is administered to patients concomitantly being treated with other drugs with which pharmacologic interactions may

occur. Examples of drugs with potential for such interaction are: quinidine and procainamide, which may antagonize cholinergic effects; cholinergic drugs, particularly cholinesterase inhibitors, where additive effects may occur. When administered to patients receiving ganglionic blocking compounds a critical fall in blood pressure may occur, usually preceded by severe abdominal symptoms.

Pregnancy:

Pregnancy Category C. Animal reproduction studies have not been conducted with bethanechol chloride. It is also not known whether bethanechol can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Bethanechol should be given to a pregnant woman only if clearly needed.

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 bethanechol is administered to a nursing woman.

Pediatric Use:

Safety and effectiveness in children below the age of 12 years have not been established.

ADVERSE REACTIONS:

Adverse reactions are infrequent with bethanechol chloride. The following may occur:

Cardiovascular: Fall in blood pressure (see WARNINGS).

Gastrointestinal: Involuntary defecation, vomiting, colicky pain, abdominal cramps, diarrhea, nausea and belching, salivation and borborygmi.

Respiratory: Asthmatic attacks and dyspnea.

Neurologic: Headache, facial flushing.

Urogenital: Urinary urgency.

Miscellaneous: Substernal pressure or pain (see WARNINGS), malaise.

OVERDOSAGE:

Maintain artificial respiration until antidote can be given. Atropine sulfate is a specific antidote and may be given in doses of 0.6mg-1.2mg intraveneously (slowly), intramuscularly, or subcutaneously to counteract severe toxic cardiovascular or bronchoconstrictor responses to bethanechol chloride.

DOSAGE AND ADMINISTRATION:

Dosage must be individualized, depending on type and severity of the condition to be treated.

Preferably give the drug on an empty stomach to minimize the possibility of nausea and vomiting.

The usual adult oral dose ranges from 10 to 50 mg three or four times a day. The minimum effective dose is determined by giving 5 or 10 mg initially, and repeating the same amount at hourly intervals until satisfactory response occurs, or until a maximum of 50 mg has been given. The effects of the drug sometimes appear within 30 minutes, and are usually maximal within 90 minutes. The drug's effects persist for about one hour.

HOW SUPPLIED:

As a pink round, scored compressed tablet impressed with SL/324 containing 10 mg of Bethanechol chloride in bottles of 100, 500, 1000:

NDC #50111-324-01, bottle of 100 Tablets
NDC #50111-324-02 bottle of 500 Tablets
NDC #50111-324-03, bottle of 1000 Tablets

As a yellow round, scored compressed tablet impressed with SL/325 containing 25 mg of Bethanechol chloride, in bottles of 100, 500 and 1000:

NDC #50111-325-01, bottle of 100 Tablets
NDC #50111-325-02, bottle of 500 Tablets
NDC #50111-325-03, bottle of 1000 Tablets

CAUTION:

Federal law prohibits dispensing without prescription.

Revised 4/84

Manufactured by
SIDMAK LABORATORIES, INC.
East Hanover, N.J. 07936

SIDMAK LABORATORIES, INC.

ORIGINAL

Labeling:

NDA No: 88441 Rc'd. 5/16/84

Reviewed by: V. Watts

§ 314.1(f)(1) LABEL AND OTHER LABELING.

Copies of the final printed label are attached.

APPROVED

MAY 29 1984

NDC 50111-325-01

Usual dosage and complete prescribing information: See accompanying literature.

Store at controlled room temperature 15° to 30°C (59° to 86°F).

This is a bulk package. Dispense contents with child-resistant closure (as required) and in tight, light resistant container as defined in the USP/NF.

Keep tightly closed.

Keep this and all medication out of the reach of children.

Bethanechol Chloride Tablets, USP 25mg.

Each tablet contains:
Bethanechol Chloride, U.S.P. 25mg.

CAUTION: Federal (USA) law prohibits dispensing without prescription

100 Tablets

Sidmak®
LABORATORIES, INC.
17 West Street
East Hanover, NJ 07936

Control No:
Exp. Date:

APPROVED

MAY 29 1984

NDC 50111-325-02

Usual dosage and complete prescribing information: See accompanying literature.

Store at controlled room temperature 15° to 30°C (59° to 86°F).

This is a bulk package. Dispense contents with child-resistant closure (as required) and in tight, light resistant container as defined in the USP/NF.

Keep tightly closed.

Keep this and all medication out of the reach of children.

Bethanechol Chloride Tablets, USP 25mg.

Each tablet contains:
Bethanechol Chloride, U.S.P. 25mg.

CAUTION: Federal (USA) law prohibits dispensing without prescription

500 Tablets

Sidmak®
LABORATORIES, INC.
17 West Street
East Hanover, NJ 07936

Control No:
Exp. Date:

APPROVED

MAY 29 1984

NDC 50111-325-03

Usual dosage and complete prescribing information: See accompanying literature.

Store at controlled room temperature 15° to 30°C (59° to 86°F).

This is a bulk package. Dispense contents with child-resistant closure (as required) and in tight, light resistant container as defined in the USP/NF.

Keep tightly closed.

Keep this and all medication out of the reach of children.

Bethanechol Chloride Tablets, USP 25mg.

Each tablet contains:
Bethanechol Chloride, U.S.P. 25mg.

