TIRZEPATIDE AND THE RISKS OF USE WITHOUT MEDICAL PRESCRIPTION

TIRZEPATIDA E OS RISCOS DO USO SEM PRESCRIÇÃO MÉDICA

TIRZEPATIDA Y LOS RIESGOS DEL USO SIN PRESCRIPCIÓN MÉDICA

https://doi.org/10.56238/sevened2026.020-055

Bruna Eduarda da Silva[1], Natalia Dame Alves[2], Jéssica da Silva Francelino[3], Amanda Oliva Spaziani[4], Bruna Marçal Guidoti Eleutério[5], Fabricio Sidnei da Silva[6], Dirce Maria Ignácio dos Santos Gonzaga[7], Rauer Ferreira Franco[8]

ABSTRACT

Tirzepatide represents a milestone in metabolic pharmacotherapy as the first dual agonist of glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptors. Although it has demonstrated unprecedented efficacy in reducing glycated hemoglobin (HbA1c) and body weight in the treatment of type 2 diabetes and obesity, its growing popularity has generated a concerning phenomenon of non-prescribed use without medical supervision. The objective of this study is to conduct a literature review on tirzepatide, emphasizing the risks associated with its use without prescription. The analysis of the safety profile indicates that the most frequent adverse events are gastrointestinal (nausea, diarrhea, and vomiting), in addition to serious and rare risks such as acute pancreatitis, gallbladder disease, acute kidney injury, and warnings regarding suicidal ideation and thyroid C-cell tumors. It is concluded that use without supervision eliminates the screening of absolute contraindications, predisposes individuals to inappropriate dose titration, nullifies the monitoring of serious drug interactions, and exposes users to the dangers of the unregulated market, including counterfeit products and improper storage.

Keywords: Tirzepatide. Dual GIP/GLP-1 Agonist. Self-Medication. Adverse Effects. Patient Safety.

RESUMO

A tirzepatida representa um marco na farmacoterapia metabólica como o primeiro agonista duplo dos receptores do polipeptídeo insulinotrópico dependente de glicose (GIP) e do peptídeo semelhante ao glucagon-1 (GLP-1). Embora tenha demonstrado uma eficácia sem precedentes na redução da hemoglobina glicada (HbA1c) e na perda de peso corporal no tratamento do diabetes tipo 2 e da obesidade , sua crescente popularização gerou um fenômeno preocupante de uso não prescrito e sem supervisão médica. O objetivo deste trabalho é realizar uma revisão bibliográfica sobre a tirzepatida, enfatizando os riscos de

[1] Undergraduate student. Universidade Brasil. E-mail: brunaaeduardasilvaa@gmail.com
[2] Undergraduate student. Universidade Brasil. E-mail: damenatalia61@gmail.com
[3] Postgraduate degree in Nursing Education. CEDES – FAMERP. E-mail: jessicafrancelino98@gmail.com
[4] Master's degree in Health Sciences. Universidade Brasil. E-mail: spazianimedicina@gmail.com
[5] Doctoral student in Biomedical Engineering. Universidade Brasil. E-mail: Bruna.eleuterio@ub.edu.br
[6] Dr. in Biomedical Engineering. Universidade Brasil. E-mail: Prof.fabricio@ymail.com
[7] Master's degree in Environmental Sciences. Universidade Brasil. E-mail: dirce.gonzaga@ub.edu.br
[8] Doctoral student in Health Sciences/FAMERP. Universidade Brasil. E-mail: rauer.franco@ub.edu.br

seu uso sem prescrição. A análise do perfil de segurança aponta que os eventos adversos mais frequentes são gastrointestinais (náuseas, diarreia e vômitos) , além de riscos graves e raros, como pancreatite aguda, doença biliar, lesão renal aguda e advertências sobre ideação suicida e tumores de células C da tireoide. Conclui-se que o uso sem supervisão elimina a triagem de contraindicações absolutas , predispõe a uma titulação inadequada de doses , anula o monitoramento de interações medicamentosas graves e expõe o usuário aos perigos do mercado não regulamentado, incluindo produtos falsificados e armazenamento inadequado.

Palavras-chave: Tirzepatida. Agonista Dual GIP/GLP-1. Automedicação. Efeitos Adversos. Segurança do Paciente.

