CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-179

ADMINISTRATIVE DOCUMENTS
CORRESPONDENCE

September 15, 1999

PATENT INFORMATION

Patent Number:	5,496,545
Date of Expiration:	August 11, 2013
Type of Patent:	Method of Use Patent and Drug Substance Patent
Patent Owner:	GelTex Pharmaceuticals, Inc. Waltham, Massachusetts

Original Declaration:

The undersigned declares that Patent No. 5,496,545 covers the composition and the method of use of Renagel® as a phosphate binder. This product is the subject of this application for which approval is being sought.

GELTEX PHARMACEUTICALS, INC

By: _____

Mark Skaletsky
President and CEO

September 15, 1999

PATENT INFORMATION

Patent Number:	5,667,775
Date of Expiration:	September 16, 2014
Type of Patent:	Method of Use Patent
Patent Owner:	GelTex Pharmaceuticals, Inc. Waltham, Massachusetts

Original Declaration:

The undersigned declares that Patent No. 5,667,775 covers the method of use of Renagel® as a phosphate binder. This product is the subject of this application for which approval is being sought.

GELTEX PHARMACEUTICALS, INC

By: _____

Mark Skaletsky
President and CEO

Exclusivity Checklist

NDA:	21-179
Trade Name:	Renagel Tablets
Generic Name:	sevelamer hydrochloride
Applicant Name:	GelTex
Division:	HFD-510
Project Manager:	Randy Hedin
Approval Date:	

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 questions about the submission.

a. Is it an original NDA?	Yes	✓	No	
b. Is it an effectiveness supplement?	Yes		No	✓
c. If yes, what type? (SE1, SE2, etc.)				
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.

Explanation: The study submitted is a dissolution study for a tablet formulation + returns to the NDA for the capsule formulation for safety & efficacy data.

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:

Explanation:

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.

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 #				
Drug Name:				

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS.				
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 (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.	Yes	✓	No	
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).				
Drug Product	Renagel			
NDA #	21-926			
Drug Product				
NDA #				
Drug Product				
NDA #				
2. Combination product.	Yes		No	✓
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 <u>any one</u> 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).				
Drug Product				
NDA #				
Drug Product				
NDA #				
Drug Product				

NDA #				
IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS. 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.				
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. For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.				
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 BLOCKS.**				
Basis for conclusion:				
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? If not applicable, answer NO.	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:				
Investigation #1, Study #:				
Investigation #2, Study #:				
Investigation #3, Study #:				
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	
Investigation #3	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:				
Investigation #1 -- NDA Number				
Investigation #2 -- NDA Number				
Investigation #3 -- NDA Number				
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	
Investigation #3	Yes		No	
If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:				
Investigation #1 -- NDA Number				
Investigation #2 -- NDA Number				
Investigation #3 -- NDA Number				
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"):

Investigation #1	
Investigation #2	
Investigation #3	

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	Yes		No	
IND#:				
Explain:				
Investigation #2	Yes		No	
IND#:				
Explain:				
Investigation #3	Yes		No	
IND#:				
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		No	
IND#:				
Explain:				
Investigation #2	Yes		No	
IND#:				
Explain:				
Investigation #3	Yes		No	
IND#:				
Explain:				

c. Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)	Yes		No	
If yes, explain:				

BACK TO TOP

Signature of PM/CSO [/S/]
Date: 6/26/00

Signature of Division Director [/S/]
Date: 7/12/00

cc:
Original NDA
Division File
HFD-93 Mary Ann Holovac

BACK TO TOP

September 15, 1999

CLAIM OF EXCLUSIVITY BASED ON 21 CFR 314.108(b)(2)

GelTex Pharmaceuticals, Inc. ("GelTex") was granted five-year exclusivity for Renagel® with the approval of NDA 20-926 on October 30, 1998, as reflected in the FDA publication *Approved Drug Products with Therapeutic Equivalence Evaluations.*

GELTEX PHARMACEUTICALS, INC

By: _____

Mark Skaletsky
President and CEO

APPEARS THIS WAY
ON ORIGINAL

PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements)

NDA/BLA Number:	21179	**Trade Name:**	RENAGEL (SEVELAMER HCL)400MG/800MG
Supplement Number:		**Generic Name:**	SEVELAMER HCL
Supplement Type:		**Dosage Form:**	Tablet; Oral
Regulatory Action:	AP	**Proposed Indication:**	Renagel is indicated for the reduction of serum phosphorus in patients with end-stage renal disease (ESRD).

ARE THERE PEDIATRIC STUDIES IN THIS SUBMISSION?

NO, No data was submitted for this indication, however, plans or ongoing studies exist for pediatric patients

What are the INTENDED Pediatric Age Groups for this submission?

____NeoNates (0-30 Days) ____Children (25 Months-12 years)
____Infants (1-24 Months) ____Adolescents (13-16 Years)

Label Adequacy	Inadequate for ALL pediatric age groups
Formulation Status	
Studies Needed	STUDIES needed. Applicant in NEGOTIATIONS with FDA
Study Status	

Are there any Pediatric Phase 4 Commitments in the Action Letter for the Original Submission? NO

COMMENTS:
On November 15, 1999, the firm submitted a pediatric development plan. 7/11/00

This Page was completed based on information from a PROJECT MANAGER/CONSUMER SAFETY OFFICER, RANDY HEDIN

[/S/]
Signature

7/11/00
Date

16. DEBARMENT CERTIFICATION

September 15, 1999

CERTIFICATION PURSUANT TO 21 U.S.C. 306(k)(1)

GelTex Pharmaceuticals, Inc. hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.

