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# An Overview on Medical Treatment of Polycystic Ovary Syndrome

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**Abstract:**

Polycystic Ovary Syndrome (PCOS) is a complex endocrine and metabolic disorder that affects up to 10–15% of women of reproductive age. It is characterized by menstrual irregularities, hyperandrogenism, and polycystic ovarian morphology. The pathophysiology of PCOS involves a combination of insulin resistance, increased luteinizing hormone (LH) secretion, and androgen excess, all of which contribute to ovarian dysfunction and metabolic derangements. Medical treatment of PCOS focuses on managing the diverse clinical manifestations rather than curing the disease, since its exact cause remains unclear. The pharmacologic approach aims to address specific symptoms and underlying hormonal imbalances. Combined oral contraceptive pills (COCs) are considered the first-line therapy for women not seeking pregnancy, as they regulate menstrual cycles, reduce androgen levels, and prevent endometrial hyperplasia. Insulin sensitizers, particularly metformin, play a key role in improving insulin resistance, restoring ovulatory cycles, and supporting weight reduction in obese patients.

**Keywords:** Polycystic Ovary Syndrome (PCOS); Hyperandrogenism; Insulin resistance; Metformin; Oral contraceptive pills; Antiandrogens; Clomiphene citrate; Letrozole; Ovulation induction; Hormonal therapy; Fertility treatment.

## Introduction:

Polycystic Ovary Syndrome (PCOS) is one of the most prevalent endocrine disorders affecting women of reproductive age, characterized by irregular menstrual cycles, hyperandrogenism, and polycystic ovaries. One of the most significant consequences of PCOS is anovulation, which can lead to infertility. As many as 70% of women with PCOS may experience difficulties in conceiving, making the induction of ovulation a critical focus in their management **(1).**

The medical management of PCOS aims to alleviate symptoms, restore ovulatory function, and prevent long-term complications. First-line treatments depend on the primary complaint—whether it is infertility, menstrual irregularity, or hyperandrogenic symptoms. Common pharmacological options include combined oral contraceptives to regulate menses and reduce androgen levels, metformin to improve insulin sensitivity, and clomiphene citrate or letrozole for ovulation induction. In some cases, antiandrogens such as spironolactone are added to manage hirsutism and acne. Lifestyle modification remains a cornerstone of therapy, often enhancing the efficacy of pharmacological interventions **(2).**

## Clomiphene Citrate

Clomiphene citrate, a selective estrogen receptor modulator, has long been established as a first-line treatment for inducing ovulation in women with PCOS. By blocking estrogen receptors in the hypothalamus, clomiphene increases the release of gonadotropins, thereby stimulating ovarian follicular development and promoting ovulation. This pharmacological approach has demonstrated effectiveness in restoring ovulation in a significant proportion of women with PCOS, facilitating their chances of conception **(3).**

In addition to its efficacy, clomiphene citrate is favored for its oral administration, cost-effectiveness, and relatively favorable side effect profile compared to more invasive procedures. Despite its widespread use,

there remains a need for a comprehensive understanding of its mechanisms, optimal dosing strategies, and potential combination with other therapies to enhance outcomes **(4).**

**Pharmacokinetics**

Clomiphene citrate induces ovulation primarily by blocking estrogen receptors in the hypothalamus, leading to increased GnRH release and subsequent elevation of LH and FSH levels. This cascade of hormonal changes promotes ovarian follicle growth and maturation, culminating in ovulation. Understanding this mechanism is crucial for optimizing treatment strategies in women with anovulatory disorders **(5).**

Clomiphene acts as a Selective Estrogen Receptor Modulator (SERM), selectively binding to estrogen receptors in the hypothalamus. By occupying these receptors, clomiphene prevents estrogen from exerting its negative feedback effect on the hypothalamus. This leads the hypothalamus to perceive lower estrogen levels. The blockade of estrogen receptors in the hypothalamus stimulates the release of gonadotropin-releasing hormone (GnRH). Increased GnRH leads to the anterior pituitary gland releasing higher levels of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), which are crucial for ovarian function **(6).**