CAUTION: Federal (USA) law prohibits dispensing without prescription

1000 Tablets

Sidmak®
LABORATORIES, INC.
17 West Street
East Hanover, NJ 07936

Control No:
Exp. Date:

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

88-441

CSO LABELING REVIEW(S)

REVIEW OF PROFESSIONAL LABELING

ANDA - Draft

DATE OF REVIEW: 8-24-83

NAME OF FIRM: Sidmark Laboratories

ANDA #: 88-441 (25 mg)
88-440 (10 mg)

NAME OF DRUG: Generic: Bethanechol Chloride Tablets

DATE OF SUBMISSION: 7-25-83

COMMENTS:

Container: Satisfactory, 100s, 500s, 1000s

Insert: Not satisfactory

a) Must be updated to provide information similar to our Labeling Guideline.

RECOMMENDATIONS:

1. Firm may prepare FPL for container labels.

2. Send insert Labeling Guideline. Request that firm prepare and submit revised insert labeling. The date of printing must appear on this labeling.

Kent T. Johnson

cc:
dup
KTJ/cl/8-24-83

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

88-441

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW
(If necessary, continue any item on 8" x 10½" paper. Key continuation to item by number.)

1. ORGANIZATION: Generic Drugs	2. NDA NUMBER: 88-441
3. NAME AND ADDRESS OF APPLICANT (City and State): Sidmak Laboratories, Inc. East Hanover, NJ 07936	4. AF NUMBER
	5. SUPPLEMENT (S) NUMBER(S) / DATE(S)
6. NAME OF DRUG: Bethanechol Chloride	7. NONPROPRIETARY NAME
8. SUPPLEMENT(S) PROVIDES FOR: original	9. AMENDMENTS AND OTHER (Reports, etc.) DATES
10. PHARMACOLOGICAL CATEGORY: urinary retention	11. HOW DISPENSED: ☒ RX ☐ OTC
12. RELATED IND/NDA/DMF(S)	
13. DOSAGE FORM (S): Tablet	14. POTENCY (Iso): 25 mg
15. CHEMICAL NAME AND STRUCTURE	16. RECORDS AND REPORTS: CURRENT ☐ YES ☐ NO; REVIEWED ☐ YES ☐ NO

APPEARS THIS WAY ON ORIGINAL

17. COMMENTS

FPL for container labels and insert labeling satis. per R.Poux 5-22-84.

Approvable letter sent 5-22-84.

Applicant not on the alert list dated May 14, 1984.

24 month expiration date approved for product packaged in HDPE containers of 100s, 500s & 1000 tablets.

18. CONCLUSIONS AND RECOMMENDATIONS

approved

19. REVIEWER

NAME	SIGNATURE	DATE COMPLETED
V.Walton	V. Walton	5-22-84

DISTRIBUTION ☒ ORIGINAL JACKET ☐ REVIEWER ☐ DIVISION FILE

CHEMIST'S REVIEW
(If necessary, continue any item on 8" x 10½" paper. Key continuation to item by number.)

1. ORGANIZATION: Generic Drugs

2. NDA NUMBER: 88-440 & 88-441

3. NAME AND ADDRESS OF APPLICANT (City and State)

Sidmak Labs
East Hanover, NJ

4. AF NUMBER

5. SUPPLEMENT (S)
NUMBER(S) | DATE(S)

6. NAME OF DRUG

7. NONPROPRIETARY NAME: Bethanechol Chloride

8. SUPPLEMENT(S) PROVIDES FOR:

original

9. AMENDMENTS AND OTHER (Reports, etc.) DATES

APPEARS THIS WAY
ON ORIGINAL

10. PHARMACOLOGICAL CATEGORY

11. HOW DISPENSED
☒ RX ☐ OTC

12. RELATED IND/NDA/DMF(S)
88-440 10 mg
88-441 25 mg

13. DOSAGE FORM (S)
tablet

14. POTENCY (Use)
10 and 25 mg

15. CHEMICAL NAME AND STRUCTURE

16. RECORDS AND REPORTS
CURRENT
☐ YES ☐ NO
REVIEWED
☐ YES ☐ NO

17. COMMENTS

Inspection:
Applicant, _____ are satis. per L.Hartley 1/3/84.

Labeling:
Insert satis. per K.Johnson 4-11-84 request FPL.

APPEARS THIS WAY
ON ORIGINAL

18. CONCLUSIONS AND RECOMMENDATIONS

approvable letters sent

19. REVIEWER

NAME: V.Walton
SIGNATURE: V.Walton
DATE COMPLETED: 4-12-84

DISTRIBUTION ☐ ORIGINAL JACKET ☐ REVIEWER ☐ DIVISION FILE

FORM FDA 2266 (7/75) PREVIOUS EDITION MAY BE USED UNTIL SUPPLY IS EXHAUSTED.

§314.1(f)(1)(i) THE COMPOSITION OF THE DRUG, STATING THE NAME AND AMOUNT OF EACH INGREDIENT CONTAINED IN A STATED QUANTITY OF THE DRUG IN THE FORM IN WHICH IT IS TO BE DISTRIBUTED.

INGREDIENT	MGS. PER TABLET
Bethanechol Chloride	* 25.50
Total Weight	320.00

APPEARS THIS WAY
ON ORIGINAL

CHEMIST'S REVIEW
(If necessary, continue any item on 8" x 10½" paper. Key continuation to item by number.)

