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Faculty of Pharmacy - Tanta University

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Inside this issue:

Evaneotrim®: A new option for chronic weight management in Egypt

Obesity has become an increasingly serious health issue worldwide, leading to various physiological impairments and associated health conditions. Evaneotrim®, introduced recently by EVA Pharma to the Egyptian market, provides a new medication option as an adjunct to lifestyle changes for chronic weight management in obese adults. Evaneotrim® is an extended-release combination product containing the active ingredients naltrexone and bupropion.

MECHANISM OF ACTION:

The precise neurochemical mechanisms behind Evaneotrim®'s effects on weight are not fully understood but likely involve complementary actions on pathways regulating food intake and energy expenditure. Evaneotrim® is theorized to act within the hypothalamus to modulate the activity of pro-opiomelanocortin (POMC) neurons that control satiety signals and metabolism. Specifically, the POMC cells produce alpha-melanocyte stimulating hormone (alpha-MSH) and beta-endorphin. Alpha-MSH reduce appetite and increase energy expenditure. Meanwhile, beta-endorphin is an endogenous opioid that binds to and inhibits mu-opioid receptors on the POMC neurons themselves, limiting their activation through a negative feedback loop.

Bupropion as an aminoketone antidepressant is thought to increase POMC cell production and secretion of both alpha-MSH and beta-endorphin. Simultaneously, the opioid antagonist naltrexone blocks the inhibitory effects of beta-endorphin binding to mu-opioid receptors. This complementary pharmacological action enhances firing of the POMC neurons, amplifying melanocortin pathway signaling and ultimately driving weight loss through diminished eating behaviors and increased metabolism.

INDICATIONS AND DOSAGE:

Evaneotrim® is indicated for chronic weight management in obese adults or overweight adults with at least one weight-related comorbid condition (e.g. hypertension, diabetes). The recommended dose is two tablets twice daily (total daily dose 32mg naltrexone/360mg bupropion ER) following initial gradual uptitration over 4 weeks. If at least 5% weight loss is not achieved after 12 weeks, Evaneotrim® should be discontinued.

DRUG INTERACTIONS

Evaneotrim®'s naltrexone component can block the effects of opioids. Bupropion has the potential to interact with many medications by inhibition of cytochrome P450 2D6. Concurrent use of Evaneotrim® with monoamine oxidase inhibitors is contraindicated. Caution should be taken when co-administering drugs that lower seizure threshold.

EFFICACY:

Four phase 3 trials demonstrated Evaneotrim® 32mg/360mg, plus lifestyle changes, achieved statistically significant greater weight loss over 56 weeks compared to placebo. Average placebo-subtracted weight loss ranged 3.7% in patients with diabetes to 8.1% using intensive behavioral modification. Improvements were also seen in waist circumference, eating control, lipids, glycemic parameters, and weight-related quality of life versus placebo.

SAFETY AND TOLERABILITY:

The most common side effects are nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, and diarrhea. Evaneotrim® has been associated with increases in resting heart rate and blood pressure. It has a boxed warning for risks of suicidal thoughts and seizures, aligned with the antidepressant class labeling for bupropion. Naltrexone-bupropion significantly reduces body weight by a small amount but significantly increases the risk of adverse events. A rigorous process of post-marketing surveillance is required.

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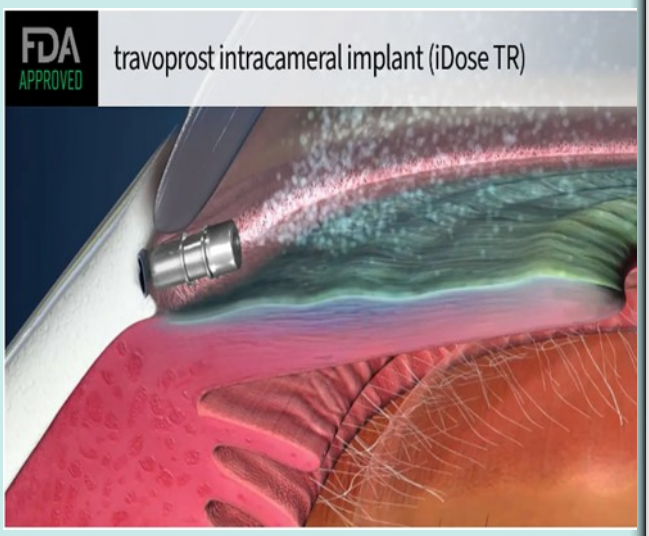
- *Thomas B, Lindblad AJ, Luu T, Paige A. Naltrexone-bupropion for weight loss. Can Fam Physician. 2023 Sep;69(9):627.*
- *Onakpoya IJ, Lee JJ, Mahtani KR, Aronson JK, Heneghan CJ. Naltrexone-bupropion (Mysimba) in management of obesity: A systematic review and meta-analysis of unpublished clinical study reports. Br J Clin Pharmacol. 2020 Apr;86(4):646-667.*

Ph. Mohammed K. Talaat, PhrmD.