Elevated levels of FSH promote the growth and maturation of ovarian follicles. As the follicles mature, they produce estradiol, which eventually leads to a surge in LH, triggering ovulation. Clomiphene can lead to the development of multiple follicles, increasing the risk of multiple pregnancies. It may also enhance ovarian response in women with diminished ovarian reserve, although this effect can vary **(7).**

**Pharmacodynamics**

**Absorption**

Clomiphene citrate is well-absorbed when taken orally, with peak plasma levels occurring within a few hours. Its high bioavailability contributes to its effectiveness in inducing ovulation in women with conditions such as PCOS. The absorption of clomiphene citrate may not be significantly affected by food, allowing for flexible dosing with or without meals. Clomiphene citrate has a relatively short half-life, which is typically around 5 to 7 days. Its effects on hormone levels, however, can persist beyond its elimination due to the changes it induces in the endocrine system **(8).**

**Distribution**

Clomiphene citrate has a large volume of distribution, indicating extensive distribution into body tissues. This characteristic suggests that the drug is widely distributed beyond the plasma into various tissues. Clomiphene citrate is approximately 99% bound to plasma proteins, primarily albumin and alpha-1 acid glycoprotein. This high level of protein binding affects its bioavailability and the free concentration of the drug available for action. Clomiphene citrate has a tendency to accumulate in ovarian tissue, which is significant for its intended effect of inducing ovulation. This localization enhances its effectiveness in stimulating follicular development. Clomiphene can cross the blood-brain barrier, which may contribute to its central effects on hormone regulation and the potential for central nervous system side effects, such as visual disturbances or mood changes **(9).**

**Metabolism**

Clomiphene citrate is primarily metabolized in the liver. The metabolism involves cytochrome P450 enzymes, particularly CYP3A4 and CYP2D6, which play significant roles in its biotransformation. Clomiphene citrate is converted into several active metabolites, including desethylclomiphene and other hydroxylated derivatives. These metabolites may have similar or varying degrees of activity compared to the parent compound. The presence of active metabolites contributes to the prolonged effects of clomiphene citrate, even after the parent drug has been cleared from the system. Factors such as genetics, liver function, and concurrent medications can influence the metabolism of clomiphene citrate, potentially affecting both its efficacy and side effects **(10).**

**Excretion**

The metabolites of clomiphene are primarily excreted through urine and feces. The elimination half-life of clomiphene citrate is generally around 5 to 7 days, but the effects may persist longer due to active metabolites **(11).**

**Uses**

Clomiphene citrate is primarily utilized for inducing ovulation in women with conditions like PCOS and other anovulatory disorders. Its effectiveness in promoting fertility makes it a cornerstone of treatment in reproductive medicine. Additionally, it may be employed in assessing ovarian function and addressing specific menstrual irregularities. Clomiphene citrate can be used in fertility assessments to evaluate ovarian reserve and responsiveness. The response to clomiphene can provide insights into ovarian function. It may be used to help restore menstrual cycles in women with hypothalamic amenorrhea due to low body weight or excessive exercise **(12).**

**Side effects**

While clomiphene citrate is an effective treatment for inducing ovulation, it can lead to side effects ranging from mild and common symptoms to more serious conditions like Ovarian Hyperstimulation Syndrome (OHSS) and visual disturbances. Regular monitoring and patient education about these potential side effects are essential to ensure safe and effective use of the medication **(13).**

Clomiphene citrate is generally well-tolerated, but it can cause a range of side effects including flushing and warmth due to hormonal changes, emotional variability or changes in mood, gastrointestinal upset can occur in some patients, discomfort or tenderness in the breasts and swelling of the ovaries, which may cause discomfort. Ovarian hyperstimulation syndrome (OHSS) is a is a rare, iatrogenic complication of ovarian stimulation by assisted reproduction technology and other infertility treatments. Following gonadotropin therapy, OHSS usually develops several days after oocyte retrieval or assisted ovulation. This syndrome is characterized by ovarian enlargement due to multiple ovarian cysts and an acute fluid shift into the extravascular space. Complications of OHSS include ascites, hemoconcentration, hypovolemia, and electrolyte imbalances **(14).**

