CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22309Orig1s000

CHEMISTRY REVIEW(S)

Memorandum	Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research
Date:	27-APR-2011
To:	NDA 22-309 CMC Review #3
From:	Hitesh Shroff, Ph.D.
Through:	Moo-Jhong Rhee, Ph.D. Chief, Branch IV ONDQA Division II
CC:	Donna Christner, Ph.D.
Subject:	**Final labels and the "Approval" recommendation.**

The previous Review #2 made a recommendation of "Approval" from the CMC perspective based on draft labels submitted via emails.

Now the sponsor has submitted the final container/carton labels on April 22, 2011 as an amendment, which are the same as the previously submitted via email and are deemed satisfactory.

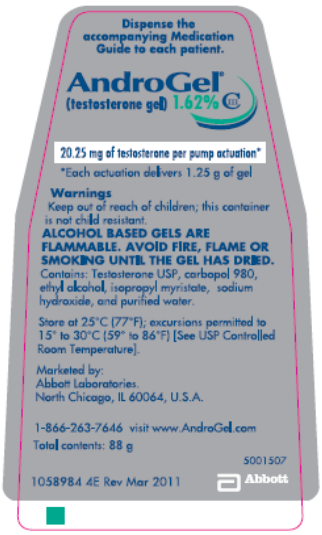
Therefore, the previous "Approval" recommendation from the CMC perspective is still effective.

Attachment.

Immediate container label:

Front

Back



Carton label:

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

HITESH N SHROFF
04/27/2011

MOO JHONG RHEE
04/27/2011
Chief, Branch IV

NDA 22-309

AndroGel® (testosterone gel) 1.62%

Unimed Pharmaceuticals, LLC

Hitesh Shroff, Ph.D.
Review Chemist

Office of New Drug Quality Assessment
Division of New Drug Quality Assessment II
Branch IV

CMC Review of NDA 22-309
For the Division of Reproductive and Urologic Drug Products (HFD-580)

Table of Contents

Chemistry Review Data Sheet

1. NDA 22-309

2. REVIEW:#3

3. REVIEW DATE: 20-Apr-2011

4. REVIEWER: Hitesh Shroff, Ph.D.

5. PREVIOUS DOCUMENTS:

Submissions	Document Date
Original	12-FEB-2009
Amendment - Package Insert Draft	11-Feb-2009
Amendment - Quality Information	04-Mar-2009
Amendment - Quality Information	10-Mar-2009
Amendment - Response to IR	03-Sept-2009
Amendment - Patient Package Insert Draft	03-Sept-2009
Amendment - Quality Information	01-Dec-2009

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment – Labeling/Patient Package Insert Draft	21-Jan-2010
Amendment – Labeling/Patient Package Insert Draft	07-Jan-2011
Amendment – Labeling	28-Feb-2011
Email – PI	04-Apr-2011
Email – Labeling	07-Apr-2011

7. NAME & ADDRESS OF APPLICANT

Name:	Abbott Products, Inc.
Address:	901 Sawyer Road Marietta, GA 30062
Representative:	Gregg A. Pratt Director Global Regulatory Affairs
Telephone:	770-578-5829

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Androgel® 1.62%
b) Non-Proprietary Name (USAN): Testosterone
c) Code Name/# (ONDQA only): None
d) Chem. Type/Submission Priority (ONDQA only):

- Chem. Type: 5
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b)(2)

10. PHARMACOL. CATEGORY: Androgen

11. DOSAGE FORM: Topical gel

12. STRENGTH/POTENCY: 1.62% w/w gel

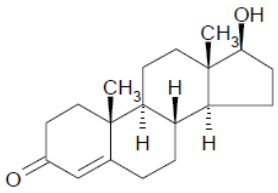
13. ROUTE OF ADMINISTRATION: Transdermal

14. Rx/OTC DISPENSED: X Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM:
_____SPOTS product – Form Completed

___X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:



Testosterone

Chemical Name: 17β-Hydroxyandrost-4-en-3-one
Androst-4-en-3-one, 17-Hydroxy-, (17β)-
Molecular Formula: $C_{19}H_{28}O_2$
Molecular Weight: 288.43

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)		3	Adequate	29-NOV-2007	Reviewed by Donald Klein for (b) (4)
	III			4			
	III			4			

