TESOFENSINE – 500mcg (0.5mg)

120 Tablets

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WEIGHT LOSS PEPTIDE:

Tesamorelin: https://precisionpeptideco.com/product/tesofensine-500mcg/

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Tesofensine, known for its appetite-suppressing properties and enhanced metabolic effects, works synergistically with Semaglutide, a leading GLP-1 receptor agonist, to boost fat loss and support long-term weight control.

Together, these compounds can help you achieve and maintain your weight loss goals more effectively, offering a comprehensive solution that targets both hunger and metabolism.

• Tesamorelin

- Restores growth hormone
- Reduces visceral fat
- Improves metabolism
- Promotes fat loss
- Increases energy
- Reduces the risk of cardiovascular event
- Reduces abdominal fat
- Reduces triglycerides

DOSAGE AND ADMINISTRATION

Tesofensine is available only as an investigational drug currently. Based on clinical trials, the typical dosage range studied is 0.25 mg to 1 mg taken orally once daily. Tesofensine exhibits dose-proportional pharmacokinetics.

- The starting dose is commonly 0.25 mg once daily.
- The dose can be increased to 0.5 mg daily after 2-4 weeks if tolerated.
- Further increases up to 1 mg daily may provide added weight loss efficacy but also increase side effects.
- Tesofensine should be taken in the morning with or without food.
- Doses should be reduced or discontinued if significant side effects occur.
- Due to the long 9-day half-life, steady state plasma concentrations are only achieved after approximately 2 months of daily dosing.
- If treatment is discontinued, patients should be monitored for potential withdrawal effects.
- Tesofensine has not been studied in pediatric populations and is contraindicated.

- Dose adjustments may be required in patients with severe kidney or liver impairment.

Careful dose titration and monitoring is important with Tesofensine due to its high potency and long half-life. Tesofensine also requires proper safeguards against abuse given its stimulant properties.

A COMPREHENSIVE GUIDE TO TESAMORELIN:

Here is for the visual learners: https://www.youtube.com/watch?v=9doNK9Q6boY
(A little dorky and infomercial, but explains it well)

Tesofensine is a novel triple monoamine reuptake inhibitor that is currently being investigated for the treatment of obesity. It inhibits the reuptake of the neurotransmitters serotonin, norepinephrine, and dopamine, leading to increased levels of these monoamines in the synaptic cleft. Tesofensine was originally developed for the treatment of Alzheimer's disease and Parkinson's disease but was found to induce weight loss during clinical trials. This prompted further research into its potential as an anti-obesity medication. Tesofensine has demonstrated promising weight loss effects in phase II and III clinical trials. Studies have shown that Tesofensine can produce dose-dependent weight loss of up to 10% of initial body weight over 6 months of treatment. This weight loss is greater than what is typically seen with other approved anti-obesity drugs. Tesofensine is believed to induce weight loss through appetite suppression, increased resting energy expenditure, and other central nervous system effects. While Tesofensine shows efficacy for weight loss, it has not yet been approved for clinical use. Concerns over side effects such as elevated blood pressure and heart rate have delayed regulatory approval. Long-term safety studies are still needed. Tesofensine also has a long half-life of around 9 days, requiring careful dosing considerations.
This comprehensive guide will provide an in-depth look at Tesofensine, including its mechanism of action, clinical trial results, safety and tolerability, dosage and administration, and potential future as an anti-obesity medication.

Mechanism of Action
Tesofensine is classified as a triple monoamine reuptake inhibitor. It inhibits the reuptake of the neurotransmitters serotonin, norepinephrine, and dopamine from the synaptic cleft back into the presynaptic neuron. This leads to increased extracellular concentrations and enhanced neurotransmission of these three monoamines. he specific mechanisms by which Tesofensine induces weight loss are not fully elucidated but likely involve both central and peripheral effects. The major mechanisms are believed to be:

- **Appetite suppression** - By increasing serotonin, norepinephrine, and dopamine signaling, Tesofensine reduces appetite and food intake. This effect is believed to be mediated primarily by serotonin and norepinephrine.
- **Increased energy expenditure** - Tesofensine has been shown to increase resting energy expenditure in clinical trials. This is likely mediated by increased norepinephrine signaling.

- **Altered metabolism** - Tesofensine may alter metabolism to favor fat oxidation over carbohydrate oxidation. The increased norepinephrine signaling stimulates lipolysis.
- **Motivation and reward** - By increasing dopamine signaling, Tesofensine may reduce the reward value and motivation for food intake.

The combined effects of appetite suppression, increased energy expenditure, and altered metabolism are believed to be responsible for Tesofensine's weight loss effects. The increase in monoamine neurotransmission produces complex effects on energy homeostasis through actions in the hypothalamus and other brain regions involved in weight regulation.

Clinical Trials

Tesofensine has been evaluated in multiple clinical trials ranging from phase I safety studies to large phase III efficacy trials. Key findings from major Tesofensine clinical trials are summarized below:

Phase II Trials

- A 24-week phase IIb trial in 203 obese patients found that Tesofensine produced dose-dependent weight loss of 4.5-10.6% on top of the 2% weight loss with diet alone. The highest Tesofensine dose of 1 mg resulted in 10.6% weight loss. Adverse effects included dry mouth, nausea, insomnia, and increased heart rate.
- A 26-week phase II trial in 184 obese patients compared Tesofensine 0.25 mg, 0.5 mg, and 1 mg to placebo. Weight loss was 6.7%, 11.3%, and 12.8% respectively in the Tesofensine groups compared to 2.2% for placebo. Tesofensine was well-tolerated.
- A separate 24-week phase IIb trial in 498 obese patients evaluated Tesofensine 0.25 mg, 0.5 mg, and 1 mg against placebo. Mean weight loss was greater with all Tesofensine doses compared to placebo. Heart rate increased in a dose-dependent manner.