RESUMEN

La tirzepatida representa un hito en la farmacoterapia metabólica como el primer agonista dual de los receptores del polipéptido insulinotrópico dependiente de glucosa (GIP) y del péptido similar al glucagón tipo 1 (GLP-1). Aunque ha demostrado una eficacia sin precedentes en la reducción de la hemoglobina glucosilada (HbA1c) y en la pérdida de peso corporal en el tratamiento de la diabetes tipo 2 y la obesidad, su creciente popularización ha generado un fenómeno preocupante de uso sin prescripción y sin supervisión médica. El objetivo de este trabajo es realizar una revisión bibliográfica sobre la tirzepatida, enfatizando los riesgos de su uso sin prescripción médica. El análisis del perfil de seguridad indica que los eventos adversos más frecuentes son gastrointestinales (náuseas, diarrea y vómitos), además de riesgos graves y raros como pancreatitis aguda, enfermedad biliar, lesión renal aguda y advertencias sobre ideación suicida y tumores de células C de la tiroides. Se concluye que el uso sin supervisión elimina el cribado de contraindicaciones absolutas, predispone a una titulación inadecuada de las dosis, anula el monitoreo de interacciones medicamentosas graves y expone al usuario a los peligros del mercado no regulado, incluidos productos falsificados y almacenamiento inadecuado.

Palabras clave: Tirzepatida. Agonista Dual GIP/GLP-1. Automedicación. Efectos Adversos. Seguridad del Paciente.

1 INTRODUCTION

Tirzepatide represents a milestone in metabolic pharmacotherapy as the first dual agonist of GIP (glucose-dependent insulinotropic polypeptide) and GLP-1 (glucagon-like peptide-1) receptors approved for clinical use.[1][2] Approved by the FDA in May 2022 for the treatment of type 2 diabetes and later in 2023 for obesity, tirzepatide has demonstrated unprecedented efficacy in reducing glycated hemoglobin (HbA1c) and losing body weight.[3][4]

However, the growing popularization of this drug has been accompanied by a worrying phenomenon: its use without prescription and without adequate medical supervision. This course completion work aims to carry out a comprehensive literature review on tirzepatide, with special emphasis on the risks associated with its use without a medical prescription, providing scientific support for the understanding of the dangers of this practice.

The relevance of this topic for biomedicine lies in the need to understand not only the pharmacological mechanisms and clinical efficacy of tirzepatide, but also the risks inherent to its inappropriate use, contributing to health education and the prevention of avoidable adverse events.

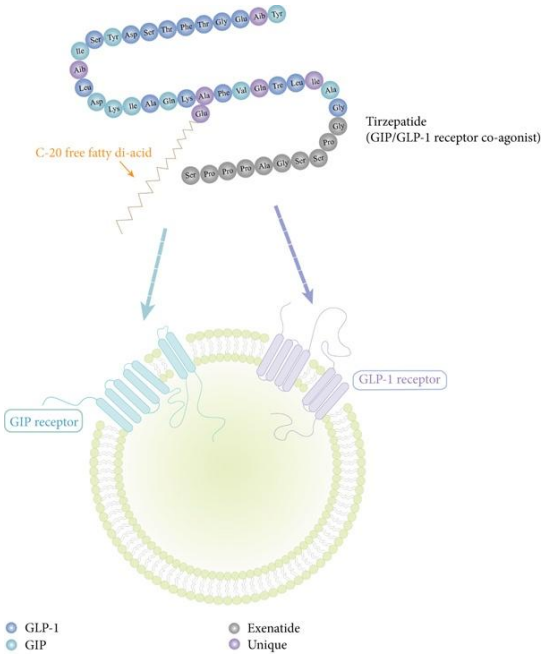
2 MOLECULAR STRUCTURE AND MECHANISM OF ACTION

2.1 CHEMICAL STRUCTURE

Tirzepatide is a synthetic acylated peptide composed of 39 amino acids, whose structure is based primarily on the sequence of the native GIP.[1][4] A distinctive feature of its structure is the presence of a C20 di-acid fatty acid chain attached to a lysine residue, a modification that facilitates binding to albumin and significantly prolongs the half-life of the molecule.[2][5]