FDA approves Travoprost implant for treatment of ocular hypertension and glaucoma

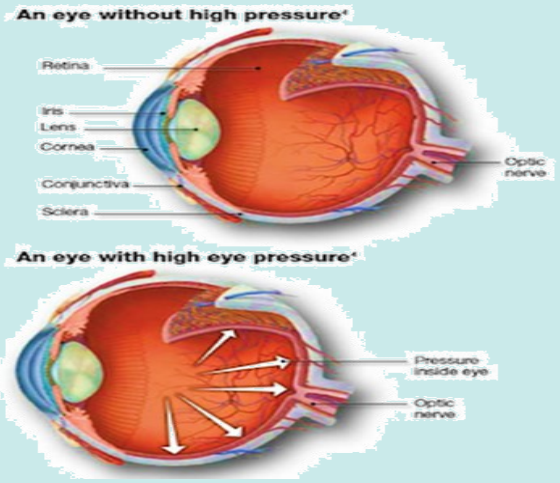
The US Food and Drug Administration (FDA) has approved an intracameral implant with 75 mcg of travoprost (iDose TR) to reduce intraocular pressure (IOP) in patients with open-angle glaucoma (OAG) or ocular hypertension (OHT). The implant is designed to provide long-duration treatment for the full range of glaucoma disease severity. The implant releases the prostaglandin analog travoprost, which is already approved for the two ocular conditions.



Pivotal phase 3 clinical trials showed the treatment resulted in sustained reductions in IOP for three months, ranging from 6.6 to 8.4 mmHg, comparable to reductions with topical timolol 0.5% drops used twice daily. These clinical data suggest that iDose TR is effective with a favorable safety profile and can potentially relieve patients from the burdens of prescription eye drops for an extended period.

The iDose TR (Glaukos Corp) is inserted into a corneal incision on the temple side of the eye, and a preloaded handheld injector is designed to deliver the implant into the eye's sclera. The implant seats in the junction of the iris, sclera, and cornea. Normal IOP is 10-21 mmHg, and glaucoma treatments are designed to reduce high IOP into the normal range.

Travoprost is a prostaglandin analog topical formulation for lowering IOP in OAG and OHT. Timolol is a topical beta-blocker widely used for the same indications. In two phase 3 clinical trials, 81% of patients who received the iDose TR did not require supplemental drops to reduce IOP after 12 months compared with 95% of those who received timolol alone.



The phase 3 trials included 1150 participants across 89 clinical sites. Both trials, GC-010 and GC-012, met the primary endpoints through 3 months and demonstrated a favorable tolerability and safety profile through 12 months.

Based on these outcomes, the FDA concluded in the prescribing information that iDose TR demonstrated non-inferiority to topical timolol in the reduction of IOP during the first three months of treatment. The agency also noted that the use of iDose TR did not demonstrate non-inferiority over the next nine months.

In the controlled studies, the most common ocular adverse reactions reported in 2% to 6% of patients who received iDose TR were increases in IOP, iritis, dry eye, and defects of the visual field, most of which were said to be mild and transient in nature.

