**Table of Contents**

1. Objective 2

2. Scope 2

3. Quality Target Product Profile 2

4. Critical Quality Attributes Designation 3

5. Conclusion 6

6. References 7

**List of Tables**

[Table 1: Gelnique 10% Manufacturing Unit Operations 2](#_Toc470248495)

[Table 2: Quality Target Product Profile for Gelnique™ (Oxybutynin Chloride) Gel 10% 2](#_Toc470248496)

[Table 3: Critical and Non-Critical Quality Attributes of Gelnique™ (Oxybutynin Chloride) Gel 10% 4](#_Toc470248497)

# Objective

The objective of this document is to define QTPP (Quality Target Product Profile), and identify Critical Quality Attributes (CQAs) and non-critical attributes for Gelnique™ (Oxybutynin Chloride) Gel 10%.

# Scope

The scope of this section includes the single concentration of Gelnique 10% manufactured at Actavis, Inc. in Salt Lake City, Utah. The unit operations and item numbers associated with the manufacturing of Gelnqiue 10% are provided below.

| Table 1: Gelnique 10% Manufacturing Unit Operations | | |
| --- | --- | --- |
| **Product Strength**  **(w/w)** | **Operation and Item Number(s)** | |
| **Mixing** | **Packaging** |
| 100 mg / g | 175547 | 52544008430 (US only) |
| 74028708430 (Canada only) |

# Quality Target Product Profile

QTPP of a product is defined as prospective quality characteristics of a drug product that ideally will be achieved to ensure the desired quality, taking into account quality of the drug product. **Table 2** lists QTPP for Gelnique™ (Oxybutynin Chloride) Gel 10%.

| Table 2: Quality Target Product Profile for Gelnique™ (Oxybutynin Chloride) Gel 10% | | |
| --- | --- | --- |
| **Profile Component** | **Target** | **Justification** |
| Dosage Form | Gel | The product rationale for dosage form, route of administration and dosage strength is provide in Gelnique™ (Oxybutynin Chloride) Gel 10% FDA submission documents (NDA# 022204) . |
| Route of Administration | Topical |
| Dosage Strength | 10% ; 100 mg / g |
| Pharmacokinetics | Oxybutynin is transported across intact skin and into the systemic circulation by passive diffusion across the stratum corneum. Steady-state concentrations are achieved within 7 days of continuous dosing. Absorption of oxybutynin is similar when Gelnique 10% is applied to the abdomen, upper arm/shoulders or thighs | Topical administration significantly reduces the formation of the active metabolite, N-desethyl Oxybutynin, by avoiding the pre-systemic metabolism. Therefore topical administration potentially provides better pharmacokinetics than oral administration. |
| Stability | Expiration date is 24 months from the date of manufacture of gel mix.  Stability studies are conducted under Controlled Room Temperature (CRT) conditions. | The expiration time is based on 24 month stability conducted on the drug product during development of Gelnique 10%. 24 month Stability data is available in FDA submission document (NDA# 022204). |
| Drug Product Quality Attributes | **Physicochemical Attributes:**   * Appearance * Identity * Assay * Ethanol * Content Uniformity * Minimum Fill * Impurities and Degradation Products * Viscosity * pH * Drug Release * Weight Loss * Microbial Limits | Pharmaceutical requirement:  Meeting the same compendial or other applicable (quality) standards (i.e., identity, assay, purity, and quality) |
| Container Closure System | The finished drug product is packaged in a 1 g (1.14mL) Sachet with tear notches. 30 Sachet units are packaged in one carton. | Suitable container closure system to achieve the target shelf-life and ensure system integrity during shipping and handling. |
| Administration/  Concurrence to labeling | Gelnique 10% is a muscarinic antagonist indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency and frequency | Safety and efficacy requirements. |

# Critical Quality Attributes Designation

The drug product quality attributes are identified from the profile components listed in **Table 2**. The quality attributes are classified as critical or non-critical based on the following characteristics:

**Critical Quality Attribute Characteristics:**

* A physical, chemical, or microbiological characteristic of a product that should be within an appropriate limit, range or distribution to ensure the desired product quality
* CQAs should only include product attributes that have the potential to be altered by changes to process parameters or formulation variables
* Attribute is directly linked to quality of the product