**Myoinositol**

Myo-inositol is a naturally occurring carbohydrate and a member of the vitamin B complex family. It has gained attention for its role in improving ovarian function and insulin sensitivity in women with Polycystic Ovary Syndrome (PCOS), a common endocrine disorder characterized by anovulation, insulin resistance, and hormonal imbalances **(15).**

**Pharmacokinetics**

Myo-inositol exerts its beneficial effects in the context of PCOS and ovulation induction primarily through improving insulin sensitivity, regulating ovarian function, and modulating hormonal pathways. These actions collectively promote follicular development and enhance the chances of ovulation, making myo-inositol a valuable adjunct in the management of fertility in women with PCOS **(16).**

Myo-inositol enhances insulin signaling by participating in the phospho-inositol signaling pathway. It helps improve the response of cells to insulin, thereby increasing glucose uptake and decreasing insulin resistance. By improving insulin sensitivity, myo-inositol can lower circulating insulin levels, which is particularly beneficial for women with PCOS, who often exhibit insulin resistance. Myo-inositol is involved in the maturation of ovarian follicles. It supports the growth and development of oocytes and enhances the quality of the follicles. Myo-inositol helps regulate the hormonal environment by reducing elevated levels of androgens (such as testosterone) that are common in PCOS. This hormonal balance can facilitate regular ovulation **(17).**

Myo-inositol may influence the secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), promoting a balanced hormonal profile conducive to ovulation. By supporting healthy follicular development, myo-inositol can also enhance estrogen production, which is essential for the ovulatory process.

Myo-inositol acts as a precursor for inositol phosphates, which are important second messengers in various signaling pathways, including those involved in cell growth and differentiation. By enhancing cellular signaling in ovarian cells, myo-inositol contributes to improved oocyte quality and developmental competence **(18).**

**Pharmacodynamics**

**Absorption**

Myo-inositol is primarily taken orally, available in various forms such as powders, capsules, and tablets. Myo-inositol is rapidly absorbed when taken orally, with high bioavailability and minimal impact from food intake. Its efficient absorption and transport to target tissues, particularly in the ovaries, contribute to its effectiveness in promoting ovarian function and improving insulin sensitivity in women with PCOS. The absorption of myo-inositol is not significantly affected by food intake, allowing flexibility in dosing with or without meals. Myo-inositol is absorbed through specific transporters in the intestinal wall, facilitating its entry into the bloodstream. Once in circulation, it can be taken up by various tissues, including the ovaries **(19).**

**Distribution**

Myo-inositol exhibits widespread distribution throughout the body, with significant concentrations in tissues like the ovaries and brain. Its ability to cross the blood-brain barrier and its efficient uptake by cells underscore its importance in metabolic and reproductive health, particularly for women with PCOS. Understanding its distribution helps inform its therapeutic applications and efficacy in clinical settings. Myo-inositol is particularly concentrated in the ovarian tissue, where it plays a critical role in follicular development and oocyte quality. This localization is important for its effectiveness in promoting ovulation in women with PCOS. Myo-inositol is taken up by cells via specific transporters, facilitating its action in insulin signaling and cellular processes. Myo-inositol has low plasma protein binding, which allows for its free circulation in the bloodstream and availability for cellular uptake **(20).**

**Metabolism**

Myo-inositol is metabolized through several biochemical pathways that involve phosphorylation and conversion to signaling molecules. It can be synthesized in the body but is also obtained from dietary sources. The metabolism of myo-inositol is closely linked to insulin signaling and is crucial for maintaining cellular function and metabolic health, particularly in conditions like Polycystic Ovary Syndrome **(21).**

