

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-015/S-008**

**ADMINISTRATIVE DOCUMENTS**

**Division of Reproductive and Urologic Drug Products**

**REGULATORY PROJECT MANAGER REVIEW**

**Application Number:** 21-015/S-008  
**Name of Drug:** AndroGel® 1% (testosterone gel) CIII  
**Applicant:** Unimed Pharmaceuticals, Inc.  
**Material Reviewed:** Physician Insert and Patient Package Insert dated 11/02  
**Submission Date:** December 04, 2002  
**Receipt Date:** December 05, 2002

**Background and Summary**

The change in alcohol content in the drug product was noted in the NDA annual report dated April 26, 2002 and in the package inserts submitted to the Agency in the CBE-0 dated December 4, 2002. Following an inquiry, the sponsor provided a justification for the change, and it is acceptable. Please see Chemistry memo in DFS dated July 30, 2003. The changes made in the PI and PPI addressing the potential hazard in gel products containing alcohol is acceptable.

Reviewed by:  
Eufrecina DeGuia  
Regulatory Health Project Manager  
Division of Reproductive and Urologic Drug Products  
HFD-580  
August 11, 2003

APPROVED FOR SIGNATURE  
ON 8/11/03

FPL October 22, 2002	December 4, 2002 S-008	Comments
<p><b>AndroGel®</b> (testosterone gel) 1% CIII</p>	<p><b>AndroGel®</b> (testosterone gel) 1% CIII</p> <p>A.09.063.0039332 80-0005-04 Issued 11/02</p>	<p>The sponsor added “A.09.063.0039332 80-0005-04 Issued 11/02”.</p> <p>This is acceptable.</p>
<p><b>DESCRIPTION</b> AndroGel® (testosterone gel) is a clear, colorless hydroalcoholic gel containing 1% testosterone. AndroGel® provides continuous transdermal delivery of testosterone, the primary circulating endogenous androgen, for 24 hours following a single application to intact, clean, dry skin of the shoulders, upper arms and/or abdomen.</p> <p>A daily application of AndroGel® 5 G, 7.5 G, or 10 G contains 50 mg, 75 mg, or 100 mg of testosterone, respectively, to be applied daily to the skin's surface. Approximately 10% of the applied testosterone dose is absorbed across skin of average permeability during 24-hour period.</p> <p>The active pharmacologic ingredient in AndroGel® is testosterone. Testosterone USP is a white to practically white crystalline powder chemically described as 17-beta</p>	<p><b>DESCRIPTION</b> AndroGel® (testosterone gel) is a clear, colorless hydroalcoholic gel containing 1% testosterone. AndroGel® provides continuous transdermal delivery of testosterone, the primary circulating endogenous androgen, for 24 hours following a single application to intact, clean, dry skin of the shoulders, upper arms and/or abdomen.</p> <p>A daily application of AndroGel® 5 G, 7.5 G, or 10 G contains 50 mg, 75 mg, or 100 mg of testosterone, respectively, to be applied daily to the skin's surface. Approximately 10% of the applied testosterone dose is absorbed across skin of average permeability during 24-hour period.</p> <p>The active pharmacologic ingredient in AndroGel® is testosterone. Testosterone USP is a white to practically white crystalline powder chemically described as 17-beta</p>	

<p>hydroxyandrost-4-en-3-one.</p> <p><i>Testosterone Structure</i></p> <p>Inactive ingredients in AndroGel® are ethanol 68.9%, purified water, sodium hydroxide, Carbomer 940 and isopropyl myristate; these ingredients are not pharmacologically active.</p>	<p>hydroxyandrost-4-en-3-one.</p> <p><i>Testosterone Structure</i></p> <p>Inactive ingredients in AndroGel® are ethanol 68.9%, purified water, sodium hydroxide, Carbomer 940 and isopropyl myristate; these ingredients are not pharmacologically active.</p>	<p>The sponsor substituted “68.9%” for “67.0%”.</p> <p><b>This is acceptable. See Chemistry memo dated July 30, 2003.</b></p>
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APPROVED THIS WAY  
ON ORIGINAL