| **Table 3: Critical and Non-Critical Quality Attributes of Gelnique™ (Oxybutynin Chloride) Gel 10%** | | | | |
| --- | --- | --- | --- | --- |
| **Quality Attributes of the Drug Product** | | **Target** | **Attribute Critical** | **Justification of Criticality** |
| Appearance | Transparent to translucent gel packaged in a heat seal sachet | | No | The appearance is established by combining all the raw materials; it does not directly impact quality of the drug product. It is a secondary outcome and it will be monitored at drug product release. |
| Identity | Matches retention times of reference standard | | Yes\* | Identity is critical for the quality of the drug product.  \*Formulation and process variables will not impact this CQA. Therefore, the CQA will not be investigated and discussed in detail in subsequent risk assessments. However, the CQA remains a target element of the QTPP and is ensured through the product and process design and the control strategy. |
| Assay | 90.0 – 110.0% LC (avg.) | | Yes | Variability in assay can affect the efficacy of the drug product.  This attributes could potentially be influenced by the formulation and process variables. |
| Content Uniformity | Confirms to USP <905> | | No | This is a transparent hydro-alocholic gel formulation where the drug substance is freely soluble in ethanol. Content uniformity is not directly related to drug product quality, therefore it is not considered critical. |
| Minimum Fill | Conforms to USP <755> | | Yes | Minimum fill is required to meet the label claim and has impact on the efficacy of the drug product. |
| Impurities and Degradation products | PCGE: NMT 0.2% (weight)  PCGA: NMT 2.0% (weight)  Total PCGE and PCGA: NMT 2.2% (weight)  Any Other Individuals: NMT 0.2% (area)  Total Unknowns: NMT 1.0% (area) | | Yes | The limits on degradation product are critical for safety and must be controlled based on compendial/ICH requirements. The limit for individual unknowns and known degradants complies with ICH Q3B. |
| Ethanol | 614 – 750 mg/g (Avg.) | | Yes | Variability in ethanol content can affect the quality of the drug product.  This attributes could potentially be influenced by the formulation and process variables. |
| Viscosity | 15,000 – 45,000 cP | | No | The finished drug product is topically applied. Therefore, variability in viscosity will not affect the efficacy of the drug product. |
| pH | 5.0 – 7.0 | | No | The pH is established by combining all the raw materials; it does not directly impact quality of the drug product. It is a secondary outcome and it will be monitored at drug product release. |
| Drug Release | **Level 1 (n = 6 sachets)**  1 hour 18 – 54% LC (Individual)  2 hours 42 – 82% LC (Individual)  12 hours NLT 80% LC (Individual)  OR  **Level 2 (n = 12 sachets)**  1 hour 18 – 54% LC (Avg.)  14 – 58% LC (Individual)  2 hours 42 – 82% LC (Avg.)  36 – 88% LC (Individual)  12 hours NLT 80% LC (Avg.)  NLT 71% LC (Individual)  OR  **Level 3 (n = 24 sachets)**  1 hour 18 – 54% LC (Avg.)  14 – 58% LC (NLT 22 Units)  11 – 61% LC (Individual)  2 hours 42 – 82% LC (Avg.)  36 – 88% LC (NLT 22 Units)  30 – 94% LC (Individual)  12 hours NLT 80% LC (Avg.)  NLT 71% LC (NLT 22 Units)  NLT 62% LC (Individual) | | Yes | The *in vitro* dissolution profile is an important tool for quality control to ensure appropriate dosage is administered consistently and to monitor batch to batch variability. Variability in drug release can affect quality of the final product.  This attribute has a potential to be influenced by the formulation variables. |
| Weight Loss | Batch Release: Report weight. (Three sample sets are required for each stability condition under which systems will be staged.)  Stability: NMT 6.2% weight loss from Batch Release weight. | | Yes\* | Weight loss is indicative of issues with Package Integrity.  \*Process parameters or formulation variables do not have a direct effect on weight loss. Therefore, the CQA will not be investigated and discussed in detail in subsequent risk assessments. Please see stage II process validation protocol titled “Performance Qualification of the Gelnqiue 10% (8709) Form/Fill/Seal Manufacturing Process using Alternate Sachet Material Item 208371” (Protocol # **M-1229**) |
| Microbial Limits | Total Aerobic Microbial Count: NMT 200 cfu/g  Total Combined Yeasts/Molds Count: NMT 200 cfu/g  *Staphylococcus aureus*: Absent  *Pseudomonas aeruginosa*: Absent | | No | The microbial limits in an important attribute that will impact drug product quality and patient safety. However, Gelnique 10% is hydro-alcoholic formulation and ethanol in the drug product functions as an anti-microbial agent. In addition, drug product will be tested for micro at batch release. |

# Conclusion

The following critical quality attributes were identified in **Table 2** and **Table 3** for the Gelnique 10%.

* + 1. Assay
    2. Minimum Fill
    3. Impurities and degradation product
    4. Ethanol
    5. Drug Release

# References

| **Document Type** | **Document Name** | **Document Number** |
| --- | --- | --- |
| Test Method | Testing of Oxybutynin Chloride Gel, 100 mg/g Mix | TM414 |
| Testing of 10% Oxybutynin Chloride Gel and Oxybutynin Chloride Placebo Gel | TM923 |
| Material Specification | Oxybutynin Chloride Gel, 100 mg/g | 175547 |
| Gelnique Oxybutynin Chloride Gel, 10% , Ctn x 30 (US) | 52544008430 |
| Gelnique Oxybutynin Chloride Gel, 10% , Ctn x 30 (Canada) | 74028708430 |