Myo-inositol undergoes phosphorylation to form inositol phosphates and inositol phospholipids. These compounds are critical for cell signaling processes, including those involved in insulin signaling and cellular growth. Inositol trisphosphate (IP3) is one of the significant metabolites derived from myo-inositol and plays a crucial role in intracellular signaling, particularly in the regulation of calcium release from the endoplasmic reticulum. Myo-inositol can be synthesized in the body from glucose through the inositol phosphate pathway, though dietary intake is often necessary to meet physiological needs. Myo-inositol can also be converted to other inositol isomers, such as D-chiro-inositol, which has distinct metabolic functions and is particularly relevant in the context of insulin sensitivity **(22).**

**Excretion**

Myo-inositol is primarily excreted in the urine. The kidneys filter myo-inositol from the blood, and excess amounts are eliminated through urination. The excretion rate can vary based on dietary intake, metabolic needs, and kidney function. Abnormal levels of myo-inositol in urine can be associated with certain metabolic disorders or conditions, such as insulin resistance or polycystic ovary syndrome **(23).**

**Uses**

Myo-inositol is a versatile compound with various biological roles and therapeutic applications. Myo-inositol is often used to improve insulin sensitivity, particularly in individuals with insulin resistance or type 2 diabetes. It is frequently recommended for managing symptoms of PCOS, including improving ovarian function and restoring menstrual regularity. It has been shown that myo-inositol may have antidepressant and anxiolytic

effects, potentially benefiting individuals with mood disorders. It has been explored as an adjunct treatment for OCD due to its role in neurotransmitter signaling **(24).**

Myo-inositol is thought to improve oocyte quality and may enhance fertility in women with PCOS. It is sometimes used to support metabolic health during pregnancy and reduce the risk of gestational diabetes. Myo-inositol is being investigated for its potential neuroprotective effects, particularly in conditions like Alzheimer's disease and other neurodegenerative disorders. Myo-inositol may aid in weight loss and body composition improvements, especially in individuals with metabolic disorders. Its anti-inflammatory properties may make it beneficial for treating acne and other skin issues. Myo-inositol is available as a dietary supplement and is often combined with other compounds, such as D-chiro-inositol, for synergistic effects, particularly in managing PCOS. Myo-inositol is generally considered safe for most people when taken at appropriate doses. However, like any supplement, it can have side effects **(25).**

**Metformin**

Metformin is a widely used medication for managing type 2 diabetes and has gained attention for its role in treating conditions like polycystic ovary syndrome (PCOS). Metformin improves insulin sensitivity, which can be beneficial for women with PCOS who often experience insulin resistance. This can help lower insulin levels, which may influence ovarian function and hormone balance. By reducing insulin levels, metformin may help decrease androgen levels (such as testosterone) that can disrupt the normal ovulatory cycle **(26).**

**Pharmacokinetics**

Metformin's multifaceted mechanism of action makes it an effective treatment for managing hyperglycemia in type 2 diabetes and improving metabolic parameters in conditions like PCOS. By targeting hepatic glucose production, enhancing insulin sensitivity, and influencing other metabolic pathways, it helps regulate blood sugar levels and supports overall metabolic health. Metformin primarily acts on the liver by reducing the production of glucose. It inhibits gluconeogenesis, the process by which the liver produces glucose from non-carbohydrate sources. It also reduces glycogenolysis, the breakdown of glycogen to glucose, further lowering blood glucose levels **(27).**

Metformin enhances the sensitivity of peripheral tissues (like muscle and fat) to insulin. This allows cells to utilize glucose more effectively, helping to lower blood sugar levels. Increased glucose uptake in muscle tissues is crucial for managing blood sugar levels, especially after meals. It has been shown that metformin may have an effect on the gut microbiome, promoting the growth of beneficial bacteria that can aid in glucose metabolism **(28).**