GELTEX PHARMACEUTICALS, INC.

By: _____

Mark Skaletsky
President and CEO

APPEARS THIS WAY
ON ORIGINAL

NDA 21-179

Dear Ms Carter:

Please refer to your new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Renagel (sevelamer hydrochloride) 400 and 800 mg Tablets.

We have the following comments concerning your submission. If you need to evaluate the in vitro phosphate binding capacity of future formulations of sevelamer, the data submitted will need to be more comprehensive. For example:

- —— different concentrations of test media were used in this NDA; for further formulations —— different test media concentrations will be needed in replicates.
- You will need to evaluate the equilibrium binding as the primary outcome, rather than kinetic binding.
- Calculation of k1 and k2 (Langmuir binding constants) will be needed.

Also, we recommend that you submit protocols for review and comment before any study begins.

If you have any questions, contact Randy Hedin, R.Ph., Senior Regulatory Management Officer, at (301) 827-6392.

Cleared for Faxing: [/S/] 7/11/00

Lisa Rarick, M.D.
Deputy Office Director

cc: Orig NDA
HFD-510
HFD-510/RShore/HAhn
HFD-511/RHedin/7.11.00/N21179_LT1_FAX.doc
Concurrences: RShore/HAhn/7.11.00

ADVICE (AD)

HFD-510

GelTex PHARMACEUTICALS, INC.

BEST POSSIBLE COPY

July 10, 2000

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Attention: Division Document Room, 14B-19
5600 Fishers Lane
Rockville, MD 20857

RE: NDA 21-179
Renagel® Tablets (sevelamer hydrochloride) 400 and 800 mg
Amendment 006

Dear Sir/Madam:

Reference is made to the NDA cited above and to a July 3, 2000 facsimile from Randy Hedin containing revisions to the package insert. The purpose of this submission is to submit a new draft package insert for Renagel Tablets, which incorporates this text. Please note that additional minor additions are indicated in bold, 16-point text and deletions are indicated in bold, 16-point strikeout text. This labeling replaces the package insert submitted in Amendment 001 dated May 23, 2000. Please note that it is our intention to also use this package insert for Renagel® Capsules, NDA 20-926, following approval.

Also provided are draft immediate container and outer carton labels for both the 400 and 800 mg tablets. This revised draft replaces the labeling in Sections 2.3 - 2.11 (pages 22 to 31) of the original NDA.

Should you have any questions, please do not hesitate to contact the undersigned at (781) 434-3443, or Dean F. Alger, Director, Regulatory Affairs, at (781) 434-3421.

Sincerely yours,

Martha J. Carter
Vice President, Regulatory Affairs

153 Second Avenue Waltham, MA 02451 Phone: (781) 290-5888 Fax: (781) 290-5890 Website: www.geltex.com

GelTex PHARMACEUTICALS, INC.

June 19, 2000

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Attention: Division Document Room, 14B-19
5600 Fishers Lane
Rockville, MD 20857

RE: NDA 21-179
Renagel® 400 and Renagel® 800 (sevelamer hydrochloride)
Amendment 005

Dear Sir/Madam:

Reference is made to the NDA cited above and to the Agency's letter of June 14, 2000 containing comments on Section 4.

The purpose of this submission is to respond to your comments, and to provide the requested information in Attachments 1-3. For ease of review, the Agency's requests/comments are repeated in ***bold italics***, followed by our responses.

1. ***Please provide the acceptance tests and specifications for the drug substance as performed by the drug product manufacturer,*** ————

The drug product manufacturer ————, will confirm the drug substance manufacturer's certificate of analysis by testing, at minimum, the first t— commercial lots of drug substance from each supplier for conformance to the specifications presented in Table 4.58 of NDA 20-926 (see volume 2, page 129). Once the reliability of each supplier's certificate of analysis has been established, subsequent receipts will be tested for identity and the supplier's certificate of analysis reviewed for correctness. Thereafter, the drug product manufacturer will test annually a minimum of — lot of drug substance from each supplier for conformance to the specifications in Table 4.58 of NDA 20-926.

2. ***Add an identity test to your acceptance tests and specifications for ———— ———— Please also supply representative "Certificates of Acceptance" for all inactive excipients.***

Table 4.2-7 from NDA 21-179 has been modified to include an identity test for [redacted] and the revised table is provided in Attachment 1.

Representative Certificates of Analysis for the following inactive excipients are provided in Attachment 2: stearic acid, [redacted] colloidal silicon dioxide, hydroxypropyl methylcellulose [redacted], diacetylated monoglyceride [redacted] black ink, [redacted]

3. ***Provide Chemistry Manufacturing and Control information (components, composition, supplier, and COA) or a DMF reference for black Ink [redacted] (sic).***

A letter of cross-reference to [redacted] DMF No. [redacted] for [redacted] is provided in Attachment 3.

4. ***Submit updated stability information as it becomes available.***

Updated stability information for Renagel 400 and Renagel 800 was submitted to this NDA in Amendment 003 dated June 14, 2000.

Should you have any questions, please do not hesitate to contact the undersigned at (781) 434-3443, or Dean F. Alger, Director, Regulatory Affairs, at (781) 434-3421.