Figure 1

The structure of tirzepatide. undefined



This structural modification allows a half-life of approximately 116.7 hours (about 5 days), making it possible to administer subcutaneously weekly.[1][2] The molecular structure has been engineered to activate both GIP receptors and GLP-1 receptors, albeit with different affinities—it has comparable affinity to GIP receptors, but weaker binding to GLP-1 receptors compared to native GLP-1.[5]

2.2 DUAL MECHANISM OF ACTION

The mechanism of action of tirzepatide involves the simultaneous activation of two complementary incretin systems:[1][6]

GLP-1 Receptor Activation: GLP-1 is an incretin hormone that stimulates insulin secretion in hyperglycemic states, suppresses glucagon secretion in hyperglycemic or euglycemic conditions, slows gastric emptying, decreases appetite, and reduces body weight.[1] GLP-1 receptors are expressed in pancreatic beta cells and in brain regions that regulate dietary intake.[1][2]

GIP Receptor Activation: GIP is the main incretin hormone in healthy individuals and has insulinotropic properties. Unlike GLP-1, GIP is glucagonotropic in a glucose-dependent manner - in hyperglycemic conditions, it stimulates insulin release and reduces glucagon levels; In euglycemic or hypoglycemic conditions, glucagon levels are increased.[1] GIP receptors are abundant in adipose tissue, where GIP enhances the postprandial lipid

buffering capacity of white adipose tissue and insulin sensitivity, potentially preventing ectopic fat deposition.[1]

Synergy of Mechanisms: Preclinical studies have shown that the combined agonism of GIP and GLP-1 produces robust weight loss effects independent of insulin sensitivity and lipid metabolism.[4] In diet-induced obese mice, combined agonism showed greater anorexic action compared to semaglutide, increasing satiety and satiety, reducing preference for high-fat diets, and decreasing preference for sweet taste.[4]

The hypothesis is that the GIP component of dual agonism acts centrally to potentiate the GLP-1-induced reduction in food intake.[1] This synergistic action results in superior effects on glycemic control and body weight reduction compared to selective GLP-1 agonists.[6][3]

2.3 PHARMACOKINETICS AND PHARMACODYNAMICS

The pharmacokinetic properties of tirzepatide have been characterized in clinical studies:[2]

- **Absorption:** Weekly subcutaneous administration
- **Half-life:** Approximately 5 days (116.7 hours)
- **Metabolism:** Metabolites are excreted through urine and feces
- **Dose adjustments:** The pharmacodynamic and pharmacokinetic properties of tirzepatide were similar in patients with renal and hepatic impairment, and no dose adjustment was required in these conditions[2][7][8]

Tirzepatide increases insulin secretion, reduces glucagon release in a glucose-dependent manner, decreases fasting and postprandial glucose levels, promotes satiety, decreases body weight, and delays gastric emptying.[2]

3 CLINICAL EFFICACY

3.1 EFFICACY IN TYPE 2 DIABETES: SURPASS PROGRAM

The SURPASS phase III clinical trial program (SURPASS-1 to SURPASS-6) evaluated the efficacy and safety of tirzepatide in patients with type 2 diabetes.[3][4][9][10]

SURPASS-1 (Monotherapy): This double-blind, randomized, phase 3 study evaluated tirzepatide as monotherapy in patients with type 2 diabetes.[4] Placebo-adjusted reductions in HbA1c were 21 mmol/mol (1.91%), 21 mmol/mol (1.93%), and 23 mmol/mol (2.11%) with tirzepatide 5, 10, and 15 mg weekly, respectively.[9] Notably, 87–92% of participants met the American Diabetes Association's target of 7.0% HbA1c, and 31–52%

achieved normoglycemia (HbA1c 5.7%) with no increased risk of clinically significant hypoglycemia.[4]

Relative to body weight, tirzepatide demonstrated significant mean reductions at all doses. The proportion of participants who achieved weight loss ≥5%, ≥10%, and ≥15% was substantial, demonstrating benefits beyond glycemic control.[4]

SURPASS-2 (Comparison with Semaglutide): This study directly compared tirzepatide with semaglutide 1.0 mg weekly, a selective GLP-1 agonist.[1] Tirzepatide has demonstrated superiority in both glycemic control and weight loss. Weight reductions were 8.5%, 11.0%, and 13.0% at the 5, 10, and 15 mg doses of tirzepatide, respectively, compared to 6.7% with semaglutide 1 mg.[1]