Metformin activates AMP-activated protein kinase (AMPK), a key regulator of cellular energy homeostasis. This activation leads to a decrease in hepatic glucose production and an increase in fatty acid oxidation. By inhibiting the mitochondrial respiratory chain, metformin shifts cellular metabolism toward increased energy expenditure rather than storage. Metformin helps lower triglyceride levels and may have a favorable effect on lipid metabolism, contributing to cardiovascular health. It has been found that metformin may exert anti-inflammatory effects, which could be beneficial in conditions like PCOS and metabolic syndrome **(29).**

**Pharmacodynamics**

**Absorption**

Metformin is well-absorbed from the gastrointestinal tract, with food intake influencing its absorption profile. The presence of food can affect the absorption of metformin. Taking it with meals can improve gastrointestinal tolerance and may slightly reduce peak plasma concentrations, but it does not significantly affect the overall bioavailability. Extended-release formulations of metformin are designed to provide a slower absorption rate, leading to prolonged drug action and potentially fewer gastrointestinal side effects. After oral administration, metformin typically reaches peak plasma concentrations within 2 to 3 hours. The extended-release formulations may have a delayed peak. Metformin has a large volume of distribution, indicating extensive distribution into body tissues. It is minimally bound to plasma proteins (about 30%), which is relatively low compared to many other medications **(30).**

**Distribution**

Metformin has a large volume of distribution and primarily concentrates in the liver, kidneys, and intestines. Its low protein binding and limited central nervous system penetration are important factors in its pharmacokinetic profile. Metformin has a large volume of distribution, estimated to be around 63 to 93 liters. This indicates that it extensively distributes into body tissues rather than remaining confined to the bloodstream. Metformin is minimally bound to plasma proteins, with only about 30% of the drug binding to proteins. This low binding allows for a higher free concentration in the plasma, facilitating its pharmacological effects. Metformin does not significantly cross the blood-brain barrier, which may limit its central nervous system effects. Metformin is primarily excreted unchanged by the kidneys. Impaired renal function can lead to increased plasma concentrations, necessitating dose adjustments to avoid toxicity **(31).**

**Metabolism**

Metformin is primarily excreted unchanged in the urine with minimal hepatic metabolism. Its pharmacological effects are largely due to its action in the liver and peripheral tissues rather than metabolic transformation. Metformin undergoes very little hepatic (liver) metabolism. Unlike many other medications, it is not significantly broken down by liver enzymes (such as cytochrome P450 enzymes). Approximately 90% of the administered dose is excreted unchanged in the urine, indicating that metformin remains largely intact throughout its passage in the body **(32).**

After oral administration, metformin is absorbed in the gastrointestinal tract and distributed primarily to the liver, kidneys, and intestines, where it exerts its effects. Metformin's pharmacological action is primarily due to its direct effects on the liver, where it reduces gluconeogenesis (the production of glucose) and enhances insulin sensitivity in peripheral tissues. Metformin is predominantly cleared by the kidneys. It is actively secreted into the renal tubules, and any impairment in renal function can lead to increased plasma levels and the potential for lactic acidosis, a rare but serious side effect **(33).**

**Excretion**

Metformin is primarily excreted unchanged in the urine through renal mechanisms. Understanding its excretion profile is vital for ensuring safe and effective use, particularly in patients with altered renal function. Regular monitoring of kidney health is essential to mitigate risks associated with elevated drug levels. Increased levels of metformin due to renal impairment can lead to lactic acidosis, a rare but potentially life-threatening condition characterized by the buildup of lactic acid in the blood **(11).**

Metformin is primarily excreted by the kidneys. Approximately 90% of an administered dose is eliminated unchanged in the urine. It is actively secreted into the renal tubules through specific transporters, mainly the organic cation transporters. The elimination half-life of metformin is typically around 4 to 8 hours in healthy individuals, but this can vary based on renal function. In patients with reduced renal function, the clearance of metformin is decreased, leading to increased plasma concentrations. This elevates the risk of side effects, particularly lactic acidosis. It is essential to monitor renal function (e.g., serum creatinine and estimated glomerular filtration rate, or eGFR) regularly in patients taking metformin, especially in those with pre-existing kidney issues **(34).**