<b>CLINICAL PHARMACOLOGY</b>	<b>CLINICAL PHARMACOLOGY</b>	No changes made.
<b>Pharmacokinetics</b>	<b>Pharmacokinetics</b>	No changes made.
<b>Absorption</b>	<u>Absorption</u>	
<b>Distribution</b>	<u>Distribution</u>	No changes made.
<b>Metabolism</b>	<u>Metabolism</u>	No changes made.
<b>Excretion</b>	<u>Excretion</u>	No changes made.
<b>Special Populations</b>	<b>Special Populations</b>	No changes made.
<b>Clinical Studies</b>	<b>Clinical Studies</b>	No changes made.
<i>Potential for testosterone transfer:</i>	<i>Potential for testosterone transfer:</i>	No changes made.
<b>INDICATIONS AND USAGE</b>	<b>INDICATIONS AND USAGE</b>	No changes made.
<b>CONTRAINDICATIONS</b>	<b>CONTRAINDICATIONS</b>	No changes made.
<b>WARNINGS</b>	<b>WARNINGS</b>	
<ol style="list-style-type: none"> <li>1. Prolonged use of high doses of orally active 17-alpha-alkyl androgens (e.g., methyltestosterone) has been associated with serious hepatic adverse effects (peliosis hepatis, hepatic neoplasms, cholestatic hepatitis, and jaundice). Peliosis hepatis can be a life-threatening or fatal complication. Long-term therapy with testosterone enanthate, which elevates blood levels for prolonged periods, has produced multiple hepatic adenomas. Testosterone is not known to produce these adverse effects.</li> <li>2. Geriatric patients treated with androgens may be at an increased risk for the development of prostatic hyperplasia and prostatic carcinoma.</li> <li>3. Geriatric patients treated and other patients with</li> </ol>	<ol style="list-style-type: none"> <li>1. Prolonged use of high doses of orally active 17-alpha-alkyl androgens (e.g., methyltestosterone) has been associated with serious hepatic adverse effects (peliosis hepatis, hepatic neoplasms, cholestatic hepatitis, and jaundice). Peliosis hepatis can be a life-threatening or fatal complication. Long-term therapy with testosterone enanthate, which elevates blood levels for prolonged periods, has produced multiple hepatic adenomas. Testosterone is not known to produce these adverse effects.</li> <li>2. Geriatric patients treated with androgens may be at an increased risk for the development of prostatic hyperplasia and prostatic carcinoma.</li> <li>3. Geriatric patients treated and other patients with</li> </ol>	

<p>clinical or demographic characteristics that are recognized to be associated with an increased risk of prostate cancer should be evaluated for the presence of prostate cancer prior to initiation of testosterone replacement therapy. In men receiving testosterone replacement therapy, surveillance for prostate cancer should be consistent with current practices for eugonadal men (see PRECAUTIONS: Carcinogenesis, Mutagenesis, Impairment of Fertility and Laboratory Tests).</p> <p>4. Edema with or without congestive heart failure may be a serious complication in patients with preexisting, cardiac, renal, or hepatic disease. In addition to discontinuation of the drug, diuretic therapy may be required.</p> <p>5. Gynecomastia frequently develops and occasionally persists in patients being treated for hypogonadism.</p> <p>6. The treatment of hypogonadal men with testosterone esters may potentiate sleep apnea in some patients, especially those with risk factors such as</p>	<p>clinical or demographic characteristics that are recognized to be associated with an increased risk of prostate cancer should be evaluated for the presence of prostate cancer prior to initiation of testosterone replacement therapy. In men receiving testosterone replacement therapy, surveillance for prostate cancer should be consistent with current practices for eugonadal men (see PRECAUTIONS: Carcinogenesis, Mutagenesis, Impairment of Fertility and Laboratory Tests).</p> <p>4. Edema with or without congestive heart failure may be a serious complication in patients with preexisting, cardiac, renal, or hepatic disease. In addition to discontinuation of the drug, diuretic therapy may be required.</p> <p>5. Gynecomastia frequently develops and occasionally persists in patients being treated for hypogonadism.</p> <p>6. The treatment of hypogonadal men with testosterone esters may potentiate sleep apnea in some patients, especially those with risk factors such as</p>	
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obesity or chronic lung diseases.	obesity or chronic lung diseases. 7. GELS ARE FLAMMABLE. AVOID FIRE, FLAME OR SMOKING DURING USE.	The sponsor added "GELS ARE FLAMMABLE. AVOID FIRE, FLAME OR SMOKING DURING USE." <b>This is acceptable.</b>
<b>PRECAUTIONS</b>	<b>PRECAUTIONS</b>	No changes made.
<b>General</b>	<b>General</b>	No changes made.
<u>Information for Patients</u>	<u>Information for Patients</u>	No changes made.
<u>Advise patients of the following:</u> <ul style="list-style-type: none"> <li>• AndroGel® should not be applied to the scrotum.</li> <li>• AndroGel® should be applied once daily to clean dry skin.</li> <li>• After application of AndroGel®, it is currently unknown for how long showering or swimming should be delayed. For optimal absorption of testosterone, it appears reasonable to wait at least 5-6 hours after application prior to showering or swimming. Nevertheless, showering or swimming after just 1 hour should have a minimal effect on the amount of AndroGel® absorbed if done very infrequently.</li> </ul>	<u>Advise patients of the following:</u> <ul style="list-style-type: none"> <li>• AndroGel® should not be applied to the scrotum.</li> <li>• AndroGel® should be applied once daily to clean dry skin.</li> <li>• After application of AndroGel®, it is currently unknown for how long showering or swimming should be delayed. For optimal absorption of testosterone, it appears reasonable to wait at least 5-6 hours after application prior to showering or swimming. Nevertheless, showering or swimming after just 1 hour should have a minimal effect on the amount of AndroGel® absorbed if done very infrequently.</li> <li>• Since gels are flammable, avoid fire, flame or smoking during use.</li> </ul>	The sponsor added "Since gels are flammable, avoid fire, flame or smoking during use." <b>This is acceptable.</b>

