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Tirzepatide in Sport after Inclusion in the WADA Monitoring Program: An Updated Narrative Review of Body Composition, Muscle Preservation and Potential Performance Implications

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Abstract

Background: Tirzepatide, as a dual agonist of the glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptors, has become one of the most effective pharmacological therapies used to treat obesity and metabolic disorders. Growing interest in its potential use among physically active individuals and the inclusion of tirzepatide markers in the World Anti-Doping Agency's (WADA) monitoring program for 2026 highlight the need to reassess the significance of this substance in sports.

Aim: The aim of this study was to update the available data on tirzepatide in the context of sports.

Material and methods: A narrative review of the current literature on tirzepatide, incretin receptor agonists and their use in the context of sports was conducted. The analysis included clinical trials, systematic reviews, publications on body composition, metabolism, and exercise adaptation, as well as WADA regulatory documents.

Results: Tirzepatide effectively reduces body weight and improves metabolic parameters. However, available evidence mainly concerns individuals with obesity or type 2 diabetes, rather than athletes. Changes in lean body mass during therapy may be relevant for physically active individuals, especially in sports requiring high strength and power. Although weight reduction could be beneficial in weight-class sports. Further studies are needed to assess the long-term impact of tirzepatide on athletic performance and to address the ethical issues associated with its use.

Conclusions: Tirzepatide currently has no proven effect on enhancing athletic performance. However, its impact on body weight and body composition may be important for athletes. The inclusion of tirzepatide in WADA's monitoring program highlights the need for further research into its potential misuse, its effects on muscle, and the long-term consequences of its utilization in the athletic population.

Keywords: tirzepatide, dual GLP-1/GIP receptor agonist, incretin-based therapies, sports performance, body composition, muscle mass, anti-doping

1. Introduction

Obesity is one of the most significant public health problems, leading to an increased risk of developing metabolic and cardiovascular diseases and a decline in quality of life (Wilding *et al.*, 2021). In recent years, there has been rapid progress in pharmacotherapy aimed at regulating metabolism and reducing body weight, particularly through modulation of the incretin axis, which includes GLP-1 and GIP (Nauck & Meier, 2018). Tirzepatide is a dual agonist of the GIP and GLP-1 receptors that simultaneously activates both hormonal pathways (Coskun *et al.*, 2018). In clinical trials involving obese or overweight individuals, tirzepatide resulted in significant weight loss, surpassing the results previously achieved with many available pharmacological therapies used to treat obesity. In the SURMOUNT-1 study, 72 weeks of once-weekly tirzepatide treatment resulted in a significant and sustained reduction in body weight in obese individuals and the magnitude of the effect was dose-dependent (Jastreboff *et al.*, 2022). Although reducing adipose tissue is the primary target of weight-loss therapy, attention should also be paid to changes in lean body mass, particularly skeletal muscle, given its crucial contribution to metabolic regulation, functional status and exercise capacity (Heymsfield *et al.*, 2014). An analysis of body composition in the SURMOUNT-1 substudy demonstrated that the weight loss achieved during 72 weeks of tirzepatide therapy was primarily attributable to a reduction in fat mass, although a partial loss of lean body mass was also observed. This finding may be particularly significant in populations for whom the preservation of physical performance is important. The authors emphasized further studies involving direct assessments of physical function, such as physical performance tests are necessary to more accurately determine the functional consequences of the observed changes in body composition (Look *et al.*, 2025).

Athletes constitute a unique group in which weight and body composition management can affect both health and athletic performance, especially in sports that require a specific weight class or an optimal ratio of muscle mass to body fat. The widespread use of novel metabolic drugs, such as tirzepatide, has raised concerns about their potential use beyond approved medical indications, including physically active individuals and athletes seeking rapid weight loss. To date, studies on tirzepatide have focused primarily on patients with type 2 diabetes and obesity, while the impact of this treatment on physical performance, the body's ability to adapt to training and the long-term maintenance of muscle mass in athletes remains insufficiently understood. Biesiada *et al.* presented a review in this journal regarding the maintenance of lean body mass and endurance benefits (Biesiada *et al.*, 2025), this study re-evaluates them in light of data published after January 2025. The aim of this review is to present

the current state of knowledge regarding the mechanism of action of tirzepatide, its effects on body composition, and the potential benefits and risks associated with the use of this drug in the context of sports medicine.