1. ORGANIZATION: Generic Drugs

2. NDA NUMBER: 88-441

3. NAME AND ADDRESS OF APPLICANT (City and State)

Sidmak Laboratories
East Hanover, NJ

4. AF NUMBER:

5. SUPPLEMENT (S)

NUMBER(S)	DATE(S)

6. NAME OF DRUG: Bethanechol Chloride

7. NONPROPRIETARY NAME:

8. SUPPLEMENT(S) PROVIDES FOR:

original

9. AMENDMENTS AND OTHER (Reports, etc.) DATES

10. PHARMACOLOGICAL CATEGORY:

11. HOW DISPENSED: [X] RX [ ] OTC

12. RELATED IND/NDA/DMF(S)

88-440 10 mg

13. DOSAGE FORM (S): tablet

14. POTENCY (Iso): 25 mg

15. CHEMICAL NAME AND STRUCTURE

$C_7H_{17}ClN_2O_2$

16. RECORDS AND REPORTS

CURRENT: [ ] YES [ ] NO

REVIEWED: [ ] YES [ ] NO

17. COMMENTS

Application date: 7-25-83
Rx statement - satis.
Signed 356H - ok
Table of contents - ok
Cover letter- o
#24 continued -

CGMP certifica

#27 continued

18. CONCLUSIONS AND RECOMMENDATIONS or

not approved

19. REVIEWER

NAME	SIGNATURE	DATE COMPLETED
	V. Watts	12-23-83

DISTRIBUTION: [X] ORIGINAL JACKET [ ] REVIEWER [ ] DIVISION FILE

Redacted 3

Page(s) of trade secret and /or confidential commercial information

DEPARTMENT OF HEALTH & HUMAN SERVICES

Memorandum

TO :Manufacturing Review Branch (HFN-322) DATE: 7-28-83
Division of Drug Quality Compliance

FROM :Division of Generic Drugs
Requester's Name D Rosen PHONE: 34080

SUBJECT: ESTABLISHMENT EVALUATION REQUEST

NDA, ANDA, AND SUPPLEMENT NUMBER: 88-440; 88-441

DRUG TRADE MARK (if any) _____

DRUG NONPROPRIETARY NAME: Bethanechol Chloride Usp Tabs

DOSAGE FORM AND STRENGTH(S): TCM 10mg; 25mg

DRUG CLASSIFICATION: PROFILE CLASS CODE:
(Priority) _____ A or B _____ 1C _____ Other _____ _____

APPLICANT'S NAME: Sidmak Laboratories'
ADDRESS: 17 West St., East Hanover, NJ 07936

FACILITIES TO BE EVALUATED: (Name, Full Address, DMF# (if any), and Responsibility)

1. Applicant
2.
3.
4.
5.
6.

Comments: ( ) See Attached.
( ) Actual on-site inspection requested.

Reason: _____

_____

****

FOR HFN-322 USE ONLY:

Request Rec'd: _____ Inspection Requested: _____
(if applicable)

Firm(s) are in Compliance With GMPs: _____
Basis for Decision: _____
Reviewing CSO: _____ Concurrance: _____

cc: HFN-____
HFN-____
HFN-322

FORM FDA 3274 (1/83)

Instructions for Completing SF ___, Software Survey *

01. Date Summary Prepared: Indicate in YYDDD format

02. Date Summary Completed or Last Updated: Indicate in YYDDD format

03. Agency Code: Insert organization code from Appendix A of latest version of OMB Circular A-11

04. Software Type:
1=individual program
2=automated data system (assembly of computer programs)

05. Type of Submission:
1=initial
2=revision
3=deletion

06. Software Function: Classify software in one of the following categories:
A=system support/utility applications
B=management/business applications
C=scientific applications
D=data/file handlers
E=bibliographic applications
F=other (specify category)

08. Software Identification: Indicate the ... agency's identification number or code for software. If none assigned, ...

11. Title: Software title should be made as descriptive as possible.

12. Acronym: Commonly used abbreviation identifying software. (optional)

13. Organization: Identify organization responsible for software as completely as possible, including Agency (Department), Office, Service, Bureau, Corporation, Commission, or Council.

14. Address: Complete mailing address for responsible organization including building name, street address, city, state, and ZIP code. Include mail stop number if applicable.

15. Technical Contact(s): Name of person(s) to be contacted for technical information. Provide organization name and mailing address if different from those indicated in items 13 and 14.

16. Telephone number(s): Telephone number of technical contact(s). Provide area code, seven-digit commercial number, and extension.

20. Computer Manufacturer and Model: Identify mainframe computer on which software is operational. Use manufacturer, model, and abbreviations and codes provided in OMB Circular A-11.

21. Computer Memory Requirements: Maximum memory required to execute software other than that required for operating system. Specify bytes or words and numbers of bits per word.

22. Computer Operating System: Name, version, and release under which software is operating. Identify any operating system enhancements.

23. Tape Drives: Identify number needed to operate software. Specify, if critical, additional requirements such as manufacturer, model, recording density, number of tracks, etc.

24. Disk/Drum Units: Identify number needed to operate software. Specify manufacturer, model, etc., where critical.

25. Keyboard Terminals: Identify number of keyboard terminals used for inquiry and response, and/or remote operations. Specify manufacturer and model.