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")
[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: N/A

18. STATUS:

ONDQA:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A		
EES	Acceptable	07-Dec-2009	Hitesh Shroff
Pharm/Tox	N/A		
Biopharm	N/A		
LNC	N/A		
Methods Validation	N/A per ONDQA policy		
DMEPA	N/A		
EA	Categorical exclusion granted (see review)	14-Sept-2009	Hitesh Shroff
Microbiology	Approval	29-Oct-2009	Robert Mello

The Chemistry Review for NDA 22-309

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Based on 1) sufficient CMC information provided to assure the identity, strength, purity and quality of the drug product; 2) "Acceptable" cGMP compliance of all facilities; and 3) adequate CMC labels/labeling information, CMC Review #2 made a recommendation of approval of this NDA.

In order to comply with the new labeling approach for the testosterone pump products, the CMC information on the label and labeling were revised and re-submitted via emails. These changes of the labels and labeling are deemed satisfactory, making the previous "Approval" recommendation from the CMC perspective still effective.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

No recommendations at this time.

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

(1) Drug Substance

The drug substance, testosterone, is manufactured by (b) (4) (b) (4) The CMC information is in DMF# (b) (4) and LoA was also provided. The DMF is adequate.

(2) Drug Product

AndroGel (testosterone gel) 1.62% is indicated for replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone. The drug product is a transparent or slightly opalescent colorless gel containing 1.62% testosterone. The gel is packaged in a multi-dose metered pump with (b) (4) gel capacity and capable of dispensing 75 g of gel. The pump delivers 1.25 g of gel equivalent to 20.25 mg of testosterone per actuation by fully depressing the pump mechanism.

The CMC information was reviewed during the initial NDA submission in 2009 and found adequate. The complete response in October 2010 included revised label and

labeling, and there was no changes in the CMC information. All the labels and physician's insert are deemed adequate from the CMC perspective.

B. Description of How the Drug Product is Intended to be Used

The drug product is recommended to adult male patients as a single daily dose of 2.5 g of gel equivalent to 40.5 mg of testosterone. The maximum dose is 5 g of gel equivalent to 81 mg of testosterone. The gel is applied once daily to shoulders and upper arms.

C. Basis for Approvability or Not-Approval Recommendation

As Review #2 indicated, the applicant has provided sufficient information on the controls for raw materials, manufacturing processes and process controls, and adequate specifications for assuring consistent product quality of the drug substance and the drug product. The container/closure system is adequate to protect the drug product. The application has also provided sufficient stability information on the drug product to assure strength, purity, and quality of the drug product over the proposed expiration dating period. Label and labeling are revised based on the new review approaches established per DMEPA for testosterone products and they are deemed satisfactory. All facilities are in compliance with cGMP.

III. Administrative

A. Reviewer's Signature

Hitesh Shroff/ April 20, 2011

B. Endorsement Block

Moo-Jhong Rhee, Branch Chief, Branch #4, Division 2
Donna Christner

C. CC Block

Jeannie Roule

4 PAGES HAVE BEEN WITHHELD IN FULL AS b4 (CCI/TS) IMMEDIATELY FOLLOWING THIS PAGE

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

HITESH N SHROFF
04/20/2011

MOO JHONG RHEE
04/20/2011
Chief, Branch IV

NDA 22-309

AndroGel® (testosterone gel) 1.62%

Unimed Pharmaceuticals, LLC

Hitesh Shroff, Ph.D.
Review Chemist

Office of New Drug Quality Assessment
Division of Pre-Marketing Assessment II
Branch III

CMC Review of NDA 22-309
For the Division of Reproductive and Urologic Drug Products (HFD-580)

Table of Contents

Chemistry Review Data Sheet

1. NDA 22-309

2. REVIEW:#2

3. REVIEW DATE: 31-DEC-2009

4. REVIEWER: Hitesh Shroff, Ph.D.

5. PREVIOUS DOCUMENTS:

Submissions	Document Date
Original	12-FEB-2009
Amendment - Package Insert Draft	11-Feb-2009
Amendment - Quality Information	04-Mar-2009
Amendment - Quality Information	10-Mar-2009
Amendment - Response to IR	03-Sept-2009
Amendment - Patient Package Insert Draft	03-Sept-2009