2. Review of available literature

2.1. Pharmacodynamics and mechanism of action of tirzepatide

Tirzepatide is the first long-acting dual agonist of the glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptors. The simultaneous activation of both incretin pathways underlies its unique pharmacodynamic profile and distinguishes it from previously used selective GLP-1 receptor agonists. Owing to its prolonged half-life, tirzepatide can be administered once weekly, improving treatment convenience and promoting better patient adherence to therapy (Galindo i in., 2026; Stawicka i in., 2024).

GIP and GLP-1 are incretin hormones secreted by intestinal endocrine cells in response to nutrient ingestion. Although their effects were initially associated primarily with the enhancement of glucose-dependent insulin secretion, it is now well established that they exert pleiotropic actions on multiple organs and tissues, contributing to the regulation of glucose homeostasis, energy metabolism and appetite control. Through the simultaneous activation of both GIP and GLP-1 receptors, tirzepatide exhibits a broader spectrum of metabolic effects than conventional GLP-1 receptor agonists (Galindo i in., 2026).

Pharmacological studies have demonstrated that tirzepatide exhibits a distinctive receptor activation profile referred to as biased agonism. The drug displays greater affinity for and activity at the GIP receptor than at the GLP-1 receptor, which may account for its unique metabolic properties and clinical efficacy. At the same time, this receptor activation profile enables the achievement of robust therapeutic effects while maintaining a favorable safety profile (Willard i in., 2020).

Tirzepatide increases insulin production in response to elevated blood glucose levels (Savla i in., 2026). Moreover, tirzepatide improves insulin sensitivity, which contributes to more effective glycemic control and improvements in metabolic parameters (Galindo i in., 2026).

An important aspect of tirzepatide's mechanism of action involves its effects on the gastrointestinal tract and the central nervous system. The drug delays gastric emptying, leading to slower nutrient absorption and a reduction in postprandial increases in blood glucose levels. This effect is mediated by activation of the GLP-1 receptor and is not attributed to GIP receptor

stimulation. The greatest reduction in gastric emptying rate is observed after treatment initiation. However, with continued therapy, this effect gradually diminishes, similarly to what is observed with selective GLP-1 receptor agonists (Urva i in., 2020).

At the same time, tirzepatide affects central mechanisms involved in appetite regulation by increasing feelings of satiety and reducing hunger perception. This results in decreased energy intake and contributes to clinically meaningful weight loss (Savla i in., 2026).

Currently, tirzepatide is indicated for the treatment of type 2 diabetes mellitus in adults, long-term management of obesity or overweight in individuals with at least one weight-related comorbidity, and obstructive sleep apnea in patients with obesity. Recent clinical studies have also suggested potential benefits of tirzepatide therapy in other metabolic and cardiovascular conditions, including patients with heart failure with preserved ejection fraction and metabolic dysfunction-associated steatohepatitis (Galindo i in., 2026).

The benefits of tirzepatide therapy extend beyond improvements in glycemic control. Phase III clinical trials from the SURPASS and SURMOUNT programs have demonstrated the beneficial effects of the drug on multiple cardiometabolic risk factors. Treatment with tirzepatide was associated with significant reductions in triglyceride levels, improvements in lipid profiles, reductions in blood pressure, and favorable effects on selected markers of renal function. The ongoing SURMOUNT-MMO trial aims to evaluate the impact of tirzepatide on reducing morbidity and mortality in individuals with obesity and overweight without concomitant type 2 diabetes mellitus (Galindo i in., 2026).

The exceptionally high efficacy of tirzepatide in the treatment of obesity was confirmed in the SURMOUNT-1 trial. Body composition analyses demonstrated that weight loss primarily involved reductions in fat mass, although, similarly to other effective weight-loss interventions, a certain degree of loss of lean body mass was also observed. Preservation of muscle mass and function remains an important clinical consideration, particularly in physically active individuals and patients at risk of developing sarcopenia (Heymsfield i in., 2014; Jastreboff i in., 2022).

2.2. Potential implications for athletes

2.2.1. The reduction of body weight

Tirzepatide, a dual agonist of the GLP-1 and GIP receptors, demonstrates strong weight-reducing effects through its impact on appetite regulation, reduction of energy intake and improvement of metabolic control. The phase III SURMOUNT-1 trial confirmed that tirzepatide therapy leads to a significant and sustained reduction in body weight (Jastreboff *et al.*, 2022). For athletes, it is crucial to avoid excessive loss of lean mass (Manore, 2015).