26. Programming Language(s): Identify programming language(s) used to generate software (include versions) e.g., ANSI COBOL, FORTRAN V, SIMSCRIPT II.5.

30. Other Operational Requirements: Identify other peripheral devices, support software, or related equipment used, but not indicated above, e.g., optical character readers, facsimile, computer-output-microfilm, graphic plotters.

35. Narrative: Describe concisely what the software functionally accomplishes, its design characteristics, specific areas of application, relationship to other software, and other significant features.

40. Keywords: List significant words or phrases which reflect the functions, applications, and features of the software. Separate entries with semicolons.

45. Status: Enter code best describing software status:
1=planned
2=under development
3=operational
4=post operational
5=other (explain in narrative)

46. Software Availability:
1=available
2=proprietary
3=classified
4=other (explain in narrative)

47. Documentation:
1=available
2=in preparation
3=unavailable

* In this draft, elements are numbered in groups for identification purposes. In the final form, elements will be numbered sequentially.

[FR Doc.73-18071 Filed 8-27-73;8:45 am]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

[DESI 6536 Docket No. FDC-D-307; NDA 6-536]

BETHANECHOL CHLORIDE

Drugs for Human Use; Drug Efficacy Study Implementation; Followup Notice

In a notice (DESI 6536) published in the FEDERAL REGISTER of May 22, 1971 (36 FR 9341), the Commissioner of Food and Drugs announced his conclusions pursuant to the evaluation of reports received from the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, on the following drugs:

NDA 6-536; Urecholine Chloride Tablets and Injection containing bethanechol chloride; Merck Sharp & Dohme, Division of Merck and Co., Inc., West Point, PA 19486.

All identical, related, or similar products, not the subject of an approved new drug application, are covered by the new drug application(s) reviewed and are subject to this notice. See 21 CFR 130 (37 FR 23185, Oct. 31, 1972). Any per... who wishes to determine whether a s... cific product is covered by this not... should write to the Food and Drug A... ministration, Bureau of Drugs, Office ... Compliance (BD-200), 5600 Fish... Lane, Rockville, MD 20852.

The notice stated that bethanech... injection was deemed effective for c... tain indications and the tablets probab... effective for these indications and th... the other labeled indications were po... sibly effective and lacking substanti... evidence of effectiveness. The possib... effective indications have been reclas... fied as lacking substantial evidence ... effectiveness in that no new eviden... of effectiveness has been received pu... suant to the notice.

Based upon reevaluation of availab... information, the indications previous... considered as probably effective are no... regarded as effective. Also, the require... ment that bioavailability data be sub... mitted has been deferred and abbrevi... ated rather than full new dru... applications and supplements may b... submitted.

Accordingly, the previous announce... ment is amended to read as follows:

A. *Effectiveness classification.*—The Food and Drug Administration has considered the Academy's reports, as wel... as other available evidence, and con... cludes that:

1. Bethanechol chloride injection and tablets are effective for treatment of acute postoperative and postpartum nonobstructive (functional) urinary retention and for neurogenic atony of the urinary bladder with retention.

2. These drugs lack substantial evidence of effectiveness for all their othe... labeled indications.

B. *Conditions for approval and marketing.*—The Food and Drug Administration is prepared to approve abbrevi... ated new drug applications and abbreviated supplements to previously approved new drug applications under conditions described herein.

1. *Form of drug.*—These preparations are in sterile aqueous solution or tablet form suitable for subcutaneous or oral administration, respectively.

2. *Labeling conditions.*—a. The labels bear the statement, "Caution: Federal law prohibits dispensing without prescription."

b. The drugs are labeled to comply with all requirements of the Act and regulations, and the labeling bears adequate information for safe and effective use of the drug(s). The "Indications" are as follows:

INDICATIONS

For the treatment of acute postoperative and postpartum nonobstructive (functional) urinary retention and for neurogenic atony of the urinary bladder with retention.

3. *Marketing status.*—Marketing of such drugs may be continued under the conditions described in the notice entitled *Conditions for Marketing New Drugs Evaluated in Drug Efficacy Study*, published in the FEDERAL REGISTER July 14, 1970 (35 FR 11273), as follows:

For holders of "deemed approved" new drug applications (i.e., an application which became effective on the basis of safety prior to October 10, 1962), the submission of a supplement for revised labeling and an abbreviated supplement for new labeling information as described in paragraphs (a)(1)(i) and (iii) of the notice of July 14, 1970.

b. For any person who does not hold an approved or effective new drug application, the submission of an abbreviated new drug application as described in paragraph (a)(3)(i) of that notice.

c. For any distributor of the drug, the use of labeling in accord with this announcement for any such drug shipped within the jurisdiction of the Act as described in paragraph (b) of that notice.

C. *Notice of opportunity for a hearing.*—Notice is given to the holder(s) of the new drug application(s) and to any other interested person that the Commissioner proposes to issue an order under section 505(e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355 (e)) withdrawing approval of the listed new drug application(s) and all amendments and supplements thereto providing for indications lacking substantial evidence of effectiveness referred to in paragraph A.2. of this notice on the grounds that new information before him with respect to the drug(s), evaluated together with theevidence available to him at the time of approval of the application(s), shows there is a lack of substantial evidence that the drug(s) will have all the effects purported or represented to have under the conditions of use prescribed, recommended, or suggested in the labeling. An order withdrawing approval will not issue with respect to any application(s) supplemented, in accord with this notice, to delete the claim(s) lacking substantial evidence of effectiveness.