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment - Quality Information	01-Dec-2009

7. NAME & ADDRESS OF APPLICANT

Name:	Unimed Pharmaceuticals, LLC
Address:	901 Sawyer Road Marietta, GA 30062
Representative:	Kathryn Penhale-Unz Director Regulatory Affairs
Telephone:	770-578-5796

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Androgel® 1.62%
b) Non-Proprietary Name (USAN): Testosterone
c) Code Name/# (ONDQA only): None
d) Chem. Type/Submission Priority (ONDQA only):

- Chem. Type: 5
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b)(2)

10. PHARMACOL. CATEGORY: Androgen

11. DOSAGE FORM: Topical gel

12. STRENGTH/POTENCY: 1.62% w/w gel

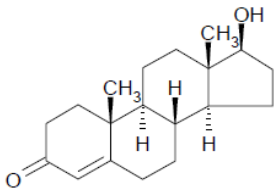
13. ROUTE OF ADMINISTRATION: Transdermal

14. Rx/OTC DISPENSED: X Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM:
_____SPOTS product – Form Completed

___X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:



Testosterone

Chemical Name: 17β-Hydroxyandrost-4-en-3-one
Androst-4-en-3-one, 17-Hydroxy-, (17β)-
Molecular Formula: $C_{19}H_{28}O_2$
Molecular Weight: 288.43

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II		(b) (4)	3	Adequate	29-NOV-2007	Reviewed by Donald Klein for (b) (4)
	III			4			
	III			4			

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: N/A

18. STATUS:

ONDC:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A		
EES	Acceptable	07-Dec-2009	Hitesh Shroff
Pharm/Tox	N/A		
Biopharm	N/A		
LNC	N/A		
Methods Validation	N/A per ONDQA policy		
DMEPA	N/A		
EA	Categorical exclusion granted (see review)	14-Sept-2009	Hitesh Shroff
Microbiology	Approval	29-Oct-2009	Robert Mello

The Chemistry Review for NDA 22-309

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This NDA has now provided sufficient CMC information to assure the identity, strength, purity and quality of the drug product. All facilities are in compliance with cGMP. Labels/labeling have required information. Therefore, from the CMC perspective, this NDA is recommended for "Approval".

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

No recommendations at this time.

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

(1) Drug Substance

The drug substance, testosterone, is manufactured by (b) (4) (b) (4) The CMC information is provided in DMF# (b) (4), which was reviewed on Nov 29, 2007 and found to be adequate. Since then there have been no significant changes in the manufacturing process and control of testosterone. The applicant provided LOA to reference the DMF for CMC information.

(2) Drug Product

The drug product is a transparent or slightly opalescent colorless gel containing 1.62% testosterone. The gel is packaged in a multi-dose metered pump with (b) (4) gel capacity and capable of dispensing 75 g of gel. The pump delivers 1.25 g of gel equivalent to 20.25 mg of testosterone per actuation by fully depressing the pump mechanism. The once daily recommended starting dose for adult males is 2.5 g gel applied to shoulders/upper arms or abdomen. Androgel® is indicated for replacement therapy in adult males associated with a deficiency or absence of endogenous testosterone.

A new gel formulation containing 1.62% testosterone with higher viscosity, reduced volume of application (b) (4)

compared to Androgel® (testosterone gel) 1% is developed. The gel is composed of excipients including ethanol, isopropyl myristate, Carbopol 980, sodium hydroxide and water. All excipients are USP/NF grade and there are no novel excipients used in this formulation. A significantly higher *in vitro* viscosity was achieved (b) (4) (b) (4) Carbopol, (b) (4) sodium hydroxide. A (b) (4)

The release specification of the finished product include appearance, identification, pH, viscosity, related substances, pump performance, dose uniformity, microbial tests and assays for testosterone, isopropyl myristate and ethanol.

The drug product container closure system is a (b) (4) enclosed in a plastic canister and equipped with multi-dose pump. (b) (4) The pump dispense (b) (4) s and delivers 1.25g of the gel per actuation. (b) (4) containing the product is placed in the canister and sealed shut with multi-dose pump. There has been no change in packaging configuration, process or equipment from Androgel® (testosterone gel) 1% product.