SURPASS-6 (Addition to Basal Insulin): This study evaluated tirzepatide versus insulin lispro added to basal insulin in patients with type 2 diabetes.[10] Tirzepatide demonstrated significant superiority in reducing HbA1c and body weight. In addition, the incidence of clinically significant hypoglycemia was substantially lower with tirzepatide (9-12% of participants) compared to insulin lispro (48%), with event rates of 0.4 versus 4.4 events/patient-year.[10] **Meta-analysis of the SURPASS Program:** A meta-analysis including seven clinical trials with 6,609 participants confirmed the dose-dependent superiority of tirzepatide in HbA1c reduction versus all comparators, with mean differences ranging from -17.71 mmol/mol (-1.62%) to -22.35 mmol/mol (-2.06%) versus placebo.[3]

3.2 EFFICACY IN OBESITY: SURMOUNT PROGRAM

The SURMOUNT program specifically investigated the efficacy of tirzepatide for the treatment of obesity.[11][12]

SURMOUNT-1: This 72-week study evaluated tirzepatide in participants with obesity without type 2 diabetes.[12] The highest dose (15 mg) resulted in an average weight reduction of 22.5%, with nearly 40% of participants losing ≥25% of body weight. The rates of participants achieving weight loss ≥5% ranged from 67-78%, ≥10% from 31-47%, and ≥15% from 13-27%.[12]

The most frequent adverse events were gastrointestinal (nausea, diarrhoea, and constipation), occurring in more participants in the tirzepatide groups than in the placebo group, being generally transient, mild to moderate in severity, and occurring mainly during the dose escalation period.[12]

SURMOUNT-2: In patients with obesity and type 2 diabetes, tirzepatide reduced weight by an average of 12.8% and 14.7% at doses of 10 and 15 mg, respectively, with a

reduction in HbA1c of 2.2%. Almost half of the participants achieved normal HbA1c values (5.7%).[11]

SURMOUNT-3 and SURMOUNT-4: These studies demonstrated that combining tirzepatide with intensive lifestyle intervention or continuing treatment for 88 weeks resulted in weight reduction of up to 26.6% and 26%, respectively.[11] In SURMOUNT-3, discontinuation rates due to adverse events were 10.5% in the tirzepatide group versus 2.1% in the placebo group.[11]

3.3 DIABETES PREVENTION AND OTHER INDICATIONS

Diabetes Prevention: A recent study published in 2025 evaluated tirzepatide for obesity treatment and diabetes prevention in participants with prediabetes.[13] The results demonstrated significant efficacy in reducing weight and preventing progression to type 2 diabetes. Four cases of adjudication-confirmed pancreatitis were reported, evenly distributed between the treatment groups, including placebo, and none were classified as severe.[13]

Obstructive Sleep Apnea: In December 2024, tirzepatide became the first prescription drug approved for the treatment of moderate to severe obstructive sleep apnea in adults with obesity.[14] The studies demonstrated significant improvement in sleep apnea parameters, with a safety profile consistent with previous studies.[14]

3.4 ADDITIONAL CARDIOMETABOLIC BENEFITS

In addition to glycemic control and weight loss, tirzepatide has demonstrated improvements in multiple cardiometabolic risk factors:[9][4]

- **Lipid profile:** Reduction of total cholesterol, triglycerides, VLDL and LDL, with an increase in HDL[4]
- **Insulin sensitivity:** Significant improvement in insulin resistance as assessed by HOMA-IR[4]
- **Blood pressure:** Reduction of systolic blood pressure- **Hepatic fat:** Improvement of liver fat content and reduction of visceral and subcutaneous abdominal adipose tissue[9]
- **Cardiovascular safety:** Pre-specified post-hoc analyses showed that tirzepatide did not increase the risk of MACE (major adverse cardiovascular events) in participants with type 2 diabetes compared to controls[3][9]

4 SAFETY PROFILE AND ADVERSE EVENTS

4.1 GASTROINTESTINAL ADVERSE EVENTS

The most frequent adverse events with tirzepatide are gastrointestinal, including nausea, diarrhea, constipation, and vomiting.[13][12][11][10][5][14] These events were generally mild to moderate, transient, and occurred primarily during the dose-escalation period.[13][12][11]

