RETATRUTIDE: REGULATORY CHALLENGES, PATIENT SAFETY, AND THE IMPACT OF THE ILLICIT SALE OF AN INVESTIGATIONAL DRUG FOR THE TREATMENT OF OBESITY

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Abstract

Obesity is one of today's foremost public health challenges, driving the development of new pharmacological therapies for body weight management. This study is a narrative literature review that aimed to analyze the regulatory challenges, patient safety considerations, and impacts arising from the illicit sale of retatrutide, a drug that remains under investigation for the treatment of obesity. The research involved an analysis of scientific articles, documents issued by national and international regulatory agencies, and technical publications addressing the clinical development of retatrutide, its mechanisms of action, preliminary efficacy, safety profile, and the risks associated with its use outside research protocols. The findings showed that, although the drug has yielded promising results in reducing body weight and improving metabolic parameters, obtaining and using it through illicit channels exposes individuals to

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significant risks, including adverse events that are not yet fully understood, counterfeit products, a lack of quality control, and the absence of professional supervision. In addition, illegal sales hinder the work of regulatory authorities, foster misinformation, and increase the risks associated with self-medication. The study concludes that strengthening health surveillance, health education, and regulatory measures is essential to protect the population until the efficacy and safety of retatrutide have been fully established through scientific evidence.

Keywords: Health surveillance, Illicit sale, Obesity, Patient safety, Retatrutide.

INTRODUCTION

Obesity is a chronic, multifactorial, and highly complex disease associated with increased morbidity and mortality and the development of several chronic noncommunicable diseases, including type 2 diabetes mellitus, systemic arterial hypertension, cardiovascular diseases, and certain types of cancer. Its prevalence has risen markedly across various countries in recent decades, making it a major challenge for healthcare systems and for the development of public policies aimed at preventing and treating this condition (World Health Organization, 2024).

In this context, the development of new pharmacological therapies has attracted growing interest from the scientific community, particularly incretin-based drugs. Among these, retatrutide stands out as an investigational molecule that acts as a triple agonist of the glucagon-like peptide-1 (GLP-1), glucose-dependent insulinotropic polypeptide (GIP), and glucagon receptors. Preliminary clinical trial results indicate significant reductions in body weight and improvements in metabolic parameters, reinforcing its therapeutic potential for the treatment of obesity (Jastreboff et al., 2023). However, the drug remains under clinical investigation and has not yet been approved for sale by the leading regulatory agencies.

Despite its investigational status, retatrutide is increasingly being promoted and sold illicitly through digital platforms and informal markets, often accompanied by information that lacks scientific support. This situation encourages the indiscriminate use of a product whose long-term safety,

manufacturing quality, and definitive efficacy remain dependent on the completion of clinical studies and assessment by the competent regulatory authorities. In addition to the risks inherent in using unauthorized drugs, the circulation of products of unknown origin increases the likelihood of counterfeiting, contamination, incorrect dosages, and potentially serious adverse events (Brazilian Health Regulatory Agency - *Agência Nacional de Vigilância Sanitária* 2024).

Against this background, the following research question arises: What are the main regulatory challenges associated with retatrutide, and what impact might the illicit sale of this investigational drug have on patient safety and public health?

The overall objective of this chapter is to analyze the regulatory challenges, patient safety considerations, and impacts arising from the illicit sale of retatrutide as an investigational drug for the treatment of obesity. Its specific objectives are to describe the molecule's mechanism of action and current stage of clinical development; discuss the risks associated with its use outside research protocols; examine the role of regulatory agencies in controlling the circulation of investigational drugs; and consider strategies capable of mitigating the harm caused by self-medication and illegal trade.

The relevance of this study lies in the growing demand for innovative obesity-management therapies and the expanding unauthorized supply of investigational drugs in digital environments, a situation that poses a major challenge to health surveillance authorities, healthcare professionals, and efforts to protect the public. The discussion contributes to a broader understanding of the risks involved in the premature use of therapies that have not yet been approved and reinforces the importance of compliance with regulatory standards as a means of promoting patient safety.

From a theoretical perspective, this chapter draws on recent scientific publications addressing obesity, incretin-based pharmacotherapy, the clinical development of retatrutide, medication safety, and health regulation. Its sources include clinical studies, technical documents issued by regulatory authorities, and specialized literature discussing the ethical and public health challenges associated with the improper availability of investigational drugs.

METHODOLOGY

RESEARCH DESIGN AND APPROACH

The study was conducted as a descriptive narrative literature review using a qualitative approach. This type of research makes it possible to gather, interpret, and discuss scientific publications and institutional documents relating to a particular topic, thereby enabling a contextualized analysis of issues that are still evolving within the scientific field. A narrative review is appropriate when the objective is to examine different theoretical, regulatory, and public health perspectives without being required to follow every stage of a systematic review (Rother, 2007).

This approach was selected because of the subject's current relevance and complexity, which encompasses pharmacological, regulatory, ethical, and patient safety considerations relating to retatrutide. Because it is an investigational drug that remains under clinical evaluation, it was necessary to consider not only the available scientific findings but also health alerts, regulatory information, and technical documents produced by official institutions.