Based on the stability data from three pilot scale batches of drug product at long term (24 months) and accelerated (6 months) conditions, the proposed 30 months expiration dating period when stored at room temperature is granted.

B. Description of How the Drug Product is Intended to be Used

The drug product is recommended to adult male patients as a single daily dose of 2.5 g of gel equivalent to 40.5 mg of testosterone. The maximum dose is 5 g of gel equivalent to 81 mg of testosterone. The gel is applied once daily to either shoulders/upper arms or abdomen.

C. Basis for Approvability or Not-Approval Recommendation

The sponsor has provided sufficient information on the controls for raw materials, manufacturing processes and process controls, and adequate specifications for assuring consistent product quality of the drug substance and the drug product. The container/closure system is adequate to protect the drug product. The application has also provided sufficient stability information on the drug product to assure strength, purity, and quality of the drug product over the proposed expiration dating period. Label and labeling are acceptable, and all facilities are in compliance with cGMP.

Therefore, this NDA is recommended for "approval" from the CMC perspective.

III. Administrative

A. Reviewer's Signature

Hitesh Shroff/ December 31, 2009

B. Endorsement Block

Moo-Jhong Rhee, Branch Chief, Branch #3, Division 2
Donna Christner
Jeanie Roule

C. CC Block

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22309	ORIG-1	UNIMED PHARMACEUTICALS INC	ANDROGEL

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

HITESH N SHROFF
01/04/2010

MOO JHONG RHEE
01/04/2010
Chief, Branch III

6 PAGES HAVE BEEN WITHHELD IN FULL AS b4 (CCI/TS) IMMEDIATELY FOLLOWING THIS PAGE

NDA 22-309

AndroGel® (testosterone gel) 1.62%

Unimed Pharmaceuticals, LLC

Hitesh Shroff, Ph.D.
Review Chemist

Office of New Drug Quality Assessment
Division of Pre-Marketing Assessment II
Branch III

CMC Review of NDA 22-309
For the Division of Reproductive and Urologic Drug Products (HFD-580)

Table of Contents

Chemistry Review Data Sheet

1. NDA 22-309

2. REVIEW:#1

3. REVIEW DATE: 14-SEPT-2009

4. REVIEWER: Hitesh Shroff, Ph.D.

5. PREVIOUS DOCUMENTS: N/A

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original	12-FEB-2009
Amendment - Package Insert Draft	11-Feb-2009
Amendment - Quality Information	04-Mar-2009
Amendment - Quality Information	10-Mar-2009
Amendment - Response to IR	03-Sept-2009
Amendment - Patient Package Insert Draft	03-Sept-2009

7. NAME & ADDRESS OF APPLICANT

Name:	Unimed Pharmaceuticals, LLC
Address:	901 Sawyer Road Marietta, GA 30062
Representative:	Kathryn Penhale-Unz Director Regulatory Affairs
Telephone:	770-578-5796

8. DRUG PRODUCT NAME/CODE/TYPE:
   a) Proprietary Name: Androgel® 1.62%
   b) Non-Proprietary Name (USAN): Testosterone
   c) Code Name/# (ONDQA only): None
   d) Chem. Type/Submission Priority (ONDQA only):
      - Chem. Type: 5
      - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b)(2)

10. PHARMACOL. CATEGORY: Androgen

11. DOSAGE FORM: Topical gel

12. STRENGTH/POTENCY: 1.62% w/w gel

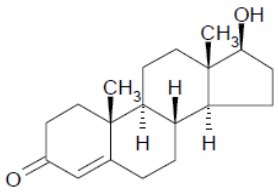
13. ROUTE OF ADMINISTRATION: Transdermal

14. Rx/OTC DISPENSED: X Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM:
_____SPOTS product – Form Completed

__X__Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:



Testosterone

Chemical Name: 17β-Hydroxyandrost-4-en-3-one
Androst-4-en-3-one, 17-Hydroxy-, (17β)-
Molecular Formula: $C_{19}H_{28}O_2$
Molecular Weight: 288.43

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)		3	Adequate	29-NOV-2007	Reviewed by Donald Klein for (b) (4)
	III			4			

(b) (4)	III	(b) (4)	(b) (4)	4			

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: N/A

18. STATUS:

ONDC:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A		
EES	Pending		
Pharm/Tox	N/A		
Biopharm	N/A		
LNC	N/A		
Methods Validation	N/A per ONDQA policy		
DMEPA	N/A		
EA	Categorical exclusion granted (see review)	14-Sept-2009	Hitesh Shroff
Microbiology	Pending		

The Chemistry Review for NDA 22-309

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The microbiology consult review has not been completed yet, so the assurance of the purity of the drug is still pending. The Office of Compliance has not made a final overall "Acceptable" recommendation for all facilities listed in the application.