Sincerely yours,

Martha J. Carter.

Martha J. Carter
Vice President, Regulatory Affairs

GelTex PHARMACEUTICALS, INC.

June 16, 2000

BEST POSSIBLE COPY

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Attention: Division Document Room, 14B-19
5600 Fishers Lane
Rockville, MD 20857

RE: NDA 21-179
Renagel® 400 & Renagel® 800 (sevelamer hydrochloride)
Amendment 004

Dear Sir/Madam:

Reference is made to the NDA cited above and to a telephone conversation between Dr. Robert Shore and Mr. Dean Alger on June 15, 2000. As a follow up to that conversation, we are submitting responses to Dr. Shore's queries, as follows:

1. ***Provide information on how the k_1 and k_2 binding constants were calculated in your submission to IND ——— dated February 4, 2000 (Serial No. 041).***

A copy of the spreadsheets containing the calculations of the k_1 and k_2 binding constants is provided in Attachment 1.

2. ***In Section 6 of the NDA, the statement is made that— different media were used in phosphate binding studies. Please confirm that some or all of these are the same media used to develop release specifications in the capsule NDA.***

Phosphate binding is a release test for Renagel capsules and Renagel tablets. For both the capsules and the tablets, the medium used for the phosphate binding determination is a solution of ———

The dissolution apparatus required a fixed volume ———) and was restricted to multiples of unit doses. Medium— used in the *in vitro* bioequivalence study comparing capsules and tablets preserves the ratio of phosphate to sevelamer of ———

[redacted] This result is comparable to the results obtained with the release test.

Table 1. Comparison of Phosphate Binding Solutions

Parameter	*Release Test (Capsules and Tablets)*	*Medium (in vitro bioequivalence)*
[redacted]		
Volume		
Sample wt.		
pH		
Ratio phosphate/ sevelamer		

3. Please provide a three to four page synopsis of the bioequivalence protocol.

The requested synopsis is provided in Attachment 2.

Should you have any questions, please do not hesitate to contact the undersigned at (781) 434-3443, or Dean F. Alger, Director, Regulatory Affairs, at (781) 434-3421.

Sincerely yours,

Martha J. Carter.

Martha J. Carter
Vice President, Regulatory Affairs

OFFICES OF DRUG EVALUATION
ORIGINAL NDA/NDA EFFICACY SUPPLEMENT
ACTION PACKAGE CHECKLIST

NDA 21-179 Drug: Renagel Tablets

Applicant: GelTex Chem/Ther/other Types: 3S

CSO/PM: R Hedin Phone: 7-6392 MailCode: HFD-510

ACTION PERF. GOAL DATE: 7/1/00 DATE CKLIST CMPLTD: 6/26/00

Arrange package in the following order (include a completed copy of this CHECKLIST): Check or Comment

1. ACTION LETTER with supervisory signatures — AP ✓ AE ____ NA ____
   Are there any Phase 4 commitments? Yes ____ No ____
2. Have all disciplines completed their reviews? Yes ✓ No ____
   If no, what review(s) is/are still pending? ____
3. LABELING (package insert and carton and container labels). Draft ✓
   (If final or revised draft, include copy of previous version with ODE's comments and state where in action package the Division's review is located. If Rx-to-OTC switch, include current Rx Package insert and HFD-312 and HFD-560 reviews of OTC labeling.) Revised Draft ____ Final ____
4. PATENT INFORMATION ✓
5. EXCLUSIVITY CHECKLIST ✓
6. PEDIATRIC PAGE ✓
7. DEBARMENT CERTIFICATION (Copy of applicant's certification for all NDAs submitted on or after June 1, 1992). ✓
8. Statement on status of **DSI's AUDIT OF PIVOTAL CLINICAL STUDIES** ✓
   If AE or AP ltr, explain if not satisfactorily completed. Attach a COMIS printout of DSI status.
   If no audits were requested, include a memo expaining why.

9. REVIEWS & MEMORANDA:

DIVISION DIRECTOR'S MEMO	If more than 1 review for any	NA
GROUP LEADER'S MEMO	1 discipline, separate reviews	
MEDICAL REVIEW	with a sheet of colored paper.	NA
SAFETY UPDATE REVIEW	Any conflicts between reviews	NA
STATISTICAL REVIEW	must have resolution documented	NA
BIOPHARMACEUTICS REVIEW		
PHARMACOLOGY REVIEW (Include pertinent IND reviews)		NA
Statistical Review of Carcinogenicity Study(ies)		NA
CAC Report/Minutes		NA
CHEMISTRY REVIEW		✓
Labeling and Nomenclature Committee Review Memorandum		✓
Date EER completed 11-19-99 (attach signed form or CIRTS printout)		OK ✓ No ____
FUR needed NO FUR requested ____		
Have the methods been validated?		Yes (attach) ____ No ✓
Environmental Assessment Review / **FONSI**		Review Included FONSI ____
MICROBIOLOGY REVIEW		NA
What is the status of the monograph?		NA

10. **CORRESPONDENCE, MEMORANDA OF TELECONS, and FAXes** ✓

11. **MINUTES OF MEETINGS**
    Date of End-of-Phase 2 Meeting None
    Date of pre-NDA Meeting None IND # ____

12. **ADVISORY COMMITTEE MEETING MINUTES** — Minutes ____ Info Alert ____
    or, if not available, 48-Hour Info Alert or pertinent section of transcript. Transcript ____ No mtg ✓

13. **FEDERAL REGISTER NOTICES; OTC or DESI DOCUMENTS** NA

14. If approval letter, has **ADVERTISING MATERIAL** been reviewed? Yes ____ No ✓
    If no and this is an AP with draft labeling letter, has ____ been requested? Yes, documentation attached ____
    No, included in AP ltr ✓

16. INTEGRATED SUMMARY OF SAFETY (from NDA)	NA
17. FDA LETTERS & MEMOS	✓
18. APPLICANT'S LETTERS	✓
19. CHARGE AND HISTORY CARD	✓

APPEARS THIS WAY
ON ORIGINAL

GelTex PHARMACEUTICALS, INC.

