Table 3: Adverse Reactions From Past Approval Experience of the Systematic Review

<table>
<thead>
<tr>
<th>Adverse Effects</th>
<th>Number of Patients</th>
<th>Number of Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td>100</td>
<td>50</td>
</tr>
<tr>
<td>Headache</td>
<td>150</td>
<td>75</td>
</tr>
<tr>
<td>Fatigue</td>
<td>200</td>
<td>100</td>
</tr>
<tr>
<td>Nausea</td>
<td>120</td>
<td>60</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>80</td>
<td>40</td>
</tr>
</tbody>
</table>

Adverse effects described in the past approval experience include dizziness, headache, fatigue, nausea, and diarrhea.

3.5.4 Conclusion

The following conclusions can be drawn from the systematic review:

1. The risk of adverse reactions from the study drug is comparable to those reported in the past approval experience.
2. Comparative studies are needed to further evaluate the adverse effects profile of the new drug.
3. The risk of adverse reactions should be monitored closely during clinical trials.

Overall, the systematic review provides valuable insights into the safety profile of the study drug, which may be beneficial for its future development and clinical use.

Graph 1: Distribution of adverse reactions reported in the systematic review.

Graph 2: Comparison of adverse reaction rates between the study drug and the comparator drug.

Graph 3: Time-to-event analysis of adverse reactions reported during clinical trials.

Graph 4: Correlation between the severity of adverse reactions and the duration of treatment.

Graph 5: Comparison of adverse reaction rates across different demographic groups.

Graph 6: Adverse reaction rates in subgroups of patients with comorbidities.

Graph 7: Trends in adverse reaction rates over time in clinical trials.

Graph 8: Adverse reaction rates in patients with specific drug interactions.

Graph 9: Analysis of adverse reaction rates in different geographical regions.

Graph 10: Predictive models for adverse reaction risk based on clinical trial data.

Graph 11: Comparison of adverse reaction rates in different patient populations.

Graph 12: Impact of adverse reactions on quality of life measures.

Graph 13: Cost-effectiveness analysis of adverse reaction management strategies.

Graph 14: Risk-benefit analysis of the study drug based on adverse reaction rates.

Graph 15: Comparison of adverse reaction rates in different treatment settings.

Graph 16: Adverse reaction rates in pediatric populations.

Graph 17: Adverse reaction rates in elderly populations.

Graph 18: Adverse reaction rates in patients with renal insufficiency.

Graph 19: Adverse reaction rates in patients with hepatic insufficiency.

Graph 20: Adverse reaction rates in patients with other comorbidities.

Graph 21: Adverse reaction rates in patients with a history of drug allergy.

Graph 22: Adverse reaction rates in patients with a history of drug abuse.

Graph 23: Adverse reaction rates in patients with a history of substance use disorder.

Graph 24: Adverse reaction rates in patients with a history of psychiatric disorder.

Graph 25: Adverse reaction rates in patients with a history of smoking.

Graph 26: Adverse reaction rates in patients with a history of alcohol use.

Graph 27: Adverse reaction rates in patients with a history of other medical conditions.

Graph 28: Adverse reaction rates in patients with a history of surgery.

Graph 29: Adverse reaction rates in patients with a history of radiation therapy.

Graph 30: Adverse reaction rates in patients with a history of chemotherapy.

Table 4: Correlation of Adverse Reactions with Clinical Parameters

<table>
<thead>
<tr>
<th>Clinical Parameter</th>
<th>Adverse Reaction Rate</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.03</td>
<td>0.05</td>
</tr>
<tr>
<td>Gender</td>
<td>0.12</td>
<td>0.08</td>
</tr>
<tr>
<td>Race</td>
<td>0.23</td>
<td>0.10</td>
</tr>
<tr>
<td>BMI</td>
<td>0.45</td>
<td>0.02</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>0.06</td>
<td>0.01</td>
</tr>
<tr>
<td>Smoking Status</td>
<td>0.08</td>
<td>0.03</td>
</tr>
<tr>
<td>Alcohol Use</td>
<td>0.11</td>
<td>0.07</td>
</tr>
<tr>
<td>History of Cancer</td>
<td>0.04</td>
<td>0.06</td>
</tr>
<tr>
<td>History of Heart Disease</td>
<td>0.07</td>
<td>0.04</td>
</tr>
<tr>
<td>History of Diabetes</td>
<td>0.15</td>
<td>0.10</td>
</tr>
</tbody>
</table>

The correlation analysis indicates that BMI, smoking status, and history of heart disease are significantly associated with adverse reaction rates.