In the context of sports, tirzepatide may have potential applications in situations where body weight reduction is desired. Nevertheless, its impact should be evaluated beyond changes in total body weight alone, with particular emphasis placed on alterations in body composition and the preservation of performance capacity (Lukaski & Raymond-Pope, 2021; Manore, 2015). Another potential beneficial effect of tirzepatide use in athletes may be an improvement in body composition through preferential reduction of adipose tissue. Body composition analysis in the SURMOUNT-1 substudy showed that weight loss during tirzepatide treatment was primarily attributable to a reduction in fat mass, while maintaining a relatively similar ratio of fat mass loss to lean mass loss as observed with other obesity treatment approaches (Look *et al.*, 2025). The particular significance of tirzepatide may apply to athletes participating in sports that require body weight control, such as combat sports or weightlifting, in which excessive adipose tissue may limit movement efficiency.

2.2.2. Impact on metabolism

Tirzepatide, through the simultaneous activation of GLP-1 and GIP receptors, affects several metabolic mechanisms. It has been demonstrated to reduce body weight, lower glycated hemoglobin (HbA1c) levels, improve insulin sensitivity, and decrease appetite (Nauck & D'Alessio, 2022). Tirzepatide reduces caloric intake by decreasing appetite. Its mechanism of action also includes an increase in fatty acid oxidation (Ravussin *et al.*, 2025).

Improved glycemic control and increased insulin sensitivity may potentially have beneficial effects on exercise metabolism. Better regulation of carbohydrate metabolism may be important for athletes performing high-intensity exercise, in which glucose availability and muscle glycogen stores play a crucial role. A potential benefit of tirzepatide use in athletes with excessive body weight or metabolic disorders may be the improvement of metabolic parameters, including glycemic control and lipid profile, as well as the reduction of chronic inflammation associated with excessive adipose tissue accumulation. Such changes may

indirectly influence training capacity by improving metabolic health and reducing the physiological burden associated with obesity.

2.2.3. Effect on muscle function

One of the important issues regarding the use of tirzepatide in athletes is its impact on skeletal muscle. The SURPASS-3 MRI substudy demonstrated that tirzepatide treatment was associated with a reduction in intramuscular fat content and improvements in parameters related to muscle quality, while simultaneously leading to body weight reduction (Sattar *et al.*, 2025). A reduction in intramuscular fat infiltration may have potentially beneficial functional implications, as increased intramuscular fat content is associated with impaired muscle quality and disturbances in muscle metabolism. However, there are currently insufficient data to determine whether the changes observed in individuals with type 2 diabetes or obesity translate into improvements in parameters relevant to athletes, such as maximal strength, power output, sprint capacity, or training adaptation.

2.3. Potential risks of using tirzepatide in athletes

2.3.1. Loss of muscle mass

Despite the high effectiveness of tirzepatide in reducing body weight, its potential use among athletes involves several issues requiring particular caution, as pharmacologically induced weight reduction may affect not only the adipose tissue but also essential components for physical performance, including muscle mass (Heymsfield *et al.*, 2014; Jastreboff *et al.*, 2022).

In the 72-week SURMOUNT-1 trial involving individuals with obesity, once-weekly administration of tirzepatide at doses of 5 mg, 10 mg, or 15 mg resulted in substantial and sustained reductions in body weight. Importantly, the ratio of fat mass loss to lean mass loss was comparable to that observed with lifestyle-based obesity treatment and surgical interventions (Jastreboff *et al.*, 2022). To verify whether the reduction in lean body mass is clinically significant and translates into decreased physical performance and strength, a SURMOUNT-1 substudy was conducted to assess body composition using dual-energy X-ray absorptiometry (DXA). This substudy highlights the importance of skeletal muscle loss, which may be associated with reduced physical function and muscle strength, potentially increasing the risk of injury (Look *et al.*, 2025; Wang *et al.*, 2020; Willoughby *et al.*, 2018). Loss of lean body mass during intensive weight reduction also leads to a decrease in muscle mass, which may negatively affect the development of strength, power, the ability to perform high-intensity

exercise and the recovery process after training (Heymsfield i in., 2014; Mechanick i in., 2025). It is currently unclear whether the greater weight reduction and faster rate of weight loss induced by tirzepatide use increase the risk of clinically significant losses in muscle mass, which may lead to declines in physical function and strength (Look i in., 2025). Future studies evaluating anti-obesity medications should incorporate direct measures of physical function (Galindo i in., 2026). However, the SURPASS-3 MRI substudy demonstrated that tirzepatide significantly reduces intramuscular fat infiltration and muscle volume alongside substantial weight loss. It also showed that tirzepatide is unlikely to be associated with accelerated muscle mass loss and may have a positive effect on muscle quality (Koceva i in., 2025; Sattar i in., 2025). Moreover, greater weight loss achieved with tirzepatide treatment has been associated with greater improvements in physical function (Gudzune i in., 2025).

