MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
TOLL-FREE: 866-333-7811
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| Suggested Formula | Naltrexone Hydrochloride 4.5 mg Oral Transmucosal Films (Solid Suspension, 30 Films) | FIN | F 009 673 |
|---|---|---|---|

## SUGGESTED FORMULATION

| Ingredient Listing | Qty. | Unit | NDC # | Supplier | Lot Number | Expiry Date |
|---|---|---|---|---|---|---|
| Naltrexone Hydrochloride, USP | TBD | | | | | |
| Bitterness Reducing Agent (NF-01) (Natural) (Powder) | 0.25 | g | | | | |
| Cellulose (Microcrystalline), NF | 1.065 | g | | | | |
| Menthol (Crystals) (Levorotatory) (Natural), USP | 0.06 | g | | | | |
| Sucralose, NF | 0.045 | g | | | | |
| Purified Water, USP | 8.0 | mL | | | | |
| NovaFilm™ Gel Base | 18.00 | g | | | | |
| Purified Water, USP | q.s. to 30.0 | mL | | | | |

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## SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

***Hygroscopic*** *(protect from moisture whenever possible):* *Naltrexone Hydrochloride, Cellulose*

***Light Sensitive*** *(protect from light whenever possible):* *Naltrexone Hydrochloride, NovaFilm™ Gel Base*

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 **12 to 15%** of the required quantities of ingredients.

Special Instruction: This formula may contain one or more Active Pharmaceutical Ingredients (APIs) that may be classified as hazardous, please refer & verify the current NIOSH list of Antineoplastic and Other Hazardous Drugs in Healthcare Settings. At this time, **General Chapter <800> Hazardous Drugs – Handling in Healthcare Settings** is informational and not compendially applicable unless otherwise specified by regulators and enforcement bodies. For information on the scope, intended applicability, and implementation context for USP General Chapter <800>, see: https://www.usp.org/compounding/general-chapter-hazardous-drugs-handling-healthcare.

This formula must be prepared within the appropriate facilities under adequate environmental conditions, following the necessary guidelines and procedures as stated within *USP 795* and *USP 800*, when handling hazardous drugs. Only trained and qualified personnel must prepare this formula.

All required personal protective equipment (hazardous if applicable), such as but not limited to, lab coat, protective sleeves, gloves both inner and outer if applicable, dedicated shoe covers, hairnet, beard cover, eyewear, appropriate face mask, respirator and face shield, etc., where applicable must be worn at all times.

If applicable, follow all required procedures for hazardous drug handling including but not limited to procurement, transport, storage, preparation, dispensing, administration, clean up (spills) & disposal.

If you are a registered 503B facility, please refer to all relevant guidance documents including but not limited to the Code of Federal Regulations (CFR), Guidance for Industry (GFIs) and Compliance Policy Guides (CPGs).

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 30 Films)

Weigh and / or measure the following ingredients when appropriate:

| Ingredient Listing | Qty. | Unit | Multiplication factor (*): ____ | Processing Error | Qty. to measure |
|---|---|---|---|---|---|
| Naltrexone Hydrochloride, USP § | TBD | | | | |
| Bitterness Reducing Agent (NF-01) (Natural) (Powder) | 0.25 | g | | | |
| Cellulose (Microcrystalline), NF § | 1.065 | g | | | |
| Menthol (Crystals) (Levorotatory) (Natural), USP | 0.06 | g | | | |
| Sucralose, NF | 0.045 | g | | | |
| Purified Water, USP | 8.0 | mL | | | |
| NovaFilm™ Gel Base § | 18.00 | g | | | |
| Purified Water, USP | q.s. to 30.0 | mL | | | |

* Takes into account increased batch size conversions and density conversions, if required.
§ Weigh / measure just prior to use.

| Preparatory Instruction | |
|---|---|
| 1. | **Preparatory Step:**<br><br>A. Preheat an appropriate convection oven.<br><br>Specifications: Temperature: 50°C. |

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2. **Ingredient quantification:**

A. Determine the potency of Naltrexone Hydrochloride based on the certificate of analysis:

| | |
|---|---|
| | 100% |
| MINUS | |
| Water and alcoholic solvents content (from certificate of analysis) | _____ % |
| DIVIDED BY | 100 |
| EQUALS | |
| Quantity of water and alcoholic solvents free Naltrexone Hydrochloride, in decimal | _____ |
| MULTIPLIED BY | |
| Assay on anhydrous, solvent free basis (from certificate of analysis) | _____ % |
| DIVIDED BY | 100 |
| EQUALS | |
| **i. Potency of Naltrexone Hydrochloride, in decimal** | _____ |