<b>Laboratory Tests</b>	<u>Laboratory Tests</u>	No changes made.
<b>Drug Interactions</b>	<u>Drug Interactions</u>	No changes made.
<b>Drug/Laboratory Test Interactions</b>	<u>Drug/Laboratory Test Interactions</u>	No changes made.
<b>Carcinogenesis, Mutagenesis, Impairment of Fertility</b>	<u>Carcinogenesis, Mutagenesis, Impairment of Fertility</u>	No changes made.
Pregnancy Category X (see Contraindications)	Pregnancy Category X (see Contraindications)	No changes made.
Nursing Mothers:	Nursing Mothers:	No changes made.
Pediatric Use:	Pediatric Use:	No changes made.
<b>ADVERSE REACTIONS</b>	<b>ADVERSE REACTIONS</b>	No changes made.
<b>DRUG ABUSE AND DEPENDENCE</b>	<b>DRUG ABUSE AND DEPENDENCE</b>	No changes made.
<b>OVERDOSAGE</b>	<b>OVERDOSAGE</b>	No changes made.
<b>DOSAGE AND ADMINISTRATION</b>	<b>DOSAGE AND ADMINISTRATION</b>	No changes made.
<b>HOW SUPPLIED</b>	<b>HOW SUPPLIED</b>	No changes made.
<b>Storage</b>	<u>Storage</u>	No changes made.
<p><b>Disposal</b> Use AndroGel® packets should be discarded in household trash in a manner that prevents accidental application or ingestion by children or pets.</p> <p>Rx Only</p> <p><b>Manufactured by Laboratories Besins Iscovesco</b> Montrouge, France</p> <p>For: Unimed Pharmaceuticals, Inc. A Solvay Pharmaceuticals, Inc. Company Deerfield, IL 60015-2544, USA</p> <p>A.09.063.0036696 80-0005-03</p>	<p><b>Disposal</b> Use AndroGel® packets should be discarded in household trash in a manner that prevents accidental application or ingestion by children or pets.</p> <p>Rx Only</p> <p>Manufactured by Laboratories Besins International Montrouge, France</p> <p>For: Unimed Pharmaceuticals, Inc. A Solvay Pharmaceuticals, Inc. Company Marietta, GA 30062-2224, USA</p> <p>A.09.063.0039332 80-0005-04 Issued 11/02</p>	<p>The sponsor substituted “International” for “Iscovesco”.</p> <p>The sponsor substituted “Marietta, GA 30062-2224, USA</p> <p>A.09.063.0039332 80-0005-04 Issued 11/02” for</p>



<p><b>Patient Information and Instructions for Using AndroGel® (testosterone gel) 1% CIII</b></p> <p>Read this information carefully before using AndroGel® [AN drow jel]. The following information about AndroGel® should not take the place of your doctor's orders or recommendations. Your doctor will tell you exactly what dose to take, how to safely take it, and when to take it. Make sure you understand the benefits and risks of AndroGel® before you use it. If you have any other questions about our AndroGel® therapy, ask your doctor or pharmacist.</p>	<p><b>Patient Information and Instructions for Using AndroGel® 1% (testosterone gel) CIII</b></p> <p>A.09.063.0039331 85-0004-02 Issued 11/02</p> <p>Read this information carefully before using AndroGel® [AN drow jel]. The following information about AndroGel® should not take the place of your doctor's orders or recommendations. Your doctor will tell you exactly what dose to take, how to safely take it, and when to take it. Make sure you understand the benefits and risks of AndroGel® before you use it. If you have any other questions about your AndroGel® therapy, ask your doctor or pharmacist.</p>	
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10/2013

