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|-------------------|--|-----|-------------|
| Suggested Formula | Hydroquinone 2%, Tretinoin 0.015% Topical Cream (Emulsion, 60 g) | FIN | F 004 625v2 |
|-------------------|--|-----|-------------|

SUGGESTED FORMULATION

| Ingredient Listing | Qty. | Unit | NDC # | Supplier | Lot Number | Expiry Date |
|--------------------------------------|--------------|------|-------|----------|------------|-------------|
| Hydroquinone, USP | 1.200 | g | | | | |
| Tretinoin 1% Stock Solution † | 0.90 | mL | | | | |
| Ascorbic Acid, USP | 1.02 | g | | | | |
| Butylated Hydroxytoluene (BHT), NF | 0.06 | g | | | | |
| Sodium Metabisulfite, NF | 0.30 | g | | | | |
| Propylene Glycol, USP | 3.0 | mL | | | | |
| Medisca HRT Cream Base | 53.41 | g | | | | |
| | | | | | | |
| † Tretinoin 1% Stock Solution | | | | | | |
| Tretinoin (Retinoic Acid), USP | 0.100 | g | | | | |
| Alcohol (95%), USP | 2.5 | mL | | | | |
| Butylated Hydroxytoluene (BHT), NF | 0.01 | g | | | | |
| Propylene Glycol, USP | 2.4 | mL | | | | |
| Acetone, NF | q.s. to 10.0 | mL | | | | |



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SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

| | |
|--|---|
| Heat sensitive (protect from heat whenever possible): | <i>Tretinoin, Butylated Hydroxytoluene</i> |
| Light sensitive (protect from light whenever possible): | <i>Hydroquinone, Tretinoin, Ascorbic Acid, Butylated Hydroxytoluene, Propylene Glycol, Sodium Metabisulfite</i> |
| Hygroscopic (protect from moisture whenever possible): | <i>Propylene Glycol</i> |
| Air sensitive (protect from air whenever possible): | <i>Sodium Metabisulfite</i> |
| Oxygen sensitive (protect from oxygen whenever possible): | <i>Hydroquinone, Tretinoin, Ascorbic Acid</i> |
| Moisture sensitive (protect from humidity whenever possible): | <i>Butylated Hydroxytoluene, Sodium Metabisulfite</i> |
| Highly Flammable (avoid exposure to heat, flame, ignition sources, light or shock): | <i>Acetone</i> |

Suggested Preparatory Guidelines

Non-Sterile Preparation Sterile Preparation

Processing Error / Testing Considerations: To account for processing error considerations during preparation, it is suggested to measure an additional **5 to 9%** of the required quantities of ingredients.

Special Instruction: Protective apparel, such as a lab coat, disposable gloves, eyewear and face-masks should always be worn.

This procedure requires the use of very small quantities of ingredients. All calculations and preparation techniques must be verified before dispensing the final product.



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SUGGESTED PREPARATION (for 60 g)

Weigh and / or measure the following ingredients when appropriate:

| Ingredient Listing | Qty. | Unit | Multiplication factor (*): ____ | Processing Error | Qty. to measure |
|--------------------------------------|--------------|------|---------------------------------|------------------|-----------------|
| Hydroquinone, USP § | 1.200 | g | | | |
| Tretinoin 1% Stock Solution † § | 0.90 | mL | | | |
| Ascorbic Acid, USP § | 1.02 | g | | | |
| Butylated Hydroxytoluene (BHT), NF § | 0.06 | g | | | |
| Sodium Metabisulfite, NF § | 0.30 | g | | | |
| Propylene Glycol, USP § | 3.0 | mL | | | |
| Medisca HRT Cream Base | 53.41 | g | | | |
| | | | | | |
| † Tretinoin 1% Stock Solution | | | | | |
| Tretinoin (Retinoic Acid), USP § | 0.100 | g | --- | --- | |
| Alcohol (95%), USP | 2.5 | mL | --- | --- | |
| Butylated Hydroxytoluene (BHT), NF § | 0.01 | g | --- | --- | |
| Propylene Glycol, USP § | 2.4 | mL | --- | --- | |
| Acetone, NF § | q.s. to 10.0 | mL | --- | --- | |

* Takes into account increased batch size conversions and density conversions, if required.