Therefore, until these issues are resolved, this application is not recommended for approval from the CMC perspective.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

No recommendations at this time.

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

(1) Drug Substance

The drug substance, testosterone, is manufactured by (b) (4) (b) (4)). The CMC information is provided in DMF# (b) (4), which was reviewed on Nov 29, 2007 and found to be adequate. Since then there have been no significant changes in the manufacturing process and control of testosterone. The applicant provided LOA to reference the DMF for CMC information.

(2) Drug Product

The drug product is a transparent or slightly opalescent colorless gel containing 1.62% testosterone. The gel is packaged in a multi-dose metered pump with (b) (4) gel capacity and capable of dispensing 75 g of gel. The pump delivers 1.25 g of gel equivalent to 20.25 mg of testosterone per actuation by fully depressing the pump mechanism. The once daily recommended starting dose for adult males is 2.5 g gel applied to shoulders/upper arms or abdomen. Androgel® is indicated for replacement therapy in adult males associated with a deficiency or absence of endogenous testosterone.

A new gel formulation containing 1.62% testosterone with higher viscosity, reduced volume of application (b) (4) compared to Androgel® (testosterone gel) 1% is developed. The gel is composed of excipients including ethanol, isopropyl myristate, Carbopol 980, sodium hydroxide and water. All excipients are USP/NF grade and there are no novel excipients used in this formulation (b) (4)

The release specification of the finished product include appearance, identification, pH, viscosity, related substances, pump performance, dose uniformity, microbial tests and assays for testosterone, isopropyl myristate and ethanol.

The drug product container closure system is a (b) (4) enclosed in a plastic canister and equipped with multi-dose pump. (b) (4) and delivers 1.25g of the gel per actuation. (b) (4) containing the product is placed in the canister and sealed shut with multi-dose pump. There has been no change in packaging configuration, process or equipment from Androgel® (testosterone gel) 1% product.

Based on the stability data from three pilot scale batches of drug product at long term (24 months) and accelerated (6 months) conditions, the proposed 30 months expiration dating period when stored at room temperature is granted.

B. Description of How the Drug Product is Intended to be Used

The drug product is recommended to adult male patients as a single daily dose of 2.5 g of gel equivalent to 40.5 mg of testosterone. The maximum dose is 5 g of gel equivalent to 81 mg of testosterone. The gel is applied once daily to either shoulders/upper arms or abdomen.

C. Basis for Approvability or Not-Approval Recommendation

The microbiology consult review is not completed yet and an "acceptable" site recommendation from the Office of Compliance is still pending.

Therefore, from the CMC perspective, this NDA is not recommended for approval until all issues are resolved.

III. Administrative

A. Reviewer's Signature

Hitesh Shroff/ October 16, 2009

B. Endorsement Block

Moo-Jhong Rhee, Branch Chief, Branch #3, Division 2
Donna Christner
Jeanie Roule

C. CC Block

47 PAGES HAS BEEN WITHHELD IN FULL AS b4 (CCI/TS) IMMEDIATELY FOLLOWING THIS PAGE

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22309	ORIG-1	UNIMED PHARMACEUTICALS INC	ANDROGEL

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

HITESH N SHROFF
10/21/2009

MOO JHONG RHEE
10/21/2009
Chief, Branch III

Initial Quality Assessment
Branch III
Pre-Marketing Assessment Division II

OND Division:	Division of Reproductive and Urologic Products
NDA:	22-309
Applicant:	Unimed
Stamp Date:	12-Feb-2009
PDUFA Date:	11-Dec-2009
Trademark:	Androgel 1.62%
Established Name:	Testosterone
Dosage Form:	Gel
Route of Administration:	Transdermal
Indication:	Replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone: Primary hypogonadism (congenital or acquired) or hypogonadotropic hypogonadism (congenital or acquired)
PAL:	Donna F. Christner Ph.D.