**Uses**

Metformin is a versatile medication with established uses in managing type 2 diabetes and PCOS, as well as potential applications in weight management, prediabetes, and other metabolic conditions. Its benefits extend beyond glycemic control, making it a valuable tool in various clinical settings. Metformin may be beneficial in managing metabolic syndrome, helping to improve insulin sensitivity, reduce waist circumference, and lower blood pressure and lipid levels. Metformin may have cardiovascular benefits, reducing the risk of cardiovascular events in patients with type 2 diabetes **(35).**

Metformin is the first-line medication for managing type 2 diabetes. It helps lower blood glucose levels by improving insulin sensitivity, reducing hepatic glucose production, and enhancing peripheral glucose uptake.

Metformin is used in individuals with prediabetes to help prevent the progression to type 2 diabetes. It can improve insulin sensitivity and lower blood glucose levels. Metformin is often prescribed to women with PCOS to help restore ovulation and regulate menstrual cycles. It can improve insulin sensitivity and lower androgen levels, which are often elevated in this condition **(36).**

**Side effects**

While metformin is generally safe and effective, it can cause side effects, particularly gastrointestinal issues and, in rare cases, lactic acidosis. t can occur in patients with impaired renal function, liver disease, or other conditions that predispose them to acidosis. Symptoms may include weakness, fatigue, muscle pain, difficulty breathing, abdominal discomfort, and unusual sleepiness. Long-term use of metformin may lead to decreased absorption of vitamin B12, potentially resulting in deficiency. This may manifest as anemia, neuropathy, or other neurological symptoms. Though rare, some individuals may experience allergic reactions, such as skin rashes, itching, or swelling. Metformin is contraindicated in individuals with significant renal impairment (eGFR < 30 mL/min) due to the increased risk of lactic acidosis. Regular monitoring of renal function and vitamin B12 levels is recommended for patients on long-term metformin therapy **(37).**

**Sitagliptin**

Sitagliptin, a DPP-4 (dipeptidyl peptidase-4) inhibitor, is primarily used to manage blood glucose levels in patients with type 2 diabetes. While sitagliptin may offer benefits in managing metabolic issues associated with PCOS and potentially aid in ovulation induction, its primary use remains in diabetes management. Women with PCOS should consult their healthcare provider to discuss the most appropriate treatment options, including the use of sitagliptin in conjunction with other therapies **(38).**

**Pharmacokinetics**

Sitagliptin's primary mechanism of action is the inhibition of the DPP-4 enzyme, leading to increased levels of incretin hormones. This results in enhanced insulin secretion, decreased glucagon release, and improved glycemic control in individuals with type 2 diabetes. Dipeptidyl peptidase-4 is an enzyme that breaks down incretin hormones, which are involved in glucose metabolism. By inhibiting the DPP-4 enzyme, sitagliptin increases the levels of active incretin hormones, primarily glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) **(39).**

Increased levels of GLP-1 and GIP enhance insulin secretion from the pancreatic beta cells in a glucose-dependent manner. This means that insulin is released when blood glucose levels are elevated, reducing the risk of hypoglycemia. Sitagliptin also decreases the secretion of glucagon, a hormone that raises blood glucose levels. This helps to lower overall blood glucose by reducing hepatic glucose production. By promoting insulin secretion and reducing glucagon levels, sitagliptin effectively lowers postprandial (after meal) blood glucose levels. Unlike some other diabetes medications, sitagliptin is generally weight neutral, meaning it does not typically cause weight gain. In the context of polycystic ovary syndrome (PCOS), sitagliptin may improve insulin sensitivity, which can help in managing metabolic aspects of the condition and potentially support ovulation **(40).**