<b>What is AndroGel®?</b>	<b>What is AndroGel®?</b>	No changes made.
<b>Who should not take AndroGel®?</b>	<b>Who should not take AndroGel®?</b>	No changes made.
<p><b>How should I use AndroGel®?</b> It is important that you read and follow these directions on how to use the AndroGel® pump properly.</p> <ol style="list-style-type: none"> <li><b>1. Apply AndroGel® at the same time each day (preferably every morning).</b> You should apply your daily dose of gel every morning to clean, dry, intact skin. If you take a bath or shower in the morning, use AndroGel® <b>after</b> your bath or shower. Your doctor will tell you how much AndroGel® to use each day.</li> <li><b>2. Be sure you skin is completely dry.</b></li> <li><b>3. Open the packet.</b> Open one AndroGel® aluminum foil packet by folding the top edge at the perforation and tearing completely across the packet along the perforation.</li> <li><b>4. Remove the contents from the packet. Squeeze the contents into the palm of your hand. Squeeze from the bottom of the packet toward the top.</b> If you like, you may squeeze a portion of the gel from the packet into the palm of your hand</li> </ol>	<p><b>How should I use AndroGel®?</b> It is important that you read and follow these directions on how to use the AndroGel® pump properly.</p> <ol style="list-style-type: none"> <li><b>1. Apply AndroGel® at the same time each day (preferably every morning).</b> You should apply your daily dose of gel every morning to clean, dry, intact skin. If you take a bath or shower in the morning, use AndroGel® <b>after</b> your bath or shower. Your doctor will tell you how much AndroGel® to use each day.</li> <li><b>2. Be sure you skin is completely dry.</b></li> <li><b>3. Open the packet.</b> Open one AndroGel® aluminum foil packet by folding the top edge at the perforation and tearing completely across the packet along the perforation.</li> <li><b>4. Remove the contents from the packet. Squeeze the contents into the palm of your hand. Squeeze from the bottom of the packet toward the top.</b> If you like, you may squeeze a portion of the gel from the packet into the palm of your hand</li> </ol>	

and apply to application site(s).

**Repeat until the entire contents of the packet have been applied.**

Men should apply gel to starred (upper arm/shoulders) or shaded (abdomen) area only.

*Pictures*

5. **Apply AndroGel® only to healthy, normal skin on your abdomen (stomach area), shoulders, or upper arms.** In this way your body will absorb the right amount of testosterone. **Never apply AndroGel® to your genitals (penis or scrotum) or to skin with open sores, wounds, or irritation.**
6. **Wash your hands with soap and water right away after application to reduce the chance that the medicine will spread from your hands to other people.**
7. **Let AndroGel® dry for a few minutes before you dress.** This prevents your clothing from wiping the gel off your skin. It ensures that your body will absorb the correct amount of testosterone.
8. **Wait 5 to 6 hours before showering or swimming.** To ensure that the greatest amount of AndroGel® is

and apply to application site(s).

**Repeat until the entire contents of the packet have been applied.**

Men should apply gel to starred (upper arm/shoulders) or shaded (abdomen) area only.

*Pictures*

5. **Apply AndroGel® only to healthy, normal skin on your abdomen (stomach area), shoulders, or upper arms.** In this way your body will absorb the right amount of testosterone. **Never apply AndroGel® to your genitals (penis or scrotum) or to skin with open sores, wounds, or irritation.**
6. **Allow gel to dry completely before smoking or going near an open flame.**
7. **Wash your hands with soap and water right away after application to reduce the chance that the medicine will spread from your hands to other people.**
8. **Let AndroGel® dry for a few minutes before you dress.** This prevents your clothing from wiping the gel off your skin. It ensures that your body will absorb the correct amount of testosterone.
9. **Wait 5 to 6 hours**

The sponsor added “6. Allow gel to dry completely before smoking or going near an open flame.” **This is acceptable.**

absorbed into your system, you should wait 5 to 6 hours after application before showering or swimming. Once in a while, you may shower or swim as soon as 1 hour after applying AndroGel®. If done infrequently, this will have little effect on the amount of AndroGel® that is absorbed by your body.

