



Regulatory Frameworks, Licensing Requirements, and Drug Accessibility: Challenges in Puerto Rico Related to Innovative Treatments for Chronic Depression

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Abstract

This study examined how licensing requirements, certifications, and regulatory frameworks influence drug pricing and access to innovative treatments in Puerto Rico, using TRANQUI-Spray (a fictitious name used for confidentiality purposes), a Risk Evaluation and Mitigation Strategy (REMS)-mandated, controlled- substance nasal spray for treatment-resistant depression as the central case study. The research analyzed how intellectual-property protections and complex approval pathways shape market dynamics, limit competition, and contribute to high medication costs. It also evaluated how FDA and DEA regulations, REMS infrastructure, and clinical certification requirements restrict the availability of novel therapies for chronic diseases. Through a qualitative approach, the study identified structural barriers to equitable access and highlighted opportunities for regulatory simplification, expanded REMS-certified capacity, and improved policy alignment. Findings underscore the need for streamlined processes that reduce administrative burden, support generic entry, and enhance affordability, ultimately promoting better health outcomes and strengthening Puerto Rico's healthcare system.

Introduction

Healthcare in Puerto Rico faces significant challenges that limit access to affordable, innovative treatments for chronic conditions. This research aims to investigate how regulatory requirements, licensing processes, patents and market access conditions influence the accessibility of innovative treatments and the affordability of drugs in Puerto Rico. The innovative TRANQUI-Spray product was used as the reference case study for this design project. TRANQUI-Spray represents a C-mine nasal spray prescribed for severe depression in adults who have not responded to conventional treatments. It is a derivative of CALMmine and is administered under medical supervision in a certified healthcare center. TRANQUI-Spray is approved for use in adults with specific conditions: Treatment-resistant depression (TRD); For patients who have not responded adequately to at least two other antidepressant medications. It is often prescribed in conjunction with an oral antidepressant. Major depressive disorder (MDD) with acute suicidal ideation or behavior: For this use, it is combined with an oral antidepressant [1].

Background- Research Description

This research examined how regulatory requirements, licensing process, patents laws and market accessibility of innovative treatments for chronic diseases in Puerto Rico. Using TRANQUI-Spray as the primary case study, the investigation explored how FDA and DEA regulatory frameworks, REMS requirements, certification processes, and market dynamics may affect treatment accessibility, pricing and patient access for treatment accessibility, pricing, and patient access for treatment-resistant depression. The study also considered the roles of regulatory and commercialization requirements, in shaping the commercialization and distribution of novel pharmaceutical therapies. Through this analysis, the relationships, among healthcare regulations, market accessibility, and the public health challenges associated with innovative treatments in Puerto Rico.

Problem

The high cost of medications is a pressing issue for patients in Puerto Rico, where many struggle to access essential treatments due to financial constraints. One key factor affecting drug prices is the presence of many regulations, patent laws, licenses, and certifications that protect pharmaceutical companies' intellectual property. While these regulated documents stimulate innovation by enabling companies to recoup their investments, they often lead to higher drug prices, limit market competition, and make healthcare unaffordable for many individuals on the island. Furthermore, the regulatory framework surrounding the development and approval of novel treatments can significantly impact patient access to essential medications. This research will specifically evaluate how regulatory processes (specifically, the documentation management process) influence the availability of innovative therapies for chronic diseases, focusing on TRANQUI-Spray, a novel treatment for resistant depression. Understanding these critical issues is essential to balancing innovation with equitable access to healthcare for Puerto Rico's population.

Methodology

This section describes the seven steps applied in the methodology.

Research Design

Qualitative approach supported by regulatory, market, and documentary analysis, combined with expert interviews and secondary data to understand factors affecting pricing and access in Puerto Rico.

Literature Review

Reviewed academic sources, legal databases, government publications, and case studies on patent impacts, regulatory effects on pricing, innovative treatments, and healthcare access.

Data Collection

Collected quantitative data on patents, licensing, certifications, and pricing; qualitative data gathered through interviews with healthcare providers, policy experts, legal professionals, and regulatory specialists.

Data Analysis

Used comparative and descriptive analysis to identify patterns in regulatory barriers, pricing structures, and treatment accessibility.

Comparative Framework

Compared Puerto Rico with mainland U.S. to evaluate how differences in patent laws, licensing, and regulatory processes affect pricing and availability.