In SURMOUNT-1, nausea occurred in 24.6-33.3% of participants on tirzepatide versus 9.5% on placebo; diarrhea in 18.7-23.0% versus 7.3%; and vomiting in 8.3-12.2% versus 1.7%.[12] In SURMOUNT-3, the three most common adverse reactions were nausea (tirzepatide: 39.7%; placebo: 14.0%), diarrhea (tirzepatide: 31.0%; placebo: 9.2%), and constipation (tirzepatide: 23.0%; placebo: 6.8%).[11] In SURPASS-6, the most frequent gastrointestinal events with tirzepatide included nausea (14-26%), diarrhea (11-15%), and vomiting (5-13%).[10] Most cases were mild to moderate in severity, transient, and occurred during the dose escalation period.[10]

Meta-analyses confirmed increased odds of gastrointestinal events, particularly nausea, with tirzepatide compared to other long-acting GLP-1 agonists.[9] Interestingly, some studies suggest that tirzepatide may have a slightly lower frequency of gastrointestinal side effects than selective GLP-1 agonists, possibly due to its unbalanced dual agonist effect favoring GIPR activity over GLP-1R.[5]

4.2 SERIOUS ADVERSE EVENTS

Pancreatitis: Rare cases of acute pancreatitis have been reported.[13][12][8][14] In SURMOUNT-1, there were four adjudication-confirmed cases, evenly distributed among treatment groups, including placebo, and none were classified as severe.[12] In the diabetes prevention study, four cases were reported (three in the tirzepatide groups and one in the placebo group).[13] In SURPASS-6, there were no cases of adjudicated pancreatitis.[10] In the sleep apnea studies, there were two confirmed cases of acute pancreatitis in the tirzepatide group of trial 2.[14]

Biliary Disease: The incidence of cholelithiasis was generally similar between the tirzepatide and placebo groups, although cholecystitis and acute cholecystitis were reported more frequently in the tirzepatide groups, with low incidences (≤0.6%).[12] In SURPASS-6, nine participants treated with tirzepatide and two treated with insulin lispro reported cholelithiasis.[10] There is a small increased risk of gallbladder or biliary diseases that may be associated with GLP-1 agonists, and may be dose-dependent, duration, or indication-dependent.[8]

Hypoglycemia: When used as monotherapy or without sulfonylureas/insulin, tirzepatide does not increase the risk of hypoglycemia.[7][5] In SURPASS-1, there were no cases of clinically significant (54 mg/dL) or severe hypoglycemia with tirzepatide.[4] In patients with type 2 diabetes, hypoglycemia occurs in about 4%, but is rare (0.5%) in patients without diabetes.[7] In SURPASS-6, when added to basal insulin, the incidence of clinically significant hypoglycemia was substantially lower with tirzepatide (9-12%) compared to insulin lispro (48%).[10]

Acute Kidney Injury: Has occurred rarely according to postmarketing reports, particularly in patients with nausea, vomiting, diarrhea, or dehydration.[7]

Cardiovascular Events and Mortality: In SURMOUNT-1, eleven deaths were reported: 4 (0.6%) in the tirzepatide 5 mg group, 2 (0.3%) in the 10 mg group, 1 (0.2%) in the 15 mg group, and 4 (0.6%) in the placebo group.[12] In the diabetes prevention study, ten deaths were reported, with seven occurring in the tirzepatide groups and three in the placebo group.[13] None of the deaths were considered treatment-related by the investigators.[10]

Mental Health: Based on experience with other weight loss medications, tirzepatide carries warnings about increased behavior and suicidal ideation.[11][7] In the sleep apnea studies, there were five cases of major depressive disorder or suicidal ideation/behavior in both studies (two with tirzepatide and three with placebo).[14] Patients should be monitored and the drug should not be prescribed to patients with a history of suicidal attempts or active ideation.[11][7]