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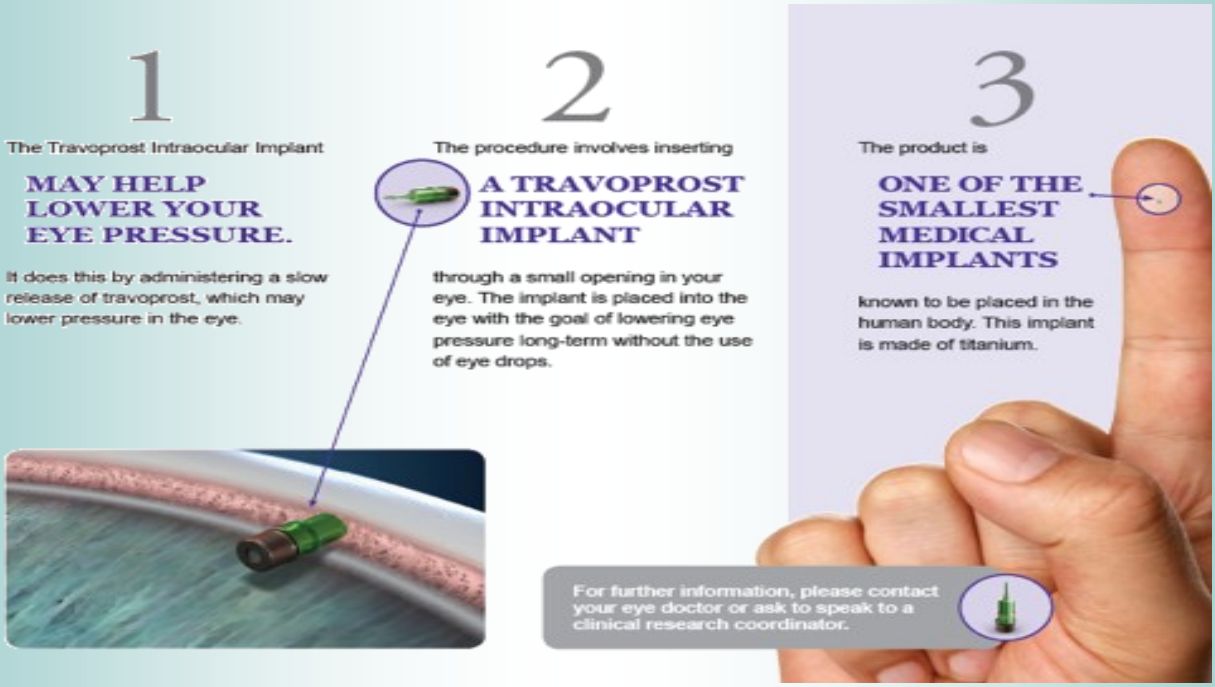
- ***FDA Approves Implant for Glaucoma. Available at: https://www.medscape.com/viewarticle/fda-approves-implant-glaucoma-2023a1000vmb. Accessed in December, 2023.***
- ***Berdahl, J.P., Sarkisian, S.R., Ang, R.E. et al. Efficacy and Safety of the Travoprost Intraocular Implant in Reducing Topical IOP-Lowering Medication Burden in Patients with Open-Angle Glaucoma or Ocular Hypertension. Drugs (2023). https://doi.org/10.1007/s40265-023-01973-7***



Ph. Mai Mousa, PharmD., M.Sc

Pfizer announces that the new experimental twice daily oral weight loss drug, danuglipron will be discontinued

⇒ On December 1, 2023, Pfizer announced that it will stop developing the twice-daily version of its experimental weight loss pill, danuglipron, and the drug will not advance into phase 3 clinical trials. Danuglipron is an oral glucagon-like peptide-1 receptor agonist (GLP-1RA) candidate, and was investigated for use in adults with obesity and without type 2 diabetes.

⇒ During the phase 2b randomized, double-blind, placebo-controlled, parallel group, dose-ranging trials evaluated the efficacy and safety of danuglipron, twice-daily dosing of danuglipron showed statistically significant reductions from baseline in body weight for all doses, with mean reductions ranging from -6.9% to -11.7%, compared to +1.4% for placebo at 32 weeks, and -4.8% to -9.4%, compared to +0.17% for placebo at 26 weeks.

⇒ While the most common adverse events were mild and gastrointestinal in nature consistent with the mechanism, high rates were observed (up to 73% nausea; up to 47% vomiting; up to 25% diarrhea).

⇒ High discontinuation rates, greater than 50%, were seen across all doses compared to approximately 40% with placebo. No new safety signals were reported and treatment with danuglipron was not associated with increased incidence of liver enzyme elevation compared to placebo. However, the once-daily version of danuglipron is still in development, with pharmacokinetic data anticipated in the first half of 2024.

⇒ Earlier this year, Pfizer has also dropped another anti-obesity drug, lotiglipron, which is a once-daily oral GLP-1RA, after pharmacokinetic data showed elevated transaminases liver enzymes in these Phase 1 studies as well as the ongoing Phase 2 study.