Graph 31: Correlation scatter plot of clinical parameters vs. adverse reaction rates.

Graph 32: Heatmap of correlation coefficients between clinical parameters and adverse reaction rates.

Graph 33: Principal Component Analysis (PCA) of clinical parameters and adverse reaction rates.

Graph 34: Partial Least Squares (PLS) regression analysis of clinical parameters and adverse reaction rates.

Graph 35: Random Forest (RF) classification model of clinical parameters and adverse reaction rates.

Graph 36: Artificial Neural Network (ANN) model of clinical parameters and adverse reaction rates.

Graph 37: Support Vector Machine (SVM) model of clinical parameters and adverse reaction rates.

Graph 38: Decision Tree (DT) classification model of clinical parameters and adverse reaction rates.

Graph 39: Naive Bayes (NB) classification model of clinical parameters and adverse reaction rates.

Graph 40: Bayesian Network (BN) model of clinical parameters and adverse reaction rates.

Graph 41: Graphical Model (GM) of clinical parameters and adverse reaction rates.

Graph 42: Graph Theory (GT) model of clinical parameters and adverse reaction rates.
MEDICATION GUIDE
Testosterone (testosterone trans-10-15-decanol) Topical Gel, 1.625 mg

Read this Medication Guide before you start using Testosterone Topical Gel, 1.625 mg and each time you get a refill. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or treatment.

What is the most important information I should know about Testosterone Topical Gel, 1.625 mg?
Early signs and symptoms of puberty have happened in young children who were accidentally exposed to testosterone through contact with men using Testosterone Topical Gel, 1.625 mg.

Signs and symptoms of early puberty in a child may include:
- enlarged penis or clitoris
- early development of pubic hair
- increased mons pubis or axillary hair
- aggressive behavior

Testosterone Topical Gel, 1.625 mg can transfer from your body to others.

Women who are pregnant should avoid contact with the unwashed or uncleaned area where Testosterone Topical Gel, 1.625 mg has been applied to your skin. 

Stop using Testosterone Topical Gel, 1.625 mg and call your healthcare provider right away if you see any signs and symptoms of in a child or a woman that may have occurred through accidental exposure to Testosterone Topical Gel, 1.625 mg.

Signs and symptoms of exposure to Testosterone Topical Gel, 1.625 mg in children may include:
- enlarged penis or clitoris
- early development of pubic hair
- increased mons pubis or axillary hair
- aggressive behavior

Signs and symptoms of exposure to Testosterone Topical Gel, 1.625 mg in women may include:
- changes in body hair
- a large increase in acne

To lower the risk of transfer of Testosterone Topical Gel, 1.625 mg from your body to others, you should follow these important instructions:
- Apply Testosterone Topical Gel, 1.625 mg only to your shoulders and upper arms that will be covered by a short sleeve or shirt.
- Wash your hands right away with soap and water after applying Testosterone Topical Gel, 1.625 mg.
- Allow the gel to dry, cover the application area with clothing.
- Keep the area covered until you have washed the application area well or have abated.
- If you expect to have skin-to-skin contact with another person, first wash the application area well with soap and water.
- If a woman or child makes contact with the Testosterone Topical Gel, 1.625 mg application area, wash the area with soap and water right away.

What is Testosterone Topical Gel, 1.625 mg?
Testosterone Topical Gel, 1.625 mg is a prescription medicine that contains testosterone.
Testosterone Topical Gel, 1.625 mg is used to treat adult males who have low or no testosterone due to certain medical conditions.

Your healthcare provider will test your blood before you start and while you are taking Testosterone Topical Gel, 1.625 mg.

It is not known if Testosterone Topical Gel, 1.625 mg is safe or effective to treat men who have low testosterone due to aging.

It is not known if Testosterone Topical Gel, 1.625 mg is safe or effective in children younger than 10 years old. Improper use of Testosterone Topical Gel, 1.625 mg may affect bone growth in children.

Testosterone Topical Gel, 1.625 mg is a controlled substance (CR) because it contains testosterone, which can be a controlled drug for people who abuse prescription medicines. Keep your Testosterone Topical Gel, 1.625 mg in a safe place to protect it. Never give your Testosterone Topical Gel, 1.625 mg to anyone else, even if they have the same symptoms you have. Selling or giving away this medicine may harm others and is against the law.

Testosterone Topical Gel, 1.625 mg is not meant for use in women.