**Pharmacodynamics**

**Absorption**

Sitagliptin is well absorbed after oral administration, with a high bioavailability and a peak concentration reached within a few hours. Its absorption is minimally affected by food, providing flexibility in dosing. Sitagliptin has an oral bioavailability of approximately 87%. This means that about 87% of the drug reaches systemic circulation after oral administration. The peak plasma concentration of sitagliptin is usually reached within 1 to 4 hours after ingestion **(41).**

**Distribution**

Sitagliptin has a large volume of distribution and moderate protein binding, indicating extensive distribution throughout the body. Sitagliptin has a volume of distribution of approximately 168 liters. This indicates that the drug extensively distributes into body tissues rather than remaining confined to the bloodstream. Sitagliptin is about 38% bound to plasma proteins. This level of protein binding is relatively low compared to many other medications, allowing a larger fraction of the drug to remain in its active form in the circulation. While specific data on the tissue distribution of sitagliptin are limited, its large volume of distribution suggests that it penetrates various tissues in the body, including pancreatic tissues where it exerts its primary effects. There is no significant evidence that sitagliptin crosses the blood-brain barrier, which may limit its central nervous system effects **(42).**

**Metabolism**

Sitagliptin has a relatively low risk of drug-drug interactions, especially those that involve cytochrome P450 enzymes. However, dose adjustments are recommended in patients with renal impairment, as the drug is predominantly eliminated through the kidneys. Sitagliptin has a high oral bioavailability of approximately 87%. It reaches peak plasma concentration within 1–4 hours after oral administration. Sitagliptin undergoes minimal metabolism by the liver. Only a small fraction (about 16%) of Sitagliptin is metabolized. The primary enzyme involved in its limited metabolism is CYP3A4, with a minor role played by CYP2C8. Sitagliptin is primarily excreted unchanged in the urine (about 79%) **(43).**

**Excretion**

Sitagliptin's reliance on renal excretion with minimal hepatic metabolism makes it less prone to interactions with other drugs metabolized by liver enzymes. Approximately 79% of an administered Sitagliptin dose is excreted unchanged in the urine. This occurs mainly through active tubular secretion, involving the organic anion transporter 3 (OAT3) and p-glycoprotein (P-gp) transporters. Sitagliptin has an elimination half-life of approximately 12.4 hours, which allows for convenient once-daily dosing. Since Sitagliptin is primarily eliminated by the kidneys, patients with renal impairment require dose adjustments to prevent drug accumulation and potential side effects **(44).**

**Uses**

Sitagliptin is an oral antidiabetic medication primarily used to manage type 2 diabetes mellitus. It belongs to the class of drugs known as dipeptidyl peptidase-4 (DPP-4) inhibitors. Sitagliptin is used to improve blood glucose control in adults with type 2 diabetes. It is effective in lowering fasting and postprandial blood glucose levels by enhancing the body's natural incretin hormones, which help regulate blood sugar levels. Sitagliptin is often used in combination with other antidiabetic medications, such as metformin, sulfonylureas, SGLT2 inhibitors, or insulin, when monotherapy is insufficient. While not a primary cardiovascular agent, Sitagliptin has been studied for cardiovascular safety and is considered safe for use in patients with type 2 diabetes who have cardiovascular disease, though it does not have proven cardiovascular benefits like some other antidiabetic agents (e.g., GLP-1 receptor agonists) **(45).**

**Side effects**

Patients on Sitagliptin should be monitored for symptoms of pancreatitis and kidney function, especially if they have preexisting conditions that increase their risk of side effects. Sitagliptin alone has a low risk of hypoglycemia, but when combined with other antidiabetic medications (e.g., insulin or sulfonylureas), the risk increases. Sitagliptin may cause severe joint pain, which may resolve upon discontinuation of the drug. Though rare, there may be an increased risk of heart failure, especially in patients with preexisting heart or kidney issues. Rarely, Sitagliptin can cause serious allergic reactions, such as angioedema, rash, or anaphylaxis **(46).**

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