4.3 DISCONTINUATION FEES

Discontinuation rates due to adverse events varied between studies. In SURMOUNT-1, 4.3-7.1% of participants on tirzepatide discontinued versus 2.6% on placebo.[12] In the combined SURMOUNT-1 and -2 studies, discontinuation due to adverse events occurred in 4.8%, 6.3%, and 6.7% of patients receiving tirzepatide 5 mg, 10 mg, and 15 mg, respectively, and 3.4% of patients receiving placebo.[11] In SURMOUNT-3, 10.5% and 2.1% of patients in the tirzepatide and placebo groups, respectively, discontinued treatment due to adverse events.[11] In SURMOUNT-4, the proportions were 1.8% and 0.9%.[11]

The 15 mg dose had a higher discontinuation rate regardless of the comparator.[12] Discontinuations due to gastrointestinal adverse events in SURPASS-1 were 2-7% with tirzepatide versus 1% with placebo.[4]

4.4 CONTRAINDICATIONS AND WARNINGS

Black-Box Warning: Tirzepatide has a black-box warning on thyroid C-cell tumors, based on rat data of uncertain significance for humans. It is contraindicated in patients with a personal or family history of medullary thyroid carcinoma and in patients with multiple endocrine neoplasia syndrome type 2 (MEN 2).[11][7][5][8]

Additional Precautions:

- Caution in patients with a history of biliary disease or pancreatitis[8]
-Caution in patients with a history of diabetic retinopathy
- Delayed gastric emptying may alter the absorption of oral medications, particularly oral contraceptives. Non-oral contraception or barrier method is recommended for 4 weeks after initiation and after each dose escalation[11][7][8]
- Should not be used in pregnant women and should be discontinued if pregnancy occurs[7][8]
- Insufficient data on presence in breast milk[7][8]
- Not studied in children[7][8]
- Does not require dose adjustment in patients with renal or hepatic impairment[7][8]

4.5 POST-MARKETING PHARMACOVIGILANCE DATA

An analysis of the FDA's adverse event reporting system (FAERS) investigated the actual safety profile of tirzepatide.[15] The study detected disproportionate reporting of gastrointestinal events (nausea with ROR 4.01, 95% CI 3.85-4.19), pancreaticobiliary disorders (pancreatitis with ROR 3.63, 95% CI 3.15-4.19), diabetic retinopathy (ROR 4.14, 95% CI 2.34-7.30), and medullary thyroid carcinoma (ROR 13.67, 95% CI 4.35-42.96).[15]

However, tirzepatide exhibited a similar risk of gastrointestinal events and medullary thyroid carcinoma and a lower risk of most pancreaticobiliary adverse events and diabetic retinopathy versus GLP-1 agonists.[15] The safety profile was similar to that of GLP-1 agonists, with no increased risk of pancreaticobiliary adverse events, diabetic retinopathy, and medullary thyroid carcinoma.[15]

5 RISKS OF USE WITHOUT A MEDICAL PRESCRIPTION

5.1 ABSENCE OF SCREENING FOR CONTRAINDICATIONS

The use of tirzepatide without medical supervision eliminates essential screening for absolute contraindications, including:

History of Medullary Thyroid Carcinoma or MEN 2: Tirzepatide is absolutely contraindicated in patients with a personal or family history of Medullary Thyroid Carcinoma

or multiple endocrine neoplasia syndrome type 2.[11][7][5][8] Without proper medical evaluation, individuals with these conditions may inadvertently use the drug, exposing themselves to serious risks.

History of Pancreatitis: Although pancreatitis is rare with tirzepatide, patients with a prior history of pancreatitis require special caution.[8] Unsupervised use prevents proper assessment of this risk.

History of Biliary Disease: Patients with a history of biliary disease require careful monitoring as there is an increased risk of cholecystitis and cholelithiasis.[12][8]

Mental Health: Tirzepatide should not be prescribed to patients with a history of suicidal attempts or active ideation.[11][7] Without adequate psychiatric evaluation, vulnerable individuals may use the drug without the necessary monitoring.