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3. **Ingredient quantification:**

A. Determine the quantity (in g) of Naltrexone Hydrochloride required to make 30 Films of Naltrexone Hydrochloride 4.5 mg:

| | |
|---|---|
| Quantity of Naltrexone Hydrochloride required for 30 Films | 0.135 g |
| DIVIDED BY | |
| Potency of Naltrexone Hydrochloride, in decimal (Step 2Ai) | _____ |
| EQUALS | |
| **i. Quantity of Naltrexone Hydrochloride needed for 30 Films** | _____ **g** |
| MULTIPLIED BY | |
| Processing error adjustments (12 to 15%) | 1.12 to 1.15 |
| EQUALS | |
| **ii. Quantity of Naltrexone Hydrochloride needed *plus* processing error adjustments** | _____ **g** |

4. **Powder-liquid preparation:**

A. By geometric addition, combine and triturate the following ingredients together to form a fine, homogeneous powder blend:

-Naltrexone Hydrochloride (amount determined from Step 3Aii)
-Bitterness Reducing Agent (NF-01) (Natural) (Powder)
-Cellulose (Microcrystalline)
-Menthol (Crystals) (Levorotatory) (Natural)
-Sucralose

B. Levigate the fine, homogeneous powder blend (Step 4A) with the Purified Water (8.0 mL *plus* processing error adjustments).

End result: Homogeneous liquid-like dispersion.

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5. **Medium incorporation:**

A. Incrementally add the homogeneous liquid-like dispersion (Step 4B) to the NovaFilm™ Gel Base.

Specifications: Continuously mix, using high-shear mixing techniques.

**NOTE: Ensure mixing process does not incorporate any air.**

End result: Homogeneous gel-like dispersion.

6. **Filling to volume:**

A. Add additional Purified Water to the mixture (Step 5A) to fill to the required batch size (30.0 mL *plus* processing error adjustments).

Specifications: Continuously mix, using high-shear mixing techniques.

**NOTE: Ensure mixing process does not incorporate any air.**

End result: Homogeneous gel-like dispersion.

7. **Mold filling and heating:**

A. Fill the 30 blister mold cavities with 1.00 mL of the homogeneous gel-like dispersion (Step 6A) per cavity. Spread the homogeneous gel-like dispersion in the cavity to a uniform thickness.

**NOTE: Ensure no air bubbles are added to the mold cavities.**

B. Heat the filled blister molds to 50°C for 60 to 90 minutes in the preheated convection oven. Do not overheat.

Specifications: Homogeneous solid dispersion.

8. **Cooling:**

A. Carefully remove the blister mold from the heated oven.

B. Allow the films to cool for an additional 15- 30 minutes in the blister molds at controlled temperature and relative humidity.

9. **Validation technique:**

A. Weigh 6 films separately.

B. The final weight of each film from Step 9A (not including the weight of blister mold) shall not be less than 90% and not more than 110% of the theoretically calculated weight in accordance to USP guidelines. The theoretically calculated weight can be determined by adding the following values: **0.154 g** + **(Step 3Ai/30)**.

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| 10. | **Product transfer:**<br><br>Transfer the final product into the specified dispensing container (see "Packaging requirements"). |

## SUGGESTED PRESENTATION

| | | | | | |
|---|---|---|---|---|---|
| Estimated Beyond-Use Date | | 180 days, controlled room temperature or refrigerator, as per USP 795*. | Packaging Requirements | | Manually lock blister molds and put into light-resistant resealable foil pouch. |
| Auxiliary Labels | 1 | Use as directed. Do not exceed prescribed dose. | 6 | | Do not take with alcohol, sleep aids, tranquilizers or other CNS depressants. |
| | 2 | Keep out of reach of children. | 7 | | Keep at controlled room temperature (20°C – 25°C) OR keep refrigerated (2°C – 8°C). Do not freeze. |
| | 3 | Keep in a dry place. | 8 | | Protect from light. |
| | 4 | May impair mental and/or physical ability. Use care when operating a car or machinery. | 9 | | Consult your health care practitioner if any other prescription or over-the-counter medications are currently being used or are prescribed for future use. |
| | 5 | Discard container after use. | 10 | | May produce psychological and/or physical dependence. |
| Pharmacist Instructions | | Add any auxiliary labels specific to the API to the dispensing container as deemed necessary. | | | |
| Patient Instructions | | Contact your pharmacist in the event of adverse reactions. | | | |

*** If the API or any other components in the CNSP have an expiration date that is earlier than the assigned BUD, the expiration date supersedes the assigned BUD and must be the assigned shortest date.**

| | | | |
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## REFERENCES


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