**9. Maintain normal activities.** Once your hands are washed and the application site is covered with clothing, there is little risk of transferring testosterone to someone else's skin due to bodily contact. If, however, you expect direct skin contact with someone else, you should wash your application site(s) with soap and water before that encounter. This will reduce the chance that the medicine will transfer to the other person.

**before showering or swimming.** To ensure that the greatest amount of AndroGel® is absorbed into your system, you should wait 5 to 6 hours after application before showering or swimming. Once in a while, you may shower or swim as soon as 1 hour after applying AndroGel®. If done infrequently, this will have little effect on the amount of AndroGel® that is absorbed by your body.

**10. Maintain normal activities.** Once your hands are washed and the application site is covered with clothing, there is little risk of transferring testosterone to someone else's skin due to bodily contact. If, however, you expect direct skin contact with someone else, you should wash your application site(s) with soap and water before that encounter. This will reduce the chance that the medicine will transfer to the other person.

<b>What to do if someone else is exposed to AndroGel®.</b>	<b>What to do if someone else is exposed to AndroGel®.</b>	No changes made.
<b>What to do if you get AndroGel® in your eyes.</b>	<b>What to do if you get AndroGel® in your eyes.</b>	No changes made.
<b>What to do if you miss a dose.</b>	<b>What to do if you miss a dose.</b>	No changes made.
<b>What should I avoid while using AndroGel®?</b> It is important that you do not spread the medicine to others, especially women and children. Be sure to wash your hands after applying AndroGel®. Do not allow other persons to contact your skin where you may have applied AndroGel®, especially pregnant or nursing women. <b>Testosterone may harm the developing baby.</b>	<b>What should I avoid while using AndroGel®?</b> It is important that you do not spread the medicine to others, especially women and children. Be sure to wash your hands after applying AndroGel®. Do not allow other persons to contact your skin where you may have applied AndroGel®, especially pregnant or nursing women. <b>Testosterone may harm the developing baby. Gels are flammable. Avoid fire, flame or smoking until gel has dried.</b>	The sponsor added “Gels are flammable. Avoid fire, flame or smoking until gel has dried.” <b>This is acceptable.</b>
<b>What are the possible side effects of AndroGel®?</b>	<b>What are the possible side effects of AndroGel®?</b>	No changes made.
<b>Other Information</b>	<b>Other Information</b>	No changes made.
Manufactured by: Laboratories Besins Iscovesco Montrouge, France For Unimed Pharmaceutical, Inc. A Solvay Pharmaceuticals, Inc. Company Deerfield, IL 60015-2544  ©Unimed Pharmaceuticals, Inc., 2002  A.09.063.0035616	Manufactured by: Laboratories Besins International Montrouge, France For Unimed Pharmaceutical, Inc. A Solvay Pharmaceuticals, Inc. Company Marietta, GA 30062-2224  ©Unimed Pharmaceuticals, Inc., 2002  A.09.063.0039331 85-0004-02 Issued 11/02	The sponsor substituted “Marietta, GA 30062-2224 ©Unimed Pharmaceuticals, Inc., 2002 A.09.063.0039331 85-0004-02 Issued 11/02” for “Deerfield, IL 60015-2544

		<p>©Unimed Pharmaceuticals, Inc., 2002</p> <p>A.09.063.0035616". <b>This is acceptable.</b></p>
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/s/

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Eufrecina deGuia  
9/17/03 09:05:58 AM  
CSO

Eufrecina deGuia  
9/17/03 09:09:52 AM  
CSO

CONFIDENTIAL  
9/17/03

# Memo

To: NDA 21-015  
 From: Swapan K. De, Ph.D.  
 Through: David T. Lin, Ph.D., Chemistry Team Leader  
 Date: 7/30/2003  
 Re: Alcohol content change for the drug product

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The change in alcohol content in the drug product was noted in the NDA annual report dated 26 April 2002 and in the package inserts submitted to FDA in the CBE-0 dated 4 December 2002. Following an inquiry, the sponsor has provided a justification for the change and is deemed satisfactory due to following reasons.