§ Weigh / measure just prior to use.



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Preparatory Instruction

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| 1. | <p>† <u>Tretinoin 1% Stock Solution preparation:</u></p> <p>A. Combine and triturate the following ingredients together to form a fine, homogeneous powder blend:</p> <ul style="list-style-type: none">-Tretinoin (Retinoic Acid) (0.100 g)-Butylated Hydroxytoluene (0.01 g) <p>B. Levigate the fine, homogeneous powder blend (Step 1A) with the Propylene Glycol (2.4 mL).</p> <p><u>End result:</u> Homogeneous liquid-like dispersion.</p> <p>C. Incrementally add the homogeneous liquid-like dispersion (Step 1B) to the Alcohol (95%).</p> <p><u>Specifications:</u> Continuously mix.</p> <p><u>End result:</u> Homogeneous liquid-like dispersion.</p> <p>D. Add Acetone to the mixture (Step 1C) to fill to the required batch size (10.0 mL).</p> <p><u>Specifications:</u> Continuously mix until all solid particles have completely dissolved.</p> <p><u>End result:</u> Homogeneous liquid-like solution.</p> |
| 2. | <p><u>Powder-liquid preparation:</u></p> <p>A. Combine and triturate the following ingredients together to form a fine, homogeneous powder blend:</p> <ul style="list-style-type: none">-Hydroquinone-Ascorbic Acid-Butylated Hydroxytoluene (BHT)-Sodium Metabisulfite <p>B. Levigate the fine, homogenous powder blend (Step 2A) with the Propylene Glycol.</p> <p><u>End result:</u> Homogeneous paste-like dispersion.</p> |



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| 3. | <p><u>Medium Integration:</u></p> <p>A. In the given order, sequentially add the following ingredients to the HRT Cream Base:</p> <ul style="list-style-type: none"> -Tretinoin 1% Stock Solution (0.90 mL <i>plus</i> processing error adjustments) -Homogeneous paste-like dispersion (Step 2B) <p><u>Specification:</u> Continuously mix, using high-shear mixing techniques.</p> <p><u>End result:</u> Homogeneous cream-like dispersion.</p> <p><u>Note:</u> Add the next ingredient, once the previous one has been completely added and dispersed.</p> |
| 4. | <p><u>Product transfer:</u></p> <p>Transfer the final product into the specified dispensing container (see “Packaging Requirements”).</p> |

SUGGESTED PRESENTATION

| Estimated Beyond-Use Date | 30 days, refrigerated, as per USP. | Packaging Requirements | Tightly closed, light-resistant ointment tube or jar. | |
|---------------------------|--|---|--|--|
| Auxiliary Labels | 1 | Use as directed. Do not exceed prescribed dose. | 7 | Keep in a dry place. |
| | 2 | Keep out of reach of children. | 8 | Keep refrigerated. Do not freeze. |
| | 3 | Do not allow to come into contact with eyes/ears/nose/mouth. | 9 | Consult your health care practitioner if any prescription or over-the-counter medications are currently being used or are prescribed for future use. |
| | 4 | For external use only. | 10 | Protect from light. |
| | 5 | Cap tightly after use. | 11 | Patient must avoid exposure to sunlight and UV rays. |
| | 6 | Do not take with alcohol, sleep aids, tranquilizers or other CNS depressants. | 12 | May impair mental and/or physical ability. Use care when operating a car or machinery. |
| Pharmacist Instructions | Add any auxiliary labels specific to the active ingredient to the dispensing container as deemed necessary. | | | |
| Patient Instructions | Contact your pharmacist in the event of adverse reactions. IMPORTANT: The quantity of active ingredient administered is directly dependent on the quantity of product applied. | | | |



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