Any manufacturer or distributor of such an identical, related, or similar product is an interested person who may in response to his notice submit data and information, request that the new drug application(s) not be withdrawn, request a hearing, and participate as a party in any hearing.

In accordance with the provisions of section 505 of the Act (21 U.S.C. 355) and the regulations promulgated thereunder (21 CFR Part 130), the Commissioner hereby gives the applicant(s) and any other interested person an opportunity for a hearing to show why approval of the new drug application(s) providing for the claim(s) involved should not be withdrawn.

On or before September 27, 1973 the applicant(s) and any other interested person may file with the Hearing Clerk, Food and Drug Administration, Room 6–86, 5600 Fishers Lane, Rockville, Maryland 20852, a written appearance electing whether or not to avail himself of the opportunity for a hearing. Failure of an applicant or any other interested person to file a written appearance of election within the specified time will constitute an election by him not to avail himself of the opportunity for a hearing. No extension of time may be granted.

If no person elects to avail himself of the opportunity for a hearing, the Commissioner without further notice will enter a final order withdrawing approval of the application(s) which have not been supplemented to delete the indication(s) lacking substantial evidence of effectiveness.

If an applicant or any other interested person elects to avail himself of the opportunity for a hearing, he must file, on or before September 27, 1973, a written appearance requesting the hearing, giving the reasons why approval of the new drug application(s) should not be withdrawn, together with a well-organized and full-factual analysis of the clinical and other investigational data he is prepared to prove in support of his opposition. A request for a hearing may not rest upon mere allegations or denials, but must set forth specific facts showing that a genuine and substantial issue of fact requires a hearing (21 CFR 130.14(b)).

If review of the data submitted by an applicant or any other interested person warrants the conclusion that there exists substantial evidence demonstrating the effectiveness of the product(s) for the labeling claim(s) involved, the Commissioner will rescind this notice of opportunity for hearing.

If review of the data in the application(s) and data submitted by the applicant(s) or any other interested person in a request for a hearing, together with the reasoning and factual analysis in a request for a hearing, warrants the conclusion that no genuine and substantial issue of fact precludes the withdrawal of approval of the application(s), the Commissioner will enter an order making findings and conclusions on such data and withdrawing approval of application(s) not supplemented to delete the claim(s) involved.

If, upon the request of the new drug applicant(s) or any other interested person, a hearing is justified, the issues will be defined, a hearing examiner will be named, and he shall issue, as soon as practicable after September 27, 1973, a written notice of the time and place at which the hearing will commence. All persons interested in identical, related, or similar products covered by the new drug application(s) will be afforded an opportunity to appear at the hearing, file briefs, present evidence, cross-examine witnesses, submit suggested findings of fact, and otherwise participate as a party. The hearing contemplated by this notice will be open to the public except that any portion of the hearing that concerns a method or process the Commissioner finds entitled to protection as a trade secret will not be open to the public, unless the respondent specifies otherwise in his appearance.

Communications forwarded in response to this notice should be identified with the reference number DESI 6536, directed to the attention of the appropriate office listed below, and addressed to the Food and Drug Administrati 5600 Fishers Lane, Rockville, MD 20852

Supplements (identify with NDA numbe Office of Scientific Evaluation (BD–10 Bureau of Drugs.

Original abbreviated new drug applicati (identify as such): Generic Drug Staff (BD–90), Bureau Drugs.

Requests for the Academy's report: Drug Efficacy Study Information Cont (BD–66), Bureau of Drugs.

Request for Hearing (identify with doc number): Hearing Clerk, (CC–20), Room 6–86, Pa lawn Building.

All other communications garding t announcement: Drug Efficacy Study Implementation P ject Manager (BD–101), Bureau of Dru

Received requests for a hearing m be seen in the office of the Hearing Cl (address given above) during regu business hours, Monday throu Friday.

This notice is issued pursuant to p visions of the Federal Food, Drug, a Cosmetic Act (Sec. 502, 505, 52 St 1050–53, as amended; 21 U.S.C. 352, 3 and the Administrative Procedure A (5 U.S.C. 554), and under the author delegated to the Commissioner of Fo and Drugs (21 CFR 2.120).

Dated August 21, 1973.

SAM D. FINE,
Associate Commissioner for Compliance

[FR Doc.73–18152 Filed 8–27–73;8:45 am

[DESI 5773 Docket No. FDC–D–642; NDA 5–773]

HOLLAND-RANTOS CO., INC.

Nylmerate Jelly; Notice of Opportunity Hearing on Proposal To Withdraw A proval of New Drug Application

In a notice (DESI 5773) published the FEDERAL REGISTER of July 27, 19 (37 FR 15030) the Commissioner of Fo and Drugs announced his conclusi pursuant to the evaluation of a rep received from the National Academy Sciences-National Research Coun Drug Efficacy Study Group, on the dr described below stating that the dr was regarded as possibly effective and lacking substantial evidence of effecti ness for the various labeled indicatio The possibly effective indications ha been reclassified as lacking substant evidence of effective in that no da have been submitted pursuant to t notice.