- The drug product specification was updated to reflect the change in the alcohol used in the manufacturing from  $\frac{\text{---}}{\text{---}}$  to  $\frac{\text{---}}{\text{---}}$ . However, the total amount of alcohol in the formulation remains the same based on absolute alcohol content.
- The previous amount of  $\frac{\text{---}}{\text{---}}$  alcohol used was  $\frac{\text{---}}{\text{---}}$  gel. The change indicates the amount of  $\frac{\text{---}}{\text{---}}$  alcohol used is  $\frac{\text{---}}{\text{---}}$  gel. The sponsor used a density conversion calculation to account for the difference between the initial (v/v) and the final (wt/wt) reporting. Both the old and new density conversions are shown below.

Old calculation:

$$\begin{array}{ccccccc} \text{Starting Material} & & \text{Formulation Record} & & \text{Target Claim (wt/wt)} & & \% \text{Label Claim} \\ \frac{\text{---}}{\text{---}} \text{ Alcohol} & \times & \frac{\text{---}}{\text{---}} \text{ g Alcohol / g gel} & = & \frac{\text{---}}{\text{---}} \text{ g alcohol/ g gel} & & \text{---} \end{array}$$

Density adjusted calculation:

$$\begin{array}{ccccccc} \text{Starting} & & \text{Density of} & & \text{Formulation Record} & & \text{Density of} & & \text{Target Claim} \\ \text{Material (v/v)} & & \text{Starting} & & & & \text{Absolute EtOH} & & \text{(wt/wt)} \\ \frac{\text{---}}{\text{---}} \text{ Alcohol} & \times & \frac{\text{ml. Alcohol solution}}{\text{g Alcohol}} & \times & \frac{\text{g Alcohol solution}}{\text{g Gel}} & \times & \frac{\text{g Alcohol}}{\text{ml. Alcohol}} & = & \frac{\text{g Alcohol}}{\text{g Gel}} \\ \text{solution} & & \text{solution} & & & & & & \text{---} \\ & & & & & & & & \% \text{Label Claim} \end{array}$$

**Conclusion:** The calculation for change in alcohol content is deemed satisfactory. Thus, the change of alcohol content from  $\frac{g(\text{---})}{g \text{ gel}}$  to  $\frac{g(\text{---})}{g \text{ gel}}$  is acceptable.

**cc:**

Orig. NDA #21-015/SLR-008

**HFD-580/Division File**  
**HFD-580/Deguaie**  
**HFD-580/DTLin/SDe**

**R/D Init by: DTLin, Ph.D.**

filename: nda21015.slr008

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/s/  
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Swapn De  
7/30/03 08:29:33 AM  
CHEMIST

David T. Lin  
7/30/03 09:21:16 AM  
CHEMIST  
I concur.

APPEARS THIS WAY  
ON ORIGINAL

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-015/S-008**

**CORRESPONDENCE**



NDA 21-015/S-008

**CBE-0 SUPPLEMENT**

Unimed Pharmaceuticals, Inc.

c/o \_\_\_\_\_  
└

Dear Dr. Mondabaugh:

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

Name of Drug Product:           AndroGel® (testosterone gel)  
NDA Number:                    21-015  
Supplement number:            008  
Date of supplement:            December 4, 2002  
Date of receipt:                 December 5, 2002

This supplemental application was submitted as a "Supplement - Changes Being Effected." This supplement provides for changes to the specific sections of the AndroGel's Patient Insert and Physician Insert (UNIMED part numbers 85-0004-02 and 85-0005-04) and also to incorporate additional safety information regarding the potential hazard of gel products containing alcohol, and name and address changes into the physician and patient inserts.

Unless we notify you within 60 days of the 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 February 3, 2003 in accordance with 21 CFR 314.101(a).

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service:  
Center for Drug Evaluation and Research  
Division of Reproductive and Urologic Drug Products, HFD-580  
Attention: Division Document Room, 8B-45  
5600 Fishers Lane  
Rockville, Maryland 20857

Courier/Overnight Mail:

Food and Drug Administration

Center for Drug Evaluation and Research

Division of Reproductive and Urologic Drug Products, HFD-580

Attention: Document Room 8B-45

5600 Fishers Lane

Rockville, Maryland 20857

If you have any question, please call Eufrecina DeGuia , Regulatory Health Project Manager, at (301) 827-4260.

Sincerely,

*{See appended electronic signature page}*

Margaret Kober, R.Ph.

Chief, Project Management Staff

Division of Reproductive and Urologic Drug Products

Office of Drug Evaluation III

Center for Drug Evaluation and Research

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/s/

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Margaret Kober  
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Chief, Project Management Staff

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