REFRENCES:

- ***Pfizer Announces Topline Phase 2b Results of Oral GLP-1R Agonist, Danuglipron, in Adults with Obesity. Available at: https://www.pfizer.com/news/press-release/press-release-detail/pfizer-announces-topline-phase-2b-results-oral-glp-1r. Accessed in December, 2023.***
- ***Pfizer to discontinue twice-daily weight loss pill due to high rates of adverse side effects. Available at: https://www.cnbc.com/2023/12/01/pfizer-to-discontinue-twice-daily-version-of-weight-loss-pill.html. Accessed in December, 2023.***
- ***Pfizer axes new weight loss pill after patients experience serious side effects. Available at: https://www.biopharma-reporter.com/Article/2023/12/04/Pfizer-axes-new-weight-loss-pill-after-patients-experience-serious-side-effects. Accessed in December, 2023.***
- ***Pfizer Provides Update on GLP-1-RA Clinical Development Program for Adults with Obesity and Type 2 Diabetes Mellitus. Available at: https://www.pfizer.com/news/press-release/press-release-detail/pfizer-provides-update-glp-1-ra-clinical-development. Accessed in December, 2023.***

Ph. Amr Noweir, B. Sc.

The top three medication classes that are effective for migraine, based on reported records from a smartphone application

According to recent findings from a comprehensive analysis of self-reported patient data in real-world settings, triptans, ergots, and antiemetics demonstrate two to five times greater efficacy in alleviating acute migraines compared to ibuprofen. Notably, acetaminophen emerges as the least effective medication for this purpose.

METHODS:

Examining data from Migraine Buddy, an electronic diary app, researchers scrutinized nearly 11 million records of migraine attacks spanning a 6-year timeframe. The study involved assessing the perceived efficacy of 25 acute migraine medications across seven categories: acetaminophen, NSAIDs, triptans, combination analgesics, ergots, antiemetics, and opioids. Employing a two-level nested multivariate logistic regression model, adjustments were made for within-subject dependence and concurrent medications taken during each analyzed migraine episode. The conclusive analysis encompassed nearly 5 million medication-outcome pairs derived from 3.1 million migraine attacks involving 278,000 individuals using medications.

KEY FINDINGS:

When compared to ibuprofen as the baseline, triptans, ergots, and antiemetics emerged as the top three medication categories, showcasing the highest effectiveness with mean odds ratios (OR) of 4.80, 3.02, and 2.67, respectively. Following closely were opioids (OR, 2.49), NSAIDs excluding ibuprofen (OR, 1.94), combination analgesics containing acetaminophen/acetylsalicylic acid/caffeine (OR, 1.69), and other classes (OR, 1.49). Acetaminophen (OR, 0.83) ranked as the least effective option. Noteworthy individual medications included eletriptan (Relpax) (OR, 6.1), zolmitriptan (Zomig) (OR, 5.7), and sumatriptan (Imitrex) (OR, 5.2) as the most efficacious choices.

LIMITATIONS:

These conclusions rely on subjective effectiveness ratings reported by users, lacking data on side effects, dosages, and formulations. The omission of newer migraine medication classes, such as gepants and ditans, results from their lower frequency of use. Notably, the regression model did not factor in variables like age, gender, pain intensity, and other associated migraine symptoms that might influence treatment effectiveness.

References:

Chiang CC, Fang X, Horvath Z, et al. Simultaneous Comparisons of 25 Acute Migraine Medications Based on 10 Million Users' Self-Reported Records From a Smartphone Application. Neurology. Published online November 29, 2023. doi:10.1212/WNL.0000000000207964.

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Vision

The vision of Tanta University DPIC is to improve national healthcare service through provision of evidence-based, unbiased, patient oriented drug information services & adverse drug reporting system.

Mission

* Responding to drug inquiries related to the use of the drug and providing the health care professionals and patients with drug information related to the patient's care to achieve the optimal use of the drug in addition to the provision of other toxicological managing information.
* Educational activities to support the rational optimal use of drugs as well, supporting research activities.
* Continuous medical education and training courses in various fields of pharmacy for students, undergraduates, postgraduate students, and researchers.
* Issuing a Drug Information Bulletin periodically to take a look at medical & pharmaceutical news.
* Supporting the National Pharmaceutical Vigilance Program by following up and monitoring side effects and problems related to use of pharmaceutical preparations within regional hospitals.
* Contributing to the establishment of various treatment protocols and prescription booklet services in regional hospitals.

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