RESEARCH QUESTION

The study was guided by the following question: What are the main regulatory challenges, patient safety risks, and public health impacts associated with the illicit sale of retatrutide as an investigational drug intended for the treatment of obesity?

Defining the research question helped define the scope of the search and organize the discussion around three main themes: the clinical development and mechanism of action of retatrutide; the risks arising from its use without regulatory approval; and the consequences of its illicit sale for health surveillance and public health.

INFORMATION SOURCES AND SEARCH STRATEGY

The literature search was conducted using recognized databases and institutional sources, including PubMed, SciELO, the Virtual Health Library (Biblioteca Virtual em Saúde), and Google Scholar. Technical documents, notices, and information made available by regulatory agencies and health organizations were also consulted, including the Brazilian Health Regulatory Agency (Agência Nacional de Vigilância Sanitária—Anvisa), the Food and Drug Administration (FDA), the European Medicines Agency (EMA), and the World Health Organization (WHO).

The following Portuguese- and English-language descriptors and keywords were used individually and in combination: “retatrutida,” “retatrutide,” “obesidade,” “obesity,” “medicamento experimental,” “investigational drug,” “segurança do paciente,” “patient safety,” “comercialização clandestina,” “illegal drug sale,” “medicamentos falsificados,” and “counterfeit medicines.” The terms were combined using the Boolean operators AND and OR to broaden or narrow the results according to their thematic relevance.

INCLUSION AND EXCLUSION CRITERIA

The review included scientific articles, clinical trials, literature reviews, regulatory documents, health alerts, and technical publications that directly addressed retatrutide, incretin receptor agonists, the pharmacological treatment of obesity, the safety of investigational drugs, or the illegal circulation of products intended for weight loss.

Priority was given to publications in Portuguese and English that were available in full text and addressed the most recent stages of retatrutide’s clinical development. Earlier studies relevant to understanding obesity, pharmacovigilance, drug counterfeiting, and health regulation were also considered.

Duplicate materials, texts without identified authorship, exclusively promotional publications, social media content lacking scientific support, and documents unrelated to the subject of the study were

excluded. Commercial information from unauthorized suppliers was considered solely as part of the contextualization of the problem and was not used as scientific evidence.

SELECTION AND ORGANIZATION OF THE MATERIAL

The titles and abstracts of the identified materials were initially reviewed. Documents considered relevant were then read in full. Selection was based on the relationship between the content identified and the objectives of the study.

Following this review, the information was organized using an instrument developed by the authors that included the following elements: authorship, year of publication, document type, objective, main findings, safety information, regulatory considerations, and contributions to the discussion of the illicit sale of retatrutide.

The sample consisted of publications and documents that met the inclusion criteria and provided sufficient content for analysis. Because this was a narrative review, no fixed number of studies was established in advance. Instead, priority was given to the relevance, currency, and consistency of the selected information.

DATA ANALYSIS

The material was analyzed through critical reading, interpretation, and thematic synthesis. The findings were grouped into categories defined according to the objectives of the study: the pharmacological characteristics and clinical development of retatrutide; efficacy and adverse events identified in clinical trials; challenges relating to approval and regulatory enforcement; risks arising from the acquisition of illicit products; and measures to protect patient safety.

The narrative synthesis made it possible to compare the findings of clinical studies with regulatory requirements and the public health risks associated with the circulation of drugs of unknown origin. According to Snyder (2019), a literature review should go beyond merely describing its sources and

should offer an interpretation capable of identifying areas of convergence, gaps, and practical implications within the field under investigation.

ETHICAL CONSIDERATIONS

Because the study used only data from scientific publications and documents available from public sources, without the direct participation of human subjects or access to personal information, submission to a Research Ethics Committee was not required. Throughout all stages, the principles of academic integrity, fidelity to the information consulted, and proper identification of the sources used were observed.

The discussion was grounded in scientific evidence and institutional documents and avoided making recommendations regarding the use, prescription, or acquisition of retatrutide. Particular consideration was given to its status as an investigational drug, emphasizing that preliminary clinical findings neither constitute regulatory approval nor guarantee safety when the drug is used outside duly authorized studies.

RESULTS AND DISCUSSION

The development of retatrutide represents one of the most recent advances in the pharmacological treatment of obesity. Unlike agonists that act solely on the GLP-1 receptor, the molecule acts simultaneously on the GLP-1, GIP, and glucagon receptors, reducing food intake, increasing energy expenditure, and improving glucose and lipid metabolism. Phase II clinical trial results demonstrated substantial reductions in body weight among individuals with obesity, with some participants losing more than 20% of their body weight after 48 weeks of treatment (Jastreboff et al., 2023). These findings position retatrutide as one of the most promising investigational drugs for obesity management.