Policy Recommendations

Developed recommendations to improve access to TRANQUI-Spray and essential medications, to be shared through executive summaries, presentations, and reports.

Ethical Considerations and Recommendations

Ensured informed consent, confidentiality, and voluntary participation; obtained IRB approval; acknowledged limitations such as data availability and interview bias.



Results and Discussion – Market and Regulatory Analysis

Provides an overview of TRANQUI-Spray's market conditions and regulatory environment, integrating expert interviews with FDA/DEA requirements that shape approval, distribution, and patient access.

Qualitative Data: Expert Interviews

Summarizes insights from three industry experts on product classification, regulatory requirements, pricing differences, and access barriers for TRANQUI-Spray in the U.S. and Puerto Rico.

Regulatory Framework for TRANQUI-Spray

Explains how TRANQUI-Spray is regulated as both a combination and parenteral product, outlining the interaction between FDA and DEA rules that govern approval, safety, and controlled-substance handling.

FDA Regulations for Combination and Parenteral Products

Describes the FDA's regulatory pathway, including classification, pre-market submissions (NDA, ANDA, PMA, 510(k)), GMP requirements, clinical data expectations, and Puerto Rico's alignment with federal standards.

Guidance Documents for Parenteral Products

Outlines the required eCTD submission structure (Modules 1–5), emphasizing sterility, aseptic processing, manufacturing controls, clinical data, and additional FDA expectations such as PAI readiness and data integrity.

Interaction Between FDA and DEA Regulatory Requirements

Highlights how FDA rules for combination products and DEA rules for controlled substances apply simultaneously, covering scheduling, registration, security, recordkeeping, labeling, and disposal requirements.

Patents Laws, Licenses, and other Regulations

Explains how multiple patents and regulatory exclusivities keep TRANQUI-Spray costly and limit competition, while REMS requirements and limited certified centers further restrict patient access.

Contraindications That Affect Public Access to TRANQUI-Spray

Identifies medical conditions and safety risks that prevent or limit treatment eligibility, along with practical barriers such as monitoring requirements, psychiatric considerations, and age restrictions.

Permits, Licenses & Certifications Required to Administer TRANQUI-Spray

Lists the mandatory certifications for clinics, including REMS enrollment, DEA registration, secure storage, pharmacy/distributor certification, and state-level facility licensing.

What the Certification Process Looks Like

Summarizes the six-step process for clinic approval, from readiness and DEA registration to REMS certification, drug supply authorization, patient enrollment, and audit-ready documentation.

Why is Access Limited?

Explains how strict medical criteria, REMS controls, DEA regulations, state licensing, and high treatment costs create significant barriers to accessing TRANQUI-Spray.

TRANQUI-Spray Pricing in U.S. vs Puerto Rico (2025–2026)

Notes that although Puerto Rico follows the same FDA/REMS rules, access is more limited due to fewer certified centers, insurance differences, and additional logistical challenges.

Why are exact numbers unavailable?

Clarifies that REMS data is not public, Puerto Rico does not track usage separately, and major insurance databases rarely include Puerto Rico, making precise access statistics unavailable.

Conclusions

The research also identified opportunities to improve access by strengthening coordination between federal and local agencies, streamlining documentation, expanding certified treatment infrastructure, and modernizing regulatory systems. Although limited by scarce Puerto Rico-specific data and few certified centers, the study suggests that targeted policy and regulatory reforms could reduce barriers, enhance healthcare accessibility, and support a more equitable pharmaceutical landscape on the island.

The study showed that regulatory requirements, licensing, certifications, and market-access conditions significantly shape the availability and affordability of TRANQUI-Spray in Puerto Rico. Complex REMS, FDA, and DEA processes combined with limited certified centers create major barriers to patient access and increase operational burdens for clinics. Expert insights highlighted how patents and intellectual-property protections support innovation but also restrict competition and keep prices high, especially in Puerto Rico where insurance coverage is more limited.

Future Work

Future work should focus on collecting Puerto Rico-specific utilization data and evaluating how REMS, DEA, and local licensing processes can be streamlined to reduce administrative barriers. Additional analysis of clinic infrastructure needs and economic modeling could help identify strategies to expand certified centers and lower treatment costs. These steps will support evidence-based policy recommendations aimed at improving access to innovative therapies like TRANQUI-Spray.

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