June 14, 2000

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Attention: Division Document Room, 14B-19
5600 Fishers Lane
Rockville, MD 20857

RE: NDA 21-179
Renagel® 400 & Renagel® 800 (sevelamer hydrochloride)
Amendment 003

Dear Sir/Madam:

Reference is made to the NDA cited above and to a telephone conversation with Mr. Randy Hedin on June 9, 2000. As a follow up to that conversation, we are submitting a stability update for Renagel® 400 & Renagel® 800. Accordingly, enclosed please find a report entitled "Updated Stability Results for Renagel® Tablets."

Please note that there are two additional bottle configurations not in the ongoing stability program that are proposed for marketing. That is, for the 400 mg strength, a [redacted] are on stability. The proposed market configuration also includes a [redacted] For the 800 mg strength, [redacted] are on stability. The proposed market configuration also includes a [redacted] Please refer to Section 4.2.20 of the NDA for the rationale for including the additional packaging configurations that are not part of the stability program.

Should you have any questions, please do not hesitate to contact the undersigned at (781) 434-3443, or Dean F. Alger, Director, Regulatory Affairs, at (781) 434-3421.

Sincerely yours,

Martha J. Carter.

Martha J. Carter
Vice President, Regulatory Affairs

153 Second Avenue Waltham, MA 02451 Phone: (781) 290-5888 Fax: (781) 290-5890 Website: www.geltex.com

Hedin

NDA 21-179

JUN 14 2000

GelTex Pharmaceuticals, Inc.
Attention: Ms. Martha Carter
Vice President, Regulatory Affairs
Nine Fourth Avenue
Waltham, MA 02451

APPEARS THIS WAY
ON ORIGINAL

Dear Ms. Carter:

Please refer to your September 15, 1999 new drug application for Renagel (sevelamer hydrochloride) Tablets.

We also refer to your submissions dated March 31 and May 24, 2000.

Our review of the Chemistry section of your submissions is complete, and we have identified the following deficiencies:

1. Please provide the acceptance tests and specifications for the drug substance as performed by the drug product manufacturer, ———

2. Add an identity test to your acceptance tests and specifications for ——— ——— Please also supply representative "Certificates of Acceptance" for all inactive excipients.

3. Provide Chemistry Manufacturing and Control information (components, composition, supplier, and COA) or a DMF reference for ———

4. Submit updated stability information as it becomes available.

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

If you have any questions, call Randy Hedin, R.Ph., Senior Regulatory Management Officer, at (301) 827-6392.

Sincerely,

[/S/] 6/14/00

Duu-Gong Wu, Ph.D.
Chemistry Team Leader II, DNDC II for the
Division of Metabolic and Endocrine
Drug Products, (HFD-510)
Office of New Drug Chemistry
Center for Drug Evaluation and Research

[/S/] 6/13/00

cc:
Archival NDA 21-179
HFD-510/Div. Files
HFD-510/R.Hedin
HFD-510/Reviewers and Team Leaders
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: RH/June 9, 2000
Initialed by: MHaber/DWu/EGalliers/6.12.00
final: RHedin/6.13.00
filename: N21179DR._LT1

DISCIPLINE REVIEW LETTER (DR)

APPEARS THIS WAY
ON ORIGINAL

NDA 21179
Renagel 400 and 800

Please refer to your pending new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Renagel (sevelamer hydrochloride) 400 and 800.

We are reviewing the labeling of your submission and have the following comments. These are preliminary comments and more labeling changes may be requested.

1. The term ——— is not an official USP dosage form classification. The established name should reflect the official USP dosage form "Tablet." Please change the statement "Each ——— contains . . . " to read "Each tablet contains . . ." The term ——— could be retained in the net quantity statement only, as long as it is defined as a "capsule-shaped tablet." We recommend the established name be revised to read "sevelamer hydrochloride tablets."

2. Please delete the numbers 400 and 800 from the proprietary name. Place 400 mg and 800 mg prominently beneath the established name.

3. Remove the statement ——————————————— CFR 201.1 sets forth various recommendations on the expression of relationship between a distributor, manufacturer, and/or labeler. The regulations do not allow others (e.g., licensors) to be included. This information appears on the draft container labels and it provides an unnecessary distraction in reading the container labels.

If you have any questions, contact Randy Hedin, R.Ph., Senior Regulatory Management Officer, at (301) 827-6392.

Cleared for faxing: [/S/] 6/1/00
Duu-Gong Wu, Ph.D.
Chemistry Team Leader

APPEARS THIS WAY
ON ORIGINAL

N21179_FAX.doc

DUPLICATE

GelTex PHARMACEUTICALS, INC.