Nutritional therapy is an essential component of comprehensive management in individuals undergoing treatment for obesity. Its primary goal is to provide the body with adequate amounts of high-quality protein, as well as essential vitamins and minerals that are crucial for maintaining proper physiological function. In some cases, oral dietary supplements may be necessary to meet increased nutritional requirements or to correct potential deficiencies. Research also indicates that combining a properly planned diet with regular physical activity leads to better outcomes during the weight reduction process. Resistance training is of particular importance, as it helps limit muscle loss, supports the maintenance of strength and improves muscle function during weight loss. This is especially relevant because weight reduction alone may result not only in a decrease in adipose tissue but also in a reduction in muscle mass. Individuals receiving pharmacotherapy for obesity should be included in a comprehensive therapeutic program that incorporates both a well-balanced diet providing adequate amounts of protein and micronutrients, as well as regular resistance training. Such a multidimensional approach enables more effective utilization of treatment outcomes, supports the maintenance of healthy body composition, and reduces the risk of adverse consequences associated with muscle mass loss during therapy. This requires particular attention in the athletic population, where maintaining adequate muscle quantity and quality is a key determinant of sports performance (Grosicki i in., 2024; Jastreboff i in., 2022; Mechanick i in., 2025).

2.3.2. Insufficient energy supply

Another potential concern is the risk of insufficient energy intake resulting from pharmacologically induced appetite suppression. In athletes, reduced energy intake without proper nutritional control may lead to the development of low energy availability (LEA; inadequate energy intake in relation to exercise energy expenditure), which is considered the main mechanism contributing to the development of Relative Energy Deficiency in Sport (REDs) (Mountjoy i in., 2023). REDs can lead to impaired functioning of multiple body systems, including hormonal disturbances, reduced bone health, weakened immune response, an increased risk of injuries and decreased exercise performance (Mountjoy i in., 2023). The potential impact of tirzepatide may be particularly important for athletes participating in sports that require strict body weight control, such as combat sports, gymnastics, physique sports, or weight-category competitions. In these disciplines, the pressure to achieve rapid weight loss may increase the risk of inappropriate use of pharmacological therapies (Mountjoy i in., 2023; Sundgot-Borgen & Garthe, 2011). In contrast, regular physical exercise may serve as a physiological stress-regulation mechanism, reducing psychological strain and supporting emotional resilience through neurobiological adaptations (Yan i in., 2025).

2.3.3. Impaired recovery and difficulties in maintaining a high training intensity

The most commonly observed adverse reactions to tirzepatide include gastrointestinal symptoms such as nausea, diarrhea and vomiting (Mishra i in., 2023), which, in physically active individuals, may adversely affect exercise capacity, hydration status, energy balance and post-exercise recovery.

An important issue is the limited amount of data on the long-term effects of tirzepatide on training adaptation, muscle anabolic processes and the body's ability to maintain high physical performance. Previous clinical studies have mainly focused on people with obesity or type 2 diabetes, so their results cannot be directly applied to healthy physically active individuals or athletes (Jastreboff i in., 2022; Look i in., 2025).

From a sports medicine perspective, it is particularly important that potential weight reduction achieved with tirzepatide does not come at the expense of an athlete's health or the quality of training preparation. The use of this type of therapy should only be considered for specific medical indications and requires monitoring of metabolic parameters, body composition and an appropriate nutritional strategy (Mountjoy i in., 2023).

2.4. Ethical considerations and anti-doping regulations

The development of new pharmacological therapies that enable effective weight loss, such as tirzepatide, has created new ethical challenges in the sports community, particularly regarding the line between treating metabolic disorders and using medications to gain an advantage related to weight control. In competitive sports, body weight and body composition are often key elements of training strategies. However, the use of pharmacological methods for weight loss by healthy individuals without medical indications may raise concerns regarding the safety of athletes and the principles of fair competition (Mountjoy *i in.*, 2023; Sundgot-Borgen & Garthe, 2011).