Nylmerate Jelly containing no oxynol 9 (previously listed as pol oxyethylenenonylphenol), phenylm curic acetate, and boric acid; market by Holland-Rantos Co., Inc., Enterpr Avenue, Trenton, N.J. 08638 (NI 5–773).

Therefore, notice is given to t holder(s) of the new drug application and to any other interested person th the Commissioner proposes to issue order under section 505(e) of the Fe eral Food, Drug, and Cosmetic Act (U.S.C. 355(e)) withdrawing approval

NOTICE OF APPROVAL
NEW DRUG APPLICATION OR SUPPLEMENT

NDA NUMBER: 88-441

DATE APPROVAL LETTER ISSUED: MAY 29 1984

TO: Press Relations Staff (HFI-40)

FROM:
- [XX] Bureau of Drugs
- [ ] Bureau of Veterinary Medicine

ATTENTION

Forward original of this form for publication only after approval letter has been issued and the date of approval has been entered above.

TYPE OF APPLICATION
- [ ] ORIGINAL NDA
- [ ] SUPPLEMENT TO NDA
- [XX] ABBREVIATED ORIGINAL NDA
- [ ] SUPPLEMENT TO ANDA

CATEGORY
- [XX] HUMAN
- [ ] VETERINAR

TRADE NAME *(or other designated name)* AND ESTABLISHED OR NONPROPRIETARY NAME *(if any)* OF DRUG

Bethanechol Chloride

DOSAGE FORM: Tablet

HOW DISPENSED
- [X] RX
- [ ] OTC

ACTIVE INGREDIENT(S) *(as declared on label. List by established or nonproprietary name(s) and include amount(s), if amount is declared on label.)*

Bethanechol Chloride, 25 mg.

APPEARS THIS WAY
ON ORIGINAL

NAME OF APPLICANT *(Include City and State)*

Sidmak Laboratories, Inc.
East Hanover, NJ 07936

PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY

Treatment of acute postoperative and postpartum nonobstructive (functional) urinary retention.

COMPLETE FOR VETERINARY ONLY

ANIMAL SPECIES FOR WHICH APPROVED

COMPLETE FOR SUPPLEMENT ONLY

CHANGE APPROVED TO PROVIDE FOR

FORM PREPARED BY

NAME	DATE
V.Walton V. Walton	5-22-84

FORM APPROVED BY

NAME	DATE

FORM FD 1642 (2/75) PREVIOUS EDITION MAY BE USED UNTIL SUPPLY IS EXHAUSTED.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

88-441

CORRESPONDENCE

Orig

idmak
LABORATORIES, INC.

17 WEST STREET • P.O. BOX 371 • EAST HANOVER, NJ 07936 • TELEPHONE: (201) 386-5566

FPL for container label and current labeling satisfactory 5/22/84

May 14, 1984

RESUBMISSION

NDA ORIG AMENDMENT

EPU

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
National Center for Drugs and Biologics
Room 16-70 (HFN-530)
FOOD AND DRUG ADMINISTRATION
5600 Fishers Lane
Rockville, MD 20852

RE: Abbreviated New Drug Application
Product: Bethanechol Chloride Tablets, 25 mg.

NDA#: 88-441

Dear Dr. Seife:

We refer to your communication dated 4/16/84 regarding the above referenced unapproved abbreviated new drug application (copy attached).

As per your request, we are herewith submitting 12 copies of the final printed label and final printed insert in order that you may complete the review of this application.

We respectfully submit this information and look forward to your prompt approval in order that we may begin marketing this drug.

Sincerely yours,

Satish P. Patel, Ph.D.
President

SIDMAK LABORATORIES, INC.

SPP:lk

encs.

RECEIVED
MAY 16 1984
GENERIC DRUGS

APR 16 8

NDA 88-441

Sidmak Laboratories, Inc.
Attention: Satish P. Patel, Ph.D.
17 West Street, P.O. Box 371
East Hanover, NJ 07936

Gentlemen:

Please refer to your abbreviated new drug application dated July 25, 1983, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Bethanechol Chloride Tablets, 25 mg.

Reference is also made to your submission of April 3, 1984.

We have completed the review of this application as submitted with draft labeling. However, before the application may be approved, it will be necessary for you to submit final printed labeling. The labeling should be identical in content to the draft copy, except the ' statement should be deleted. If additional information relating to the safety or effectiveness of this drug becomes available before we receive the final printed labeling, revision of that labeling may be required.

Please submit 12 copies of the final printed labels and other labeling.

In addition, we would appreciate your submitting, in duplicate, the advertising copy which you intend to use in your immediate or proposed promotional or advertising campaign. Please submit this information to the Division of Drug Advertising and Labeling HFN-240.

The drug may not be legally marketed until you have been notified in writing that the application is approved.

Sincerely yours,

Marvin Seife 4/16/84

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drugs and Biologics

cc: NWK-DO

HFN-530 V. Walton
HFN-616 JMeyer 4/13/84
KJohnson/JMeyer/VWalton
R/D INITIAL JMeyer
mm:4/13/84 (2019A)
Approvable

idmak
LABORATORIES, INC.