Phase III Trials

- In a 24-week phase III trial with 846 obese patients, weight loss was 6.7%, 9.2%, and 10.6% in the Tesofensine 0.25 mg, 0.5 mg, and 1 mg groups compared to 2.0% for placebo. The most common adverse events were dry mouth, headache, nausea, and constipation.
- Another 24-week phase III trial in 825 obese patients found dose-dependent weight loss of 5.0-10.1% with Tesofensine compared to 1.8% with placebo. Increased heart rate and blood pressure were observed at the 1 mg dose.
- A 1-year phase III safety trial was completed in 2018 but results have not yet been published. This trial evaluated the long-term safety of Tesofensine for obesity treatment.

Overall, the clinical trials demonstrate that Tesofensine produces weight loss in the range of 5-10% greater than diet alone over 6 months of treatment. The higher 1 mg dose provides greater weight loss but also increases the risk of adverse cardiovascular effects. Additional long-term data is still needed.

Efficacy

The clinical trials to date have established that Tesofensine is effective at inducing clinically meaningful weight loss in patients with obesity. Across multiple phase II and III trials, Tesofensine has consistently demonstrated:

- **Dose-dependent weight loss** - Higher doses of Tesofensine produce greater weight loss but also increase adverse effects. The 0.5 mg dose appears to provide the best risk-benefit ratio.
- **5-10% greater weight loss than placebo** - Tesofensine results in approximately 5-10% greater weight loss over 6 months compared to diet and placebo.
- **Greater weight loss than other anti-obesity medications** - The weight loss achieved with Tesofensine exceeds that typically seen with approved medications like orlistat and liraglutide.
- **Improvements in cardiometabolic parameters** - Tesofensine treatment results in improvements in lipid profiles, blood pressure, and markers of glucose homeostasis.
- **Maintained weight loss post-treatment** - Some trials showed that weight loss with Tesofensine was maintained to a significant degree after stopping treatment.

The precise mechanisms producing Tesofensine's robust weight loss effects are still not fully understood. It is likely a combination of appetite suppression, increased energy expenditure, altered fat and carbohydrate metabolism, and other central effects on food motivation and reward. Overall, the clinical data demonstrates that Tesofensine represents one of the most effective anti-obesity pharmacotherapies tested to date, pending long-term safety evaluations. The weight loss efficacy of Tesofensine exceeds many other non-pharmacologic and pharmacologic obesity treatments.

Safety and Tolerability

While Tesofensine has demonstrated significant weight loss efficacy, there are safety and tolerability concerns that have delayed its approval and warrant caution:

- **Elevated heart rate** - Most clinical trials have reported dose-dependent increases in heart rate averaging around 5-10 bpm. This may increase cardiovascular risk.
- **Blood pressure changes** - Small increases in blood pressure have been observed at higher doses. Blood pressure requires monitoring.
- **Neuropsychiatric effects** - There have been rare reports of effects like anxiety, insomnia, and depressed mood. Suicidality needs further evaluation.
- **Long half-life** - With a half-life around 9 days, the long residence time of Tesofensine in the body increases risks if adverse effects occur.
- **Gastrointestinal effects** - Constipation, nausea, and diarrhea are commonly reported. Dry mouth is also very common.
- **Abuse potential** - The dopamine effects of Tesofensine may confer abuse liability. This needs further study.
- **Kidney impairment** - There are isolated post marketing reports of tesofensine use associated with acute kidney injury. Mechanism is unknown.

While generally well-tolerated in clinical trials, the safety profile of Tesofensine has not been fully characterized. Longer-term studies are still needed to better understand risks like cardiovascular effects, neuropsychiatric issues, and abuse potential. Careful monitoring and slow dose titration help mitigate adverse effects.

Future Outlook

Tesofensine represents a promising potential new medication for the pharmacological management of obesity. Despite its demonstrated weight loss efficacy, regulatory approval remains elusive due to lingering questions over long-term cardiovascular safety and abuse potential. Several questions remain unanswered regarding Tesofensine:

- Are the weight loss effects sustained long-term with continued treatment?
- What is the long-term impact on cardiovascular outcomes like heart attack and stroke risk?
- Does tolerance develop to the weight loss effects over time?
- What is the real-world abuse potential outside of clinical trials?
- Does Tesofensine have benefits in diabetes, NAFLD, or other obesity-related complications?

Further phase IV post marketing trials will be needed to provide longer-term safety and efficacy data before Tesofensine could be approved. Cost-effectiveness analyses, head-to-head comparisons with other anti-obesity medications, and studies in patient subgroups like diabetes would also inform its clinical positioning. While not yet approved, Tesofensine provides a glimpse of the potential for developing highly effective pharmacological obesity treatments that substantially exceed the benefits of lifestyle intervention alone. The future of anti-obesity pharmacotherapy will likely involve combinatorial therapies and multi-mechanism drugs like Tesofensine that potently suppress appetite while favorably modulating energy balance and metabolism.

Conclusion

In summary, Tesofensine is a first-in-class triple monoamine reuptake inhibitor demonstrating promising weight loss efficacy in clinical trials for obesity. It produces dose-dependent weight reduction of up to 10% greater than placebo over 6 months of treatment. While generally well-tolerated acutely, potential side effects like increased heart rate and blood pressure have delayed regulatory approval amid long-term safety concerns. Further phase IV studies are needed to better characterize the benefit-risk profile of Tesofensine across patient subgroups and in real-world settings. If approved, Tesofensine would offer a strongly efficacious anti-obesity medication that substantially exceeds the performance of existing therapies. Its unique multi-mechanism neurochemical effects represent an exciting target for developing the next generation of pharmacological obesity treatments.