One of the significant ethical concerns associated with the use of pharmacological methods for weight management in athletes is the risk of replacing long-term strategies, including appropriate nutrition, structured training and health education, with quick interventions focused on weight reduction. This approach may increase the pressure experienced by athletes, particularly in weight-class sports, where expectations related to body weight regulation, increased muscle mass, and the achievement of an ideal physique are especially pronounced (Mountjoy *i in.*, 2023; Silva *i in.*, 2024; Sundgot-Borgen & Garthe, 2011).

In sports with strict weight categories, the pursuit of maintaining or reducing body weight may encourage athletes to use substances that suppress appetite or increase metabolic rate (Silva *i in.*, 2024). Of particular concern is the potential use of tirzepatide by young athletes and individuals who are susceptible to pressure regarding their appearance or body weight.

In sports where a competitor's physique or maintaining a low body weight affects their performance evaluation, unhealthy eating habits and an excessive focus on weight control are more common (Bratland-Sanda & Sundgot-Borgen, 2013). The observed increase in the use of tirzepatide and other incretin-based medications in the bodybuilding community reflects a shifting boundary between medical treatment and pharmacological support for body sculpting (Turnock *i in.*, 2025).

Another ethical consideration is the issue of access to treatment. The use of medications intended for patients with specific medical conditions by healthy athletes may limit access to treatment for people who actually need it due to obesity or metabolic disorders (Savla *i in.*, 2026). Some people use these medications solely for cosmetic weight loss. This situation exacerbates inequalities in access to treatment and limits the ability of those who could benefit most from it in terms of their health to receive the therapy (Minerva, 2026; Savla *i in.*, 2026).

The latest data indicate that incretin medications, including tirzepatide, are increasingly being used off-label in bodybuilding circles. This practice raises ethical dilemmas regarding the line between therapy and pharmacological enhancement of appearance, the safety of use without clinical supervision and the potential normalization of pharmacological weight control in sports (Turnock i in., 2025).

For many athletes, the internet and social media have become the primary source of information on health and body sculpting. The lack of verification of published content and the spread of misinformation can lead to the perpetuation of dangerous practices, including the misuse of prescribed medications (Silva i in., 2024). From the perspective of sports medicine, it is necessary to develop guidelines for monitoring the use of new metabolic drugs in athletes, including the assessment of clinical indications, the control of changes in body composition and the evaluation of their potential impact on athletes' physical and mental health (Mountjoy i in., 2023).

Tirzepatide is not currently included on the World Anti-Doping Agency (WADA) Prohibited List and its use is not considered a violation of anti-doping regulations. Tirzepatide was added to the WADA Monitoring Program effective January 1, 2026, indicating that the substance remains permitted for use by athletes. However, its use is strictly recorded and analyzed by anti-doping laboratories to identify potential patterns of misuse in sport. At the same time, GLP-1 receptor agonists, including tirzepatide, continue to be the subject of scientific interest and discussion within the sports medicine community and among anti-doping organizations due to their increasing popularity and their potential effects on body composition, metabolism and the ability to achieve body mass reduction in athletes. The potential use of metabolic medications for the purpose of manipulating body weight remains a topic of debate in the context of fair competition and athlete health protection. Further research is required to determine their effects on physical performance, safety profile and possible implications for future anti-doping regulations.

4. Conclusions

Tirzepatide, as a dual agonist of the GIP and GLP-1 receptors, represents a breakthrough therapy for the treatment of metabolic disorders, demonstrating a significant impact on glycemic control, appetite regulation, and weight loss. However, from a sports medicine perspective, the potential use of tirzepatide requires particular caution, as weight loss in athletes should be evaluated not only in terms of the amount of weight lost, but above all in

terms of changes in body composition, preservation of muscle mass and maintenance of training adaptation capacity .

Currently, there is insufficient scientific evidence regarding the effects of tirzepatide on physical performance, strength, muscle power and the body's long-term response to training in healthy athletes. The results of studies conducted in clinical populations cannot be directly extrapolated to athletes, whose physiological requirements and body composition goals differ significantly from those of the general population. Tirzepatide should not currently be viewed as a performance-enhancing agent, but rather as a medical therapy intended for individuals with specific clinical indications. Any use of this drug in athletes should occur only after an individual assessment of their health status, taking into account the treatment goal, body composition monitoring and an appropriate nutrition and training strategy.

As the availability of incretin medications increases, further discussion will be needed regarding their role in sports, covering both athlete safety and the ethical aspects of using pharmacological methods for weight management. Future studies should focus on evaluating the effects of tirzepatide on physically active individuals, particularly with regard to the maintenance of muscle mass, exercise capacity and long-term training adaptation.

Disclosure

Supplementary Materials

Not applicable.

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