17 WEST STREET • P.O. BOX 371 • EAST HANOVER, NJ 07936 • TELEPHONE: (201) 386-5566

April 3, 1984

RESUBMISSION

NDA ORIG AMENDMENT

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
National Center for Drugs and Biologics
Room 16-70 (HFN-530)
FOOD AND DRUG ADMINISTRATION
5600 Fishers Lane
Rockville, MD 20852

DRAFT LABELING

RE: Abbreviated New Drug Application
Product: Bethanechol Chloride Tablets, 25 mg.
NDA # : 88-441

Dear Dr. Seife:

Reference is made to your letter dated March 2, 1984 concerning the above referenced pending application (see attached copy).

We have enclosed in this amendment a draft copy of the revised package insert. This draft is in accord with the most current (March 1983) labeling guidelines.

As regards the stability indicating assay methodology you requested, I submit the following: We have checked with the FDA (Dr. Eric B. Shenin), with the USP (Ms. Barbara Hubert -, New Monographs), with holders of other approved abbreviated applications for this product, and our supplier of the active new-drug substance. None of the above sources has an approved, validated procedure for detecting and/or quantitating any degradation by-products for Bethechol Chloride. Also, chemically, this drug substance is very stable under normal storage conditions.

At the present time, we are working to solve this problem, both with [redacted] and [redacted] procedures. We have not been totally successful to date. However, we would request that you allow us to market this product while we continue to try to develop a satisfactory method which is stability indicating.

We look forward to your favorable response for conditional approval.

Sincerely yours,

Satish P. Patel, Ph.D.
President

SIDMAK LABORATORIES, INC.
SPP:lk
encs.

GENERIC DRUGS

NDA 88-441

Sidmak Laboratories, Inc.
Attention: Satish P. Patel, Ph.D.
17 West Street, P.O. Box 371
East Hanover, NJ 07936

Gentlemen:

Please refer to your abbreviated new drug application dated July 25, 1983, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for the preparation Bethanechol Chloride Tablets, 25 mg.

Reference is also made to your submission dated January 30, 1984 and to our letter dated December 29, 1983.

The application is deficient and therefore not approvable under Section 505(b) of the Act as follows:

1. It fails to include adequate information in the labeling. We recommend that you revise the package insert in accord with the labeling guidelines previously sent.

2. It fails to include a stability indicating assay method. We recommend that you develop and submit a ——— procedure or submit data indicating that the USP XX assay method is stability indicating.

The file is now closed. If you wish to reopen it, the submission should be in the form of an amendment to this application, adequately organized, which represents the information necessary to remove all deficiencies we have outlined.

If you do not agree with our conclusions, you may make a written request to file the application over protest, as authorized by 21 CFR 314.110(d). If you do so, the application shall be re-evaluated and within 90 days of the date of receipt of such request (or additional period as we may agree upon), the application shall be approved or you shall be given a written notice of opportunity for a hearing on the question of whether the application is approvable.

Sincerely yours,

Marvin Seife 3/7/84

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
National Center for Drugs and Biologics

cc: NWK-DO
HFN-530
KJohnson/JMeyer/VWalton
R/D INITIAL JMeyer/KJohnson/MSeife
mm:2/29/84 (0781A)
Not Approvable

JMeyer 3/1/84

V. Walton

sidmak
LABORATORIES, INC.

17 WEST STREET • P.O. BOX 371 • EAST HANOVER, NJ 07936 • TELEPHONE: (201) 386-5566

Orig

January 30, 1984

RESUBMISSION

NDA ORIG AMENDMENT

FPL

The container labels are satisf.
Insert labeling is not satisf
Must revise as directed
12-29-83. Kenfel 2-7-84

Marvin Seife, M.D.
Director
Division of Generic Drug Monographs
Office of the Associate Director for Drug Monographs
Office of Drugs
National Center for Drugs and Biologics
5600 Fishers Lane
Rockville, MD 20852

RE: Abbreviated New Drug Application
Product: Bethanechol Chloride Tablets, USP 25mg.
NDA#: 88-441

Dear Dr. Seife:

We refer to our above referenced Abbreviated New Drug Application, NDA 88-441, and we refer to your letter dated December 29, 1983 (copy enclosed).

In order to remove all deficiencies as cited in your letter and in order to complete our application, we are herewith submitting the following information to serve as an Amendment:

Exhibit 1: Twelve copies of the final printed label for each package size;

Exhibit 2: Twelve copies of the final printed insert, which incorporates the changes you suggested in your letter of 12/29/83;

Exhibit 3: An amended page 72. This correctly cites the stability indicating assay being used, and makes reference to the pages of the application (pages 66-67) which outline these procedures;

Exhibit 4: Enclosed in this exhibit are copies of all tests [redacted] containers to meet the requirements of the Code of Federal Regulations.

We respectfully submit this information and trust it will meet with your approval.

RECEIVED
FEB
GENERIC DRUGS

Sincerely yours,

Satish P. Patel, Ph.D.
President
SIDMAK LABORATORIES, INC.

encs.

DEC 29 1983

NDA 88-441

Sidmak Laboratories, Inc.
Attention: Satish P. Patel, Ph.D.
17 West Street
P.O. Box 371
East Hanover, NJ 07936

Gentlemen:

Please refer to your abbreviated new drug application dated July 25, 1983, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for the preparation Bethanechol Chloride Tablets, 25 mg.

Reference is also made to your submission of October 13, 1983.