Who should not use Testosterone Topical Gel, 1.625 mg?
Do not use Testosterone Topical Gel, 1.625 mg if you:
- have breast cancer
- have or might have prostate cancer
- are pregnant or may become pregnant or are breastfeeding.

Testosterone Topical Gel, 1.625 mg may harm your unborn baby or breast-feeding baby. Women who are pregnant or who may become pregnant should avoid contact with the area of skin where Testosterone Topical Gel, 1.625 mg has been applied.

Talk to your healthcare provider before taking this medicine if you have any of the above conditions.

What should I tell my healthcare provider before using Testosterone Topical Gel, 1.625 mg?
Before you use Testosterone Topical Gel, 1.625 mg, tell your healthcare provider if you:
- have breast cancer
- have or might have prostate cancer
- have urinary problems due to an enlarged prostate
- have heart problems
- have liver or kidney problems
- have problems breathing while you sleep (sleep apnea)
- have any other medical conditions.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

Using Testosterone Topical Gel, 1.625 mg with certain other medicines can affect each other. Especially tell your healthcare provider if you take:
- insulin
- medications that decrease blood clotting (anticoagulants)

Know the medicines you take. Ask your healthcare provider or pharmacist for a list of all the medicines you take. Keep a list of them and show it to your healthcare provider and pharmacist when you get a new medicine.

How to use Testosterone Topical Gel, 1.625 mg?

It is important that you apply Testosterone Topical Gel, 1.625 mg exactly as your healthcare provider tells you.

Your healthcare provider will tell you how much Testosterone Topical Gel, 1.625 mg to apply and when to apply it.

Your healthcare provider may change your Testosterone Topical Gel, 1.625 mg dose. Do not change your Testosterone Topical Gel, 1.625 mg dose without talking to your healthcare provider.

Testosterone Topical Gel, 1.625 mg is to be applied to the area of your shoulders and upper arms that will be covered by a short sleeve or shirt. Do not apply Testosterone Topical Gel, 1.625 mg to any other parts of your body such as your trunk, back area (lumbar), pelvic, scrotum, chest, armpits (axillae), or hands.

Apply Testosterone Topical Gel, 1.625 mg the same time each morning. Testosterone Topical Gel, 1.625 mg should be applied after shaving or bathing.

Wash your hands right away with soap and water after applying Testosterone Topical Gel, 1.625 mg.

Avoid shaving, swimming, or bathing for at least 2 hours after you apply Testosterone Topical Gel, 1.625 mg.

Testosterone Topical Gel, 1.625 mg is flammable until it is dry. Let Testosterone Topical Gel, 1.625 mg dry before using or going near an open flame.

Let the application site dry completely before putting on a shirt.

Applying Testosterone Topical Gel, 1.625 mg:
Testosterone Topical Gel, 1.625 mg comes in a pump or in packets.

Before applying Testosterone Topical Gel, 1.625 mg, make sure that your shoulders and upper arms are clean, dry, and that there is no broken skin.
The application site for Testosterone Topical Gel, 1.62% are the upper arms and shoulders that will be covered by a short sleeve t-shirt (See Figure A).

If you are using Testosterone Gel, 1.62% pump:

- Before using a new bottle of Testosterone Gel, 1.62% for the first time, you will need to prime the pump. To prime the pump, the Testosterone Gel, 1.62% pump, already push the pump all the way down 3 times. The best use any Testosterone Gel, 1.62% that comes out with the priming. Wash it down in the sink to avoid accidental exposure to others. Your Testosterone Gel, 1.62% pump is now ready to use.
- Remove the cap from the pump. Then, position the nozzle over the part of your hand and firmly push the pump all the way down. Wash the test site with soap and water. 1.62% to the application site. You may also apply Testosterone Gel, 1.62% directly to the application site.
- Wash your hands with soap and water right away.

Find Your Dose as Prescribed by Your Healthcare Provider

1 PUMP DEPRESSIONS (20.25 mg) Apply 1 pump depression of Testosterone Gel, 1.62% to upper arm and shoulder.
2 PUMP DEPRESSIONS (40.5 mg) Apply 2 pump depressions of Testosterone Gel, 1.62% to upper arm and shoulder and then apply 1 pump depression of Testosterone Gel, 1.62% to the opposite upper arm and shoulder.
3 PUMP DEPRESSIONS (60.75 mg) Apply 3 pump depressions of Testosterone Gel, 1.62% to upper arm and shoulder and then apply 2 pump depressions of Testosterone Gel, 1.62% to the opposite upper arm and shoulder.
4 PUMP DEPRESSIONS (81 mg) Apply 4 pump depressions of Testosterone Gel, 1.62% to upper arm and shoulder and then apply 3 pump depressions of Testosterone Gel, 1.62% to the opposite upper arm and shoulder.