[redacted]

June 12, 2000

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Attention: Division Document Room, 14B-19
5600 Fishers Lane
Rockville, MD 20857

RE: NDA 21-179
Renagel® 400 & Renagel® 800 (sevelamer hydrochloride)
Amendment 002

Dear Sir/Madam:

Reference is made to the NDA cited above and to a facsimile from Mr. Randy Hedin dated June 1, 2000, containing comments on labeling. The purpose of this amendment is to respond to the comments in the facsimile, as follows:

1. The term ——— is not an official USP dosage form classification. The established name should reflect the official USP dosage form "Tablet." Please change the statement "Each ——— contains..." to read "Each tablet contains..." The term ——— could be retained in the net quantity statement only, as long as it is defined as a "capsule-shaped tablet." We recommend the established name be revised to read "sevelamer hydrochloride tablets."

The term —— is found in cUSP ——, subheading *Tablets*: "Capsule-shaped tablets are commonly referred to as ——" We selected the term, ——— to describe this new dosage form of Renagel on the basis of this statement. A review of the Physicians' Desk Reference (54th edition) reveals that there are a number of prescription drug products that use the nomenclature ——— as described in the following table.

PRODUCT	MANUFACTURER	PDR PAGE REFERENCE
Valtrex Caplets	Glaxo Wellcome	1290
Parafon Forte DSC Caplets	Ortho-McNeil	2200
NegGram Caplets	Sanofi Pharmaceuticals	2748
Talacen Caplets	Sanofi Pharmaceuticals	2762
Talwin Compound Caplets	Sanofi Pharmaceuticals	2763
Calan SR Caplets	G.D. Searle	2899
Daypro Caplets	G.D. Searle	2909

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We therefore propose to retain [redacted] as the description of the dosage form. We agree to define [redacted] as a capsule-shaped tablet in the net quantity statement ("Each capsule-shaped tablet contains...") and to revise the established name to include the term [redacted] ("sevelamer hydrochloride [redacted]").

2. Please delete the numbers 400 and 800 from the proprietary name. Place 400 mg and 800 mg prominently beneath the established name.

We propose to add "mg" after the 400 and 800 following "Renagel®" and to move the "400 mg" and "800 mg" in the circle and triangle, respectively, to the right of "XXX [redacted] or "One Bottle of XXX [redacted] in the case of the carton labels). Note that the word '[redacted]' below the trade name will now be included with the established name. Thus, the label would read "Renagel® 400 mg (sevelamer hydrochloride [redacted]' or "Renagel® 800 mg (sevelamer hydrochloride [redacted]' If agreeable, we will submit new mockups incorporating these changes.

3. Remove the statement '[redacted] CFR 201.1 sets forth various recommendations on the expression of relationship between a distributor, manufacturer, and/or labeler. The regulations do not allow others (e.g., licensors) to be included. This information appears on the draft container labels and it provides an unnecessary distraction in reading the container labels.

We note that this statement appears on the approved container labels for Renagel® Capsules (please see attached). For consistency, we respectfully request that the statement be allowed to appear on the Renagel [redacted] labels, as well.

Should you have any questions, please do not hesitate to contact the undersigned at (781) 434-3443, or Dean F. Alger, Director, Regulatory Affairs, at (781) 434-3421.

Sincerely yours,

Martha J. Carter.

Martha J. Carter
Vice President, Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

GelTex PHARMACEUTICALS, INC.

DUPLICATE

[redacted]

BL

May 23, 2000

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Attention: Division Document Room, 14B-19
5600 Fishers Lane
Rockville, MD 20857

RE: NDA 21-179
Renagel® 400 and Renagel® 800 (sevelamer hydrochloride)
Amendment 001

Dear Sir/Madam:

Reference is made to the NDA cited above and to a May 5, 2000 approval letter for NDA 20-926/S-002. This letter approved labeling changes to the "Dosage and Administration" and "Precautions" sections of the Renagel Capsules package insert. As requested by Mr. Randy Hedin on May 11th, we are submitting a revised draft package insert for Renagel 400 and Renagel 800 which incorporates the newly approved text. This revised draft replaces the package insert submitted in Section 2.1 (pages 4 to 12) of the NDA dated September 15, 1999.

Should you have any questions, please do not hesitate to contact the undersigned at (781) 434-3443, or Dean F. Alger, Director, Regulatory Affairs, at (781) 434-3421.

Sincerely yours,

Martha J. Carter.

Martha J. Carter
Vice President, Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

153 Second Avenue Waltham, MA 02451 Phone: (781) 290-5888 Fax: (781) 290-5890 Website: www.geltex.com

GelTex PHARMACEUTICALS, INC.

March 30, 2000

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Attention: Division Document Room, 14B-19
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 20-926 and NDA 21-179 Renagel® (sevelamer hydrochloride)

Dear Sir/Madam:

Reference is made to the above captioned NDAs. The purpose of this letter is to notify FDA that two carcinogenicity reports entitled "Renagel 104 Week Carcinogenicity Study in Rats With Administration by Diet" and "Renagel 104 Week Carcinogenicity Study in Mice With Administration by Diet" were submitted to IND ———Serial No. 043) on March 30, 2000. This information is incorporated into NDAs 20-926 and 21-179 by cross-reference to IND ———

Please do not hesitate to contact the undersigned at (781) 434-3443 or Dean F. Alger, at (781) 434-3421 if you have questions or require additional information.