Table 1

Main Characteristics of Retatrutide

Characteristic	Description
Pharmacological class	Triple agonist of the GLP-1, GIP, and glucagon receptors
Indications under investigation	Treatment of obesity and metabolic diseases
Regulatory status	Investigational drug under clinical development
Main observed effects	Significant reduction in body weight and improvements in glycemic control and metabolic parameters
Main risks	Gastrointestinal adverse events, long-term safety still under investigation, and illicit use

Source: Adapted from Jastreboff et al. (2023) and Lilly (2025).

Although the clinical findings are considered highly promising, the use of retatrutide remains restricted to authorized clinical research protocols. To date, the leading regulatory agencies have not granted final approval for its sale as a drug intended for the treatment of obesity. According to the Food and Drug Administration (2025), investigational drugs may be made available only after efficacy, safety, and quality have been consistently demonstrated throughout all phases of clinical development. In Brazil, the Brazilian Health Regulatory Agency (Agência Nacional de Vigilância Sanitária—Anvisa, 2024) emphasizes that drugs without marketing authorization must not be sold or used outside the circumstances provided for by law.

Despite these restrictions, the illicit sale of retatrutide through digital platforms, social media, and parallel markets is increasing. This practice constitutes a major public health problem because it facilitates the circulation of products whose origin, storage conditions, composition, and active ingredient concentrations cannot be verified. As emphasized by the World Health Organization (2017), falsified or substandard medical products are a major cause of adverse events, therapeutic failure, and increased morbidity and mortality, particularly when sold without any health oversight.

In addition to the possibility of counterfeiting, another cause for concern is the self-medication encouraged by the dissemination of preliminary clinical study findings. The widespread attention given to the weight loss observed in scientific studies has fostered the mistaken belief that retatrutide is safe and available for routine clinical use. However, several adverse events remain under investigation, including gastrointestinal symptoms, metabolic changes, and potential effects arising from prolonged use

(Jastreboff et al., 2023). The indiscriminate use of the drug before these studies have been completed therefore undermines the principles of patient safety and evidence-based medicine.

From a regulatory perspective, illegal sales directly undermine pharmacovigilance activities. When investigational drugs circulate outside clinical studies, it becomes impossible to monitor adverse events adequately, trace product batches, or ensure minimum quality standards. According to Edwards and Aronson (2000), the continuous monitoring of medication-related risks is an essential component of pharmacovigilance and depends on traceability and the systematic reporting of adverse events.

Another issue identified concerns the role of digital media in increasing demand for weight-loss drugs. The dissemination of content lacking scientific support, combined with easy access to illicit sales platforms, contributes to the spread of false information and the downplaying of the risks associated with the use of investigational drugs. In this context, it is essential to strengthen health education strategies, improve public scientific literacy, and enhance the oversight of online drug sales.

Table 2

Main Impacts of the Illicit Sale of Retatrutide

Area	Observed Impacts
Patient safety	Exposure to products lacking quality control and an increased risk of adverse events
Health surveillance	Difficulties in inspecting and tracing products
Public health	Increased self-medication and circulation of counterfeit drugs
Regulatory compliance	Violations of health regulations and the sale of unregistered products
Scientific research	Impaired interpretation of safety data when the drug is used outside clinical trials

Source: Prepared by the authors based on Anvisa (2024), World Health Organization (2017), Food and Drug Administration (2025), and Jastreboff et al. (2023).

The findings demonstrate that the therapeutic potential of retatrutide must be interpreted with caution, given that its incorporation into clinical practice depends on the completion of phase III studies, rigorous assessment by regulatory authorities, and conclusive evidence establishing its benefit-risk profile. Until these stages have been completed, combating illicit sales and strengthening health

surveillance measures remain essential to protect the population and preserve the credibility of scientific efforts to develop new obesity therapies.

CONCLUSION

This study aimed to analyze the regulatory challenges, patient safety considerations, and impacts of the illicit sale of retatrutide, an investigational drug under development for the treatment of obesity. The review of scientific literature and technical documents issued by regulatory authorities showed that, although clinical trial results indicate substantial therapeutic potential for reducing body weight and improving metabolic parameters, its use remains restricted to research settings and is not recommended outside authorized clinical protocols.

The main findings showed that the illicit sale of retatrutide constitutes a major public health problem because it facilitates access to products whose origin, quality, efficacy, and safety cannot be guaranteed. In addition, the indiscriminate use of this investigational drug may increase the risk of adverse events, hinder pharmacovigilance activities, encourage self-medication, and compromise the work of the regulatory agencies responsible for overseeing the safety of medicines.

This research contributes to the broader discussion of the need to strengthen health surveillance policies, oversight of online drug sales, and health education strategies aimed at promoting the rational use of medicines. It also reinforces the importance of disseminating information grounded in scientific evidence, particularly given the widespread circulation of digital media content concerning new pharmacological therapies for obesity.

Future research should monitor the results of phase III clinical studies of retatrutide and investigate the impact of health misinformation, illegal drug sales, and the influence of social media on the behavior of individuals seeking obesity treatment. Studies evaluating regulatory enforcement strategies and educational initiatives developed by regulatory authorities may also contribute to improving public policies designed to protect population health.

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