	YES	NO
ONDQA Fileability:	x	☐
Comments for 74-Day Letter	☐	x

Summary and Critical Issues:

A. Summary

The drug product is a testosterone gel that is a transparent or slightly opalescent colorless gel containing 1.62% testosterone. It is applied topically to either the shoulders/upper arms or (b) (4) to provide transdermal delivery of testosterone to the systemic circulation. The gel is packaged in a multi-dose pump (b) (4) pump, capable of dispensing 75 g of gel), which consists of (b) (4) a plastic canister with an airless pump dispenser. Upon priming (3 actuations), each actuation dispenses 1.25 g of gel. It is indicated for replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone.

The sponsor has developed the 1.62% formulation in order to reduce the volume necessary to be applied to the skin, and has based the development of this product on the approved Androgel 1%.

B. Critical issues for review

The drug product specifications appear to be adequate to allow review. While the additional identification test and tightening of the shelf-life specification for alcohol appear to be adequate, deletion of tests for pump performance and microbial testing is a review issue that will need careful consideration prior to concurrence with the sponsor.

A microbiology consult has been sent to determine if it is acceptable to delete the test for microbial limits.

C. Comments for 74-Day Letter

There are no CMC comments for the 74-day letter.

D. Recommendation:

This NDA is fileable from a CMC perspective. A single reviewer, Hitesh Shroff, has been assigned.

_____

Donna F. Christner, Ph.D.

NDA Number: 22-308 **Applicant: Unimed** **Stamp Date: 12-Feb-2009**

Drug Name: Androgel 1.62% **NDA Type: 3S**

On **initial** overview of the NDA/BLA application for RTF:

	Content Parameter	Yes	No	Comment
1	Is the section legible, organized, indexed, and paginated adequately?	X		
2	Are ALL of the manufacturing and testing sites (including contract sites) identified with full street addresses (and CFNs, if applicable)?	X		Confirmed with sponsor
3	Is a statement provided to indicate whether each manufacturing or testing site is ready for inspection or, if not, when it will be ready?	X		
4	Is a statement on the Environmental Impact provided as required in 21 CFR 314.50(d)(1)(iii)?	X		Categorical exclusion as per 21 CFR 25.31(b)
5	Is information on the Drug Substance provided as required in 21 CFR 314.50(d)(1)(i)?	X		DMF (b) (4)
6	Is information on the Drug Product provided as required in 21 CFR 314.50(d)(1)(ii)?	X		
7	If applicable, has all information requested during the IND phases, and at the pre-NDA meetings been included?	X		
8	Have draft container labels and package insert been provided?	X		
9	Have all DMF References been identified?	X		
10	Is information on the investigational formulations included?	X		
11	Is information on the Methods Validation included?	X		
12	If applicable, is documentation on the sterilization process validation included?	X		N/A

IS THE CMC SECTION OF THE APPLICATION FILEABLE? _Yes_____

If the NDA/BLA is not fileable from chemistry, manufacturing, and controls perspective, state the reasons and provide comments to be sent to the Applicant.

Please identify and list any potential review issues to be forwarded to the Applicant for the 74-day letter.

Donna F. Christner, Ph.D. 26-Mar-2009

Pharmaceutical Assessment Lead Date

Moo-Jhong Rhee, Ph.D.

Branch Chief Date

DMF No.	Holder	Description	LOA	Status
(b) (4)			Yes	Acceptable on 29-Nov-2007 for NDA (b) (4) (b) (4) **May require review if substantial updates submitted since last review.**
			Yes	(b) (4)
			Yes	**No review performed. Review will be needed if adequate information is not found in the NDA.**

6 PAGES HAS BEEN WITHHELD IN FULL AS b4 (CCI/TS) IMMEDIATELY FOLLOWING THIS PAGE

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Donna Christner
4/9/2009 09:36:43 AM
CHEMIST

Changes made as per your comments. Hard copy signed 31-Mar-2009

Moo-Jhong Rhee
4/9/2009 01:35:02 PM
CHEMIST
Chief, Branch III