SUGGESTED FORMULATION

<table>
<thead>
<tr>
<th>Ingredient Listing</th>
<th>Qty.</th>
<th>Unit</th>
<th>NDC #</th>
<th>Supplier</th>
<th>Lot Number</th>
<th>Expiry Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diazepam, USP</td>
<td>0.500</td>
<td>g</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silica Gel</td>
<td>2.50</td>
<td>g</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propylene Glycol, USP</td>
<td>5.0</td>
<td>mL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medisca Polypeg (Suppository base)</td>
<td>TBD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SPECIAL PREPARATORY CONSIDERATIONS

**Controlled substance** (adhere to proper handling and documentation procedures)
- Diazepam

*Light sensitive* (protect from light whenever possible):
- Diazepam
- Propylene Glycol

*Hygroscopic* (protect from moisture whenever possible):
- Silica Gel
- Propylene Glycol

**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 100 x 1.3 mL suppositories)**

Weigh and / or measure the following ingredients when appropriate:

<table>
<thead>
<tr>
<th>Ingredient Listing</th>
<th>Qty.</th>
<th>Unit</th>
<th>Multiplication factor(*)</th>
<th>Processing Error</th>
<th>Qty. to measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diazepam, USP §</td>
<td>0.500</td>
<td>g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silica Gel §</td>
<td>2.50</td>
<td>g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propylene Glycol, USP §</td>
<td>5.0</td>
<td>mL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medisca Polypeg (Suppository base)</td>
<td>TBD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

**Preparatory Instruction**

1. **Preparatory step:**
   A. Prepare a hot water bath
      Specifications: Temperature: 60 to 65°C.

2. **Ingredient quantification (mold calibration):**
   Calculate the quantity of Polypeg (Suppository Base) required for 100 suppositories. Refer to the Appendix for details.
Suggested Formula: Diazepam 5 mg Rectal Suppositories (Solid Suspension, 100 x 1.3 mL Suppositories)

3. **Powder-liquid preparation:**
   A. Combine and triturate the following ingredients together to form a fine, homogeneous powder blend:
      - Diazepam
      - Silica Gel
   B. Levigate the fine, homogeneous powder blend (Step 3A) with the following ingredient:
      - Propylene Glycol

   End result: Homogeneous paste-like dispersion.

4. **Medium preparation:**
   A. Using the hot water bath, melt the following ingredient:
      - Polypeg (Suppository base) (amount determined from Appendix, Step 7B)

   Specifications: Maintain temperature between 60 and 65°C

   End result: Homogeneous liquid-like solution

   IMPORTANT: Do not allow the temperature to exceed 65°C.

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Suggested Formula: Diazepam 5 mg Rectal Suppositories (Solid Suspension, 100 x 1.3 mL Suppositories)

5. **Powder-liquid to medium integration:**
   - A. Using the hot water bath, incrementally add the homogeneous paste-like dispersion (Step 3B) to the following ingredient:
     - Homogeneous liquid-like solution (Step 4A).
   - **Specifications:** Continuously mix. Maintain temperature between 60 and 65°C.
   - **End result:** Homogeneous liquid-like dispersion.
   - **IMPORTANT:** Do not add the homogeneous paste-like dispersion (Step 3B) until the temperature of the Polypeg reaches 60 - 65°C. Do not allow the temperature to exceed 65°C.

6. **Mold filling:**
   - A. Remove the homogeneous liquid-like dispersion (Step 5A) from the hot water bath. With continuous stirring, allow to cool slightly, until the mixture is thicker (with a lotion-like consistency).
   - B. Fill each of 100 mold cavities with the mixture. If the mixture starts to solidify, reheat to 60 - 65°C, and repeat the filling procedure.
   - C. Once the cavities have been filled, allow the suppositories to cool to room temperature.
   - D. If necessary, trim the tops of the suppositories with a sharp blade or a hot spatula.

7. **Validation technique (average solid dose weight):**
   - A. Weigh 20 suppositories.
   - B. The final weight of each suppository (not including suppository mold) shall not be less than 90% and not more than 110% of the theoretically calculated weight for each unit (Appendix, Step 7A) in accordance to USP guidelines.

8. **Product transfer (solid-to-dispensing container filling):**
   - Transfer the final product into the specified dispensing container (see “Packaging Requirements”).
**SUGGESTED PRESENTATION**

<table>
<thead>
<tr>
<th>Estimated Beyond-Use Date</th>
<th>Packaging Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 days, refrigerated.</td>
<td>Individually wrapped in a tight, light-resistant foil and placed in a box or wide-mouth container.</td>
</tr>
</tbody>
</table>

**Auxiliary Labels**

1. Use as directed. Do not exceed prescribed dose.
2. Keep out of reach of children.
3. For rectal use only.
5. Do not take with alcohol, sleep aids, tranquilizers or other CNS depressants.
6. May impair mental and or physical ability. Use care when operating a car or machinery.
7. Protect from light.
8. Keep in a dry place.
9. Equilibrate to room temperature before use.
10. Controlled substance. Dangerous unless used as directed.
11. Consult your health care practitioner if any other prescription or over-the-counter medications are currently being used or are prescribed for future use.
12. 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.

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Suggested Formula

Diazepam 5 mg Rectal Suppositories (Solid Suspension, 100 x 1.3 mL Suppositories)

FIN F 001 603v2

REFERENCES


## Appendix

### Suppository mold calibration

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**SUGGESTED CALCULATION**

### Preparatory Instruction

1. **Preparatory step:**
   
   A. Prepare a hot water bath

   **Specifications:** Temperature: 60 to 65°C.

2. **Vehicle preparation:**

   Weigh and/or measure the following ingredients:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silica Gel</td>
<td>0.25 g</td>
</tr>
<tr>
<td>Propylene Glycol, USP</td>
<td>0.5 mL</td>
</tr>
<tr>
<td>Medisca Polypeg (Suppository Base)</td>
<td>14.32 g</td>
</tr>
</tbody>
</table>

3. **Powder-liquid preparation:**

   A. Triturate the following ingredient to form a fine, homogeneous powder:
   - Silica Gel

   B. Levigate the fine homogeneous powder (Step 3A) with following ingredient:
   - Propylene Glycol

   **End result:** Homogeneous paste-like dispersion.

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Appendix: Suppository mold calibration

7. **Ingredient calculation:**
   
   A. Calculate the average weight of a suppository (not including weight of the empty suppository mold):

   | Weight of the 5 suppositories: | ________ g |
   | DIVIDED BY                     | 5          |
   | Number of suppositories:       | ________  |
   | **Average (theoretical) weight of a suppository:** | ________ g |

   B. Calculate the quantity of Polypeg (Suppository Base) contained in a single suppository:

   | Average weight of a suppository (from Step 7A): | ________ g |
   | MINUS                                            |           |
   | Combined quantity of Diazepam, Silica Gel and    | 0.082 g   |
   | Propylene Glycol in each suppository:             | ________  |
   | **Quantity of Polypeg (Suppository Base) contained in a single suppository:** | ________ g |
   | MULTIPLIED BY                                    |           |
   | Number of suppositories in batch:                | 100       |
   | **Quantity of Polypeg (Suppository Base) required for 100 suppositories** | ________ g |
   | MULTIPLIED BY                                    |           |
   | Processing error adjustments (5 to 9%)           | 1.05 to 1.09 |
   | **Quantity of Polypeg (Suppository Base) required plus processing error** | ________ g |