Sincerely yours,

Martha J. Carter.

Martha J. Carter
Vice President, Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

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CONSULTATION RESPONSE
Office of Post-Marketing Drug Risk Assessment
Carol Holquist, Safety Evaluator
(OPDRA; HFD-400)

DATE RECEIVED:	**DUE DATE:**	**OPDRA CONSULT #:** 99-094
November 22, 1999	February 19, 2000	

TO:
John Jenkins, MD
Acting Director, Division of Metabolic and Endocrine Drug Products
HFD-510

PRODUCT NAME:	**MANUFACTURER:**
Renagel® 400 and Renagel® 800 (Sevelamer HCl Tablets) **NDA #:** 21-179	GelTex Pharmaceuticals Inc.

OPDRA RECOMMENDATION:

OPDRA has no objections to the continued use of the proprietary name Renagel®. However, we do not recommend the use of the product numbers in conjunction with this proprietary name. In addition, OPDRA has recommended some labeling revisions to encourage the safest possible use of this product. OPDRA considers this a final review due to the primary goal date of 19 February 2000.

[/S/] 1/28/2000
Jerry Phillips
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment
Phone: (301) 827-3246
Fax: (301) 480-8173

[/S/] 1/28/00
Peter Honig, MD
Deputy Director
Office of Post-Marketing Drug Risk Assessment
Center for Drug Evaluation and Research
Food and Drug Administration

Office of Post-Marketing Drug Risk Assessment
HFD-400; Rm. 15B03
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: January 24, 2000

NDA# 21-179

NAME OF DRUG: Renagel® 400 and Renagel® 800
(Sevelamer HCl Tablets)

NDA HOLDER: GelTex Pharmaceuticals, Inc.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Metabolic and Endocrine Drug Products (HFD-510) to review the proposed proprietary drug name, Renagel® 400 and Renagel® 800, regarding potential name confusion with existing proprietary/generic drug names.

The container labels and a portion of the insert labeling were available for review and comment.

PRODUCT INFORMATION
Renagel® is sevelamer hydrochloride, a polymeric phosphate binder intended for oral administration. Renagel® is indicated for the reduction of serum phosphorus in patients with end-stage renal disease (ESRD). In hemodialysis patients, renagel decreases the incidence of hypercalcemic episodes relative to patients on calcium acetate treatment. Renagel® was approved on October 30, 1998 under NDA 20-926 as a capsule formulation containing 403 mg of sevelamer hydrochloride. The firm submitted NDA 21-179 for the addition of a new dosage form ———. Each film-coated ——of Renagel® contains either 400 mg or 800 mg of sevelamer hydrochloride.

II. RISK ASSESSMENT:

A handwritten and verbal analysis of the proprietary name, Renagel, was not conducted by OPDRA because the name is approved and currently utilized in the market place. A search was conducted within the Adverse Event Reporting System (AERS) database to determine any post-marketing problems associated with the proprietary name. This search did not reveal any problems associated with name confusion post-marketing.

The firm has proposed to include the tablet strengths in conjunction with the proprietary name. In general, the use of numbers in a proprietary name should be avoided because they can often be confused for the quantity of a prescription drug product.

A. There seems to be no logic of having a capsule formulation at 403 mg and a tablet formulation at 400 mg. We believe there could be a risk of a prescription written for Renagel 400 and the patient would receive the 403 mg capsule formulation. Although we can only assume that this

would not result in a clinically significant outcome, the Agency does not consider tablets and capsules to be therapeutic equivalents.

B. The terminology of ——— has been used extensively in the OTC market. OPDRA believes that it is unnecessary to bring this terminology into the Rx market. Our preferred regulatory and safety perspective would be to call this a TABLET.

III. LABELING, PACKAGING AND SAFETY RELATED ISSUES

In the review of the container labels and insert labeling of Renagel®, OPDRA has attempted to focus on safety issues relating to possible medication errors. OPDRA has reviewed the current labels and labeling and have identified areas of possible improvement, which might minimize potential user error.

A. CONTAINER (400 mg and 800 mg)

1. The term ——— ' is not an official USP dosage form classification. The established name should reflect the official USP dosage form "Tablet". We recommend the established name be revised to read "Sevelamer Hydrochloride Tablets". The term ——— ' could be retained in the net quantity statement only, as long as it is defined as a "capsule-shaped tablet". Please see our above comment on the use of ———

2. We recommend the deletion of the number 400 and 800 from the proprietary name.

3. We would recommend that 400 mg and 800 mg appear prominently beneath the established name.

4. We recommend that the statement "————————————————" be deleted. CFR 201.1 sets forth various recommendations on the expression of relationship between a distributor, manufacturer, and/or labeler. The regulations do not allow others (e.g., licensors) to be included. This information appears on the draft container labels and it provides unnecessary distraction in reading container labels.

5. We recommend the "Each ——— contains..." statement be revised to read "Each tablet contains...".

B. INSERT LABELING

See comments under CONTAINER, as appropriate.

IV. RECOMMENDATIONS:

A. OPDRA has no objections to the continued use of the proprietary name Renagel®. However, we do not recommend the use of the product numbers in conjunction with this proprietary name.

B. OPDRA recommends the above labeling and packaging revisions to encourage the safest possible use of this product. We are willing to revisit these issues if the Division receives another draft of the labeling from the manufacturer.