The application is deficient and therefore not approvable under Section 505(b) of the Act as follows:

1. It fails to include correct labeling. In this regard:

   Container: Satisfactory, 100s, 500s, 1000s.

   Insert: Not Satisfactory.

   a) Must be updated to provide information similar to our Labeling Guideline.

   You may prepare and submit FPL for container labels. You may also prepare and submit revised insert labeling. The date of printing must appear on this labeling.

2. It fails to include the stability indicating assay procedure referred to on page 72 of your application.

3. It fails to indicate which ——— is used by each supplier of the HDPE containers. Also assurances must be made that each ——— meets the requirements of the Food Additive Regulations.

The file is now closed. If you wish to reopen it, the submission should be in the form of an amendment to this application, adequately organized, which represents the information necessary to remove all deficiencies we have outlined.

If you do not agree with our conclusions, you may make a written request to file the application over protest, as authorized by 21 CFR 314.110(d). If you do so, the application shall be re-evaluated and within 90 days of the date of receipt of such request (or additional period as we may agree upon), the application shall be approved or you shall be given a written notice of opportunity for a hearing on the question of whether the application is approvable.

Sincerely yours,

/s/ Marvin Seife 12/29/83

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
National Center for Drugs and Biologics

cc: NWK-DO
HFN-530
KJohnson/JMeyer/VWalton
R/D INITIAL JMeyer/MSeife
mm:12/27/83 (3942c)
Not Approvable

V. Walton

JMeyer 12/28/83

Sidmak LABORATORIES, INC.

17 WEST STREET • P.O. BOX 371 • EAST HANOVER, NJ 07936 • TELEPHONE: (201) 386-5566

Orig

October 13, 1983

ORIG NEW CORRES

Marvin Seife, M.D.
Director
Division of Generic Drug Monographs
Office of the Associate Director for Drug Monographs
Office of Drugs
National Center for Drugs and Biologics
5600 Fishers Lane
Rockville, MD 20857

REF: NDA 88-441
Amendment to Abbreviated, Unapproved Application
Three Month Stability Studies
Product: Bethanechol Chloride Tablets, USP 25mg.

Dear Dr. Seife:

We refer to our Abbreviated New Drug Application, NDA 88-441, dated July 25, 1983, for the pharmaceutical dosage form Bethanechol Chloride Tablets, USP 25mg.

Pursuant to applicable regulations, we herewith submit and enclose the following supplemental information, as outlined below, in triplicate:

1. Three Month Stability Studies, Stability Condition: R.T. for the above referenced product, in package size of 1000 Tablets per bottle;

2. Three Month Stability Studies, Stability Conditions: 37°C-75% R.H., for the above referenced product in package size of 1000 Tablets per bottle;

3. Three Month Stability Studies, Stability Condition: R.T. for the above referenced product, in package size of 100 Tablets per bottle;

4. Three Month Stability Studies, Stability Conditions: 37°C-75% R.H., for the above referenced product in package size of 100 tablets per bottle.

We respectfully submit this information and trust it will meet with your approval, and remain,

Sincerely yours,

Satish P. Patel, Ph.D., President
SIDMAK LABORATORIES, INC.
encs.

RECEIVED
OCT 18 1983
GENERIC DRUGS

SPP:lk

AUG 1 1983

NDA 88-441

Sidmak Laboratories, Inc.
Attention: Satish Patel, Ph.D.
17 West Street
P.O. Box 371
East Hanover, NJ 07936

Gentlemen:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

NAME OF DRUG: Bethanechol Chloride Tablets, USP, 25 mg.

DATE OF APPLICATION: July 25, 1983

DATE OF RECEIPT: July 27, 1983

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the NDA number shown above.

Sincerely yours,

Marvin Seife 8/1/83

Marvin Seife, M.D.
Director
Division of Generic Drug Monographs
Office of the Associate Director for
Drug Monographs
Office of Drugs
National Center for Drugs & Biologics

cc:
NWK-DO
HFN-530
JLMeyer/cjl/7-28-83
ack

JLMeyer 7/29/83

Sidmak
LABORATORIES, INC.

17 WEST STREET • P.O. BOX 371 • EAST HANOVER, NJ 07936 • TELEPHONE: (201) 386-5566

July 25, 1983

Marvin Seife, M.D., Director
Division of Generic Drug Monographs
Office of the Associate Director for Drug Monographs
Office of Drugs
National Center for Drugs and Biologics
5600 Fishers Lane
Rockville, Maryland 20852

ABBREVIATED
NEW DRUG APPLICATION
88 491

Re: Abbreviated New Drug Application
Product: Bethanechol Chloride Tablets, USP 25mg.

Dear Dr. Seife:

Pursuant to section 505(b) of the Federal Food, Drug and Cosmetic Act, we are submitting herewith, in triplicate, an Abbreviated New Drug Application for the product mentioned above.

Included in this submission are:

1. Form 356-H
2. Volume No. 1 Copy No. 1 (Blue Folder)
3. Volume No. 1 Copy No. 2 (Red Folder)
4. Volume No. 1 Copy No. 3 (Yellow Folder)

Respectfully Submitted,

SIDMAK LABORATORIES, INC.

Satish Patel, Ph.D.
President

RECEIVED
JUL 27 1983

GENERIC DRUGS