5.2 INADEQUATE TITRATION AND GASTROINTESTINAL ADVERSE EVENTS

Tirzepatide requires careful titration starting at 2.5 mg weekly with monthly tapering to minimize gastrointestinal adverse events.[4][11] The optimized escalation schedule was developed specifically to improve gastrointestinal tolerability.[4]

Risks of Improper Titration:

- **Severe gastrointestinal events:** Severe nausea, vomiting, and diarrhea may occur in up to 3% of patients. Without proper titration, these events can be more frequent and severe[7]
- **Dehydration and electrolyte imbalances:** Serious gastrointestinal events can lead to significant dehydration and electrolyte imbalances, particularly dangerous in vulnerable patients- **Acute kidney injury:** Dehydration secondary to gastrointestinal events can precipitate acute kidney injury, as reported in post-marketing data[7]
- **Premature discontinuation:** Serious adverse events due to improper titration can lead to premature discontinuation of treatment, preventing patients who could benefit from the drug from using it properly

5.3 LACK OF MONITORING OF ORAL CONTRACEPTIVE DRUG INTERACTIONS

Tirzepatide delays gastric emptying, which may reduce the efficacy of oral contraceptives.[11][7][8] Patients should use non-oral contraception or add barrier method for 4 weeks after initiation and after each dose escalation.[11][7][8] Without medical advice, women of childbearing age may experience contraceptive failure.

Sulfonylureas and Insulin: When tirzepatide is used in combination with sulfonylureas or insulin, there is a significantly increased risk of hypoglycemia.[10][5] In

SURPASS-6, the incidence of clinically significant hypoglycemia was 9-12% with tirzepatide versus 48% with insulin lispro when added to basal insulin.[10] Without medical supervision, patients may not properly adjust the doses of these medications, resulting in severe hypoglycemia.

Other Oral Medications: Delayed gastric emptying may affect the absorption of several oral medications.[11][8] Without medical evaluation, clinically significant interactions may go unnoticed.

5.4 USE IN UNSTUDIED POPULATIONS

Pregnancy: Tirzepatide should not be used in pregnant women and should be discontinued if pregnancy occurs.[7][8] Data are insufficient to determine risk in pregnant women.[8] Without medical supervision, women may inadvertently use tirzepatide during pregnancy, exposing the fetus to unknown risks.

Lactation: There are no data on the presence of tirzepatide in breast milk.[7][8] Without medical advice, breastfeeding women may use the drug without knowledge of the potential risks to the infant.

Children and Adolescents: Tirzepatide has not been studied in children.[7][8] Unsupervised use in pediatric populations exposes developing individuals to unknown risks.

Elderly: Only small proportions of patients in clinical trials were over 65 years of age.[7] Elderly patients may be more vulnerable to adverse events, particularly dehydration and acute kidney injury.

5.5 IMPOSSIBILITY OF MANAGING COMPLICATIONS

Acute Pancreatitis: Although rare, acute pancreatitis is a potentially serious complication that requires prompt recognition and management.[13][12][8][14] Without medical supervision, patients may not recognize symptoms or seek appropriate care in a timely manner.

Acute Kidney Injury: As reported in postmarketing data, acute kidney injury may occur, particularly in the context of dehydration.[7] Without medical monitoring, this complication can progress to severe kidney failure.

Acute Biliary Disease: Acute cholecystitis requires appropriate medical or surgical management.[12][10] Patients without medical supervision may not recognize symptoms or seek appropriate treatment.

Severe Hypoglycemia: In patients using tirzepatide with sulfonylureas or insulin, severe hypoglycemia may occur.[10] Without guidance on recognizing and managing

hypoglycemia, patients are at risk for serious complications, including loss of consciousness, seizures, and death.

5.6 SPECIFIC RISKS OF THE UNREGULATED MARKET

Counterfeit Products: The unregulated market may contain counterfeit products without the proper active ingredient, with incorrect dosages, or contaminated with hazardous substances.

Inadequate Storage: Tirzepatide requires proper refrigerated storage. Products obtained outside of regulated channels may have been improperly stored, compromising efficacy and safety.

Lack of Traceability: Products obtained without a medical prescription lack traceability in case of recalls or identification of problematic batches.

Improper Administration Technique: Without medical or nursing advice, patients may use inappropriate injection technique, resulting in erratic absorption, injection site infections, or other complications.

6 ETHICAL AND LEGAL CONSIDERATIONS

Tirzepatide is a prescription drug approved by the FDA and international regulatory agencies. Their dispensation without a medical prescription violates health regulations and exposes suppliers to legal sanctions. Health professionals, including biomedical professionals, have an ethical responsibility to promote the rational use of medications and educate the population about the risks of unsupervised use of prescription medications. It is essential to develop public health education strategies to make the population aware of: The risks of using over-the-counter medications; The importance of medical supervision in the treatment of obesity and diabetes; Safe and effective alternatives to us treatments.