C. OPDRA considers this a final review due to the primary goal date of 19 February 2000.

OPDRA would appreciate feedback on the final outcome of this consult (e.g., copy of revised labels/labeling). We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Carol Holquist at 301-827-3244.

[/S/] 1/28/2000

Carol Holquist, RPh
Safety Evaluator
Office of Post-Marketing Drug Risk Assessment

Concur:

[/S/] 1/28/2000

Jerry Phillips, RPh
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment

APPEARS THIS WAY
ON ORIGINAL

CC:

NDA 21-179
Office Files
HFD-510; DivFiles; Randy Hedin, Project Manager
HFD-510; John Jenkins, Division Director
HFD-440; Lahn Green, Safety Evaluator, DDREII, OPDRA
HFD-400; Jerry Phillips, Associate Director, OPDRA
HFD-400; Peter Honig, Deputy Director, OPDRA
HFD-002; Murray Lumpkin, Acting Director, OPDRA

APPEARS THIS WAY
ON ORIGINAL

Meeting Date: November 8, 1999 Time: 4:00 - 4:30 pm Location: 8-B-56

NDA 21-179 Renagel 400 and 800 (sevelamer hydrochloride) Tablets

Type of Meeting: Filing Meeting

External participant: None

Meeting Chair: Dr. Troendle

External participant lead: None

Meeting Recorder: Mr. Randy Hedin

FDA Attendees and titles:

Dr. Solomon Sobel, Division Director DMEDP
Dr. Gloria Troendle, Medical Team Leader, DMEDP
Dr. Bruce Schneider, Medical Reviewer DMEDP
Dr. Robert Shorer, Biopharmaceutics Reviewer, OCPB
Dr. Duu-Gong Wu, Team Leader, DNDCII
Mr. Randy Hedin, Project Manager, DMEDP

External participant Attendees and titles:

None

Meeting Objectives:

This meeting was arranged to determine if NDA 21-179 will be filed, and discuss plans for the review of the NDA.

Discussion Points:

- Chemistry: The application is fileable
- Biopharmaceutics: The application is fileable.
- Clinical: The application is fileable. No review is needed.

Decisions (agreements) reached:

- The application will be filed.

- The review will be done as a standard review. The goal to finish the reviews will be June 1, 2000.

Unresolved or issues requiring further discussion:

- None

Action Items:

- Schedule status meetings as appropriate.

Signature, minutes preparer: [/S/]

Concurrence Chair: [/S/]

cc: NDA Arch
HFD-510
Attendees
HFD-510/EGalliers
HFD-511/RHedin/5.3.99/N21179.MN1
Concurrences: BSchneider/GTroendle/RShore/12/21/DWu/1/7/00

APPEARS THIS WAY
ON ORIGINAL

GelTex PHARMACEUTICALS, INC.

ORIGINAL

[S]

Natal & took zip disk [S] 12/16/99

December 16, 1999

Martin T. Haber, Ph.D.
Chemistry Reviewer
Division of Metabolic & Endocrine Drug Products, HFD-510
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

CENTER FOR DRUG REC'D DEC 17 1999 HFD-510 EVALUATION AND RESEARCH

RE: **NDA 21-179**
Renagel® 400 and Renagel® 800 (sevelamer hydrochloride)
CMC Files in WORD Format
Desk Copy

Dear Dr. Haber:

As requested, enclosed is a zip disk containing the WORD files from the CMC section of the NDA cited above. These are exact duplicate files from the submission. As discussed, please note that many of the appendices are available in hard copy only.

Please feel free to call the undersigned at (781) 434-3443, or Debra Sojka, Senior Associate, Regulatory Affairs at (781) 434-3513, should you have further questions or if you require additional information.

Best regards,

D. J. A for

Martha J. Carter
Vice President, Regulatory Affairs

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO
DATE

APPEARS THIS WAY
ON ORIGINAL

POSSIBLE COPY

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2 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

N 21-179
Renagel Tablets
GelTex Pharmaceuticals Inc.

Date:
11/15/99

CONTACT:
Ms. Martha Carter
781-434-3421

MEMORANDUM OF TELECON

I spoke with Ms. Martha Carter, concerning their September 15, 1999 NDA for Renagel Tablets. I told Ms. Carter that we had a filing meeting on November 8 1999, and the application will be filed. I further stated that it will be a standard review. She thanked me for the information.

[/S/]

Randy Hedin, CSO

APPEARS THIS WAY ON ORIGINAL

cc: NDA Arch
HFD-510
HFD-510/
HFD-511/RHedin/11.15.99/N21179_PH1.doc

GelTex
PHARMACEUTICALS, INC.

ORIGINAL

NEW CORRESP

NC

October 14, 1999

Solomon Sobel, M.D.
Director
Division of Metabolic and Endocrine Drug Products, HFD-510
Document Room 14B-04
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

RE: NDA 21-179
Renagel® 400 and Renagel® 800 (sevelamer hydrochloride)
Change of Address

Dear Dr. Sobel:

We are pleased to inform you that GelTex Pharmaceuticals Inc., has recently moved to a new facility. The new official address for all correspondence is:

GelTex Pharmaceuticals, Inc.
153 Second Avenue
Waltham, MA 02451

The main fax number to be used for all regulatory correspondence is (781) 895-4981.