Instruction: Wear this pocket kit completely at all times. Squeeze from the bottom of the pump to the top.

For Testosterone Gel, 1.62% out of the pocket into the palm of your hand. Apply Testosterone Gel, 1.62% to the application site. You may also apply Testosterone Gel, 1.62% directly to the application site. Testosterone Gel, 1.62% should be applied right away.
- Wash your hands with soap and water right away.

Find Your Dose as Prescribed by Your Healthcare Provider

One (0.25 mg) packet Apply 1 packet of Testosterone Gel, 1.62% to upper arm and shoulder.
One (0.45 mg) packet Apply 1 packet of Testosterone Gel, 1.62% to upper arm and shoulder and then apply the remaining portion to the opposite upper arm and shoulder.
One (0.45 mg) packet and One (0.25 mg) packet Apply 1 packet of Testosterone Gel, 1.62% to upper arm and shoulder and then apply 1 packet of Testosterone Gel, 1.62% to the opposite upper arm and shoulder.
Two (0.45 mg) packets Apply 2 packets of Testosterone Gel, 1.62% to upper arm and shoulder and then apply 1 packet of Testosterone Gel, 1.62% to the opposite upper arm and shoulder.

What are the possible side effects of Testosterone Gel, 1.62%?

"What is the most important information I should know about Testosterone Topical Gel, 1.62%?

Testosterone Gel, 1.62% can cause serious side effects including:
- If you already have enlarged prostate gland your signs and symptoms can get worse while you are using Testosterone Gel, 1.62%.
This can include:
- Increased urinary tract infection
- Trouble starting your urine stream
- Feeling to pass urine many times during the day
- Feeling to have to go to the bathroom right away
- Feeling to have a urinary accident

- Being unable to pass urine or urine flow weak

- Possible increased risk of prostate cancer: your healthcare provider need should be notified before you are prostate cancer. If you have started or have you have been told you have Testosterone Gel, 1.62%.
- Blood in your prostatic fluid. Signs and symptoms of a blood clot in your leg can include leg pain, swelling, or redness. Signs and symptoms of a blood clot in your lung can include chest pain, shortness of breath or (less often) skin

- Possible increased risk of heart attack or stroke

- May cause Testosterone Gel, 1.62% may lower your sperm count.

- Swelling of your ankles, feet, or body, with or without heart failure.

- Enlarged or painful breasts

- Have problems breathing while you sleep (sleep apnea).

Call your healthcare provider right away if you have any of the serious side effects listed.

The most common side effects of Testosterone Topical Gel, 1.62% include:
- Wetting your bed (prostate specific antigen is used to screen for prostate cancer)
- Mixed emotions
- Hypersensitivity
- Increased or reduced seed output
- Infertility where stimulation by Testosterone Gel, 1.62% is applied.

Other side effects include more reactions than are normal for you or sensations that last longer than 1 week.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of Testosterone Gel, 1.62%.
For more information, ask your healthcare provider or pharmacist.

Call your doctor about additional side effects. You may report side effects to FDA at 1-800-FDA-1088.

How store testosterone Topical Gel, 1.62%?

- Store this product at room temperature.
- Store this product, 1.62% at 60°F (15°C to 30°C).
- Do not use nonprescription Testosterone Topical Gel, 1.62% for any condition that was not prescribed.
- Do not give Testosterone Gel, 1.62% to other people, even if they have similar symptoms.

- Keep Testosterone Gel, 1.62% away from fire.

Keep Testosterone Gel, 1.62% and all medicines out of the reach of children.

Storage of the active and inactive ingredients of Testosterone Topical Gel, 1.62%

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. You may use Testosterone Gel, 1.62% for a condition that was not prescribed. Do not give Testosterone Gel, 1.62% to other people, even if they have similar symptoms. You may throw them away.

This Medication Guide summarizes the most important information about Testosterone Topical Gel, 1.62% that you should need before you take it. Other information about Testosterone Topical Gel, 1.62% is available from your pharmacist.

For more information, go to www.perrigo.com or call 1-866-364-9920.

When to stop testosterone Topical Gel, 1.62%?

Active ingredient: testosterone

Inactives ingredients: cacodylic acid 98%, ethyl alcohol, lauric acid methylester, parabens water and sodium hydroxide.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured By Perrigo

Allegan, MI 49010

(877) 661-6827

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