REFERENCES

1. Frías, J. P., Davies, M. J., Rosenstock, J., et al. (2021). Tirzepatide versus semaglutide once weekly in patients with type 2 diabetes. The New England Journal of Medicine, 385(6), 503-515. https://doi.org/10.1056/NEJMoa2107519

2. Wong, E., Cope, R., Dima, L., & Nguyen, T. (2023). Tirzepatide: A dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 agonist for the management of type 2 diabetes mellitus. American Journal of Therapeutics, 30(1), e26-e35. https://doi.org/10.1097/MJT.0000000000001588

3. Nauck, M. A., & D'Alessio, D. A. (2022). Tirzepatide, a dual GIP/GLP-1 receptor co-agonist for the treatment of type 2 diabetes with unmatched effectiveness regrading

glycaemic control and body weight reduction. Cardiovascular Diabetology, 21(1), 169. https://doi.org/10.1186/s12933-022-01604-7

4. Rosenstock, J., Wysham, C., Frías, J. P., et al. (2021). Efficacy and safety of a novel dual GIP and GLP-1 receptor agonist tirzepatide in patients with type 2 diabetes (SURPASS-1): A double-blind, randomised, phase 3 trial. The Lancet, 398(10295), 143-155. https://doi.org/10.1016/S0140-6736(21)01324-6

5. Ma, Z., Jin, K., Yue, M., Chen, X., & Chen, J. (2023). Research progress on the GIP/GLP-1 receptor coagonist tirzepatide, a rising star in type 2 diabetes. Journal of Diabetes Research, 2023, 5891532. https://doi.org/10.1155/2023/5891532

6. Campbell, J. E., Müller, T. D., Finan, B., et al. (2023). GIPR/GLP-1R dual agonist therapies for diabetes and weight loss-chemistry, physiology, and clinical applications. Cell Metabolism, 35(9), 1519-1529. https://doi.org/10.1016/j.cmet.2023.07.010

7. Coppenrath, V., & Mazyck, B. (2024). Tirzepatide (Zepbound) for the treatment of obesity. American Family Physician, 110(2), 199-200.

8. Rebitch, C. B. (2023). Tirzepatide (Mounjaro) for the treatment of type 2 diabetes mellitus. American Family Physician, 108(1), 93-94.

9. Davies, M. J., Aroda, V. R., Collins, B. S., et al. (2022). Management of hyperglycemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care, 45(11), 2753-2786. https://doi.org/10.2337/dci22-0034

10. Rosenstock, J., Frías, J. P., Rodbard, H. W., et al. (2023). Tirzepatide vs insulin lispro added to basal insulin in type 2 diabetes: The SURPASS-6 randomized clinical trial. JAMA, 330(17), 1631-1640. https://doi.org/10.1001/jama.2023.20294

11. Apovian, C. M., Aronne, L., & Barenbaum, S. R. (2025). Clinical management of obesity (3rd ed.). The Obesity Society.

12. Jastreboff, A. M., Aronne, L. J., Ahmad, N. N., et al. (2022). Tirzepatide once weekly for the treatment of obesity. The New England Journal of Medicine, 387(3), 205-216. https://doi.org/10.1056/NEJMoa2206038

13. Jastreboff, A. M., le Roux, C. W., Stefanski, A., et al. (2025). Tirzepatide for obesity treatment and diabetes prevention. The New England Journal of Medicine, 392(10), 958-971. https://doi.org/10.1056/NEJMoa2410819

14. Malhotra, A., Grunstein, R. R., Fietze, I., et al. (2024). Tirzepatide for the treatment of obstructive sleep apnea and obesity. The New England Journal of Medicine, 391(13), 1193-1205. https://doi.org/10.1056/NEJMoa2404881

15. Caruso, I., Di Gioia, L., Di Molfetta, S., et al. (2024). The real-world safety profile of tirzepatide: Pharmacovigilance analysis of the FDA Adverse Event Reporting System (FAERS) database. Journal of Endocrinological Investigation, 47(11), 2671-2678. https://doi.org/10.1007/s40618-024-02441-z