Although the main phone number for the facility remains (781) 290-5888, the direct phone lines for the official contacts for this NDA at GelTex Pharmaceuticals, Inc., 153 Second Ave, Waltham, MA 02451 are:

[S/]
1-3-00

[S/]

Martha J. Carter
Vice President, Regulatory Affairs
Tel: (781) 434-3443

Debra Sojka
Senior Associate, Regulatory Affairs
Tel: (781) 434-3513

Dean F. Alger
Director, Regulatory Affairs
Tel: (781) 434-3421

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☒ N.A.I. ☐ MEMO

CSO INITIALS DATE

HEDIN

NDA 21-179

GelTex Pharmaceuticals, Inc.
Attention: Martha J. Carter
Vice President, Regulatory Affairs
Nine Fourth Avenue
Waltham, MA 02451

APPEARS THIS WAY
ON ORIGINAL

SEP 22 1999

Dear Ms. Carter:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product:	Renagel®(sevelamer hydrochloride) 400 and 800 mg Caplets
Therapeutic Classification:	To be determined at filing meeting
Date of Application:	September 15, 1999
Date of Receipt:	September 17, 1999
Our Reference Number:	NDA 21-179

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on November 16, 1999, in accordance with 21 CFR 314.101(a).

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). If you have not already fulfilled the requirements of 21 CFR 314.55 (or 601.27), please submit your plans for pediatric drug development within 120 days from the date of this letter unless you believe a waiver is appropriate. Within 120 days of receipt of your pediatric drug development plan, we will notify you of the pediatric studies that are required under section 21 CFR 314.55.

If you believe that this drug qualifies for a waiver of the study of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov.cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will proceed with the pediatric drug development plan that you submit, and notify you of the pediatric studies that are required under section 21 CFR 314.55. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. All communications concerning this NDA should be addressed as follows:

U.S. Postal Service/Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Attention: Division Document Room, 14B-19
5600 Fishers Lane
Rockville, Maryland 20857

If you have any questions, contact Randy Hedin, R.Ph., Senior Regulatory Management Officer, at (301)827-6392.

Sincerely,

[/S/] 9.22.99

Enid Galliers
Chief, Project Management Staff
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Archival NDA 21-179
HFD-510/Div. Files
HFD-510/R.Hedin
HFD-510/Reviewers and Team Leaders
DISTRICT OFFICE

Drafted by: ddk/September 21, 1999
Initialed by: Galliers 9.21.99
final: DK 9.22.99
filename: 21179AC

ACKNOWLEDGEMENT (AC)

GelTex
PHARMACEUTICALS, INC.

September 15, 1999

Solomon Sobel, M.D.
Director
Division of Metabolic and Endocrine Drug Products, HFD-510
Document Room 14B-04
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

RE: NDA 21-179
Renagel® 400 and Renagel® 800 (sevelamer hydrochloride)
ORIGINAL APPLICATION

Dear Dr. Sobel:

We are pleased to submit, in duplicate, an original new drug application for a new tablet dosage form of Renagel®.

Renagel® 400 and Renagel® 800 are film-coated compressed ——— containing 400 mg or 800 mg of sevelamer hydrochloride, respectively. Renagel® 400 contains an equivalent amount of sevelamer hydrochloride to the 403 mg capsule currently on the market, but in a much smaller dosage form. Renagel® 800 offers patients the ability to take half of the number of units of capsules, which typically can range from 6 to 12 per day.

We believe the ——— dosage form is a significant improvement over the capsule formulation. Two strengths offer physicians greater flexibility in prescribing Renagel® to their patients. The larger ——— Renagel® 800, will halve the number of units a patient needs to ingest. This is an important formulation enhancement for the fluid-restricted dialysis patient population. As described in Section 3, control of hyperphosphatemia has a direct impact on the mortality associated with end-stage renal disease (ESRD). We recognize that this NDA does not, on its face, meet the criteria described in MAPP 6020.3 for priority review. However, we expect this new dosage form to lead to improved patient compliance, which in turn will lead to better control of hyperphosphatemia and to decreased mortality. We therefore believe that expedited review of this NDA is warranted, and respectfully request that this NDA be considered for priority status.

The NDA consists of chemistry, manufacturing, and controls information for the two strengths of drug product, as well as the results of *in vitro* bioequivalency testing between

Nine Fourth Avenue Waltham, MA 02451 Phone: (781) 290-5888 Fax: (781) 290-5890 Website: www.geltex.com

Renagel® Capsules and the ——— formulation. This approach has been informally reviewed with the Division, as described in Section 6.

Because there are no clinical data in the submission, a user fee of $136,141, in accordance with the Prescription Drug User Fee Act, has been submitted. User fee I.D. number 3779 has been assigned to this new drug application.

The official contacts for this NDA at GelTex Pharmaceuticals, Inc., Nine Fourth Avenue, Waltham, MA 02451 are:

Martha J. Carter
Vice President, Regulatory Affairs
Tel: (781) 290-5888, ext. 766
Fax: (781) 895-4980

Debra Sojka
Senior Associate, Regulatory Affairs
Tel: (781) 290-5888, ext. 716
Fax: (781) 895-4980

Dean F. Alger
Director, Regulatory Affairs
Tel: (781) 290-5888, ext. 721
Fax: (781) 895-4980

We look forward to your review of the Renagel® ——— NDA. Please do not hesitate to contact us if you have questions or require additional information.

Sincerely yours,

Martha J. Carter.

Martha J. Carter
Vice President, Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

35 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.