FDA Update on Oversight of Prescription Drug Promotion

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Director
Office of Prescription Drug Promotion
Food and Drug Administration
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Qsymia Untitled Letter

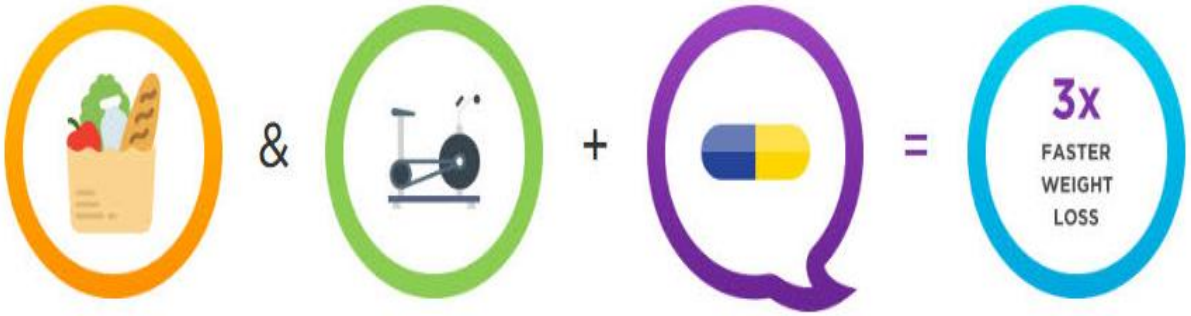
- Consumer website
- Indication:
  - Qsymia is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of:
    - 30 kg/m^2 or greater (obese) or
    - 27 kg/m^2 or greater (overweight) in the presence of at least one weight related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia.
  - **<u>Limitations of Use</u>**
    - The effect of Qsymia on cardiovascular morbidity and mortality has not been established.
    - The safety and effectiveness of Qsymia in combination with other products intended for weight loss, including prescription and over-the-counter drugs, and herbal preparations, have not been established.

Risk Information for Qsymia

- Contraindications include:
  - Pregnancy
  - Glaucoma
  - Hyperthyroidism
  - During or within 14 days following the administration of monoamine oxidase inhibitors
- Warnings and precautions include:
  - Fetal toxicity
  - Increase in heart rate
  - Suicidal behavior and ideation
  - Acute myopia and secondary angle closure glaucoma
  - Mood and sleep disorders
  - Cognitive impairment
  - Metabolic acidosis
  - Elevated creatinine

On average, prescription Qsymia can help you lose weight 3 times faster than diet and exercise alone.[1,2‡]

Losing weight has constantly tested your willpower and left you feeling frustrated. Qsymia can power your weight-loss plan and help you achieve results more quickly.



‡ Qsymia was studied in 2 large trials supporting FDA approval that involved 3754 patients whose BMI was 27 kg/m^2 or greater. Patients were randomized to placebo, phentermine 3.75 mg/topiramate 23 mg, phentermine 7.5 mg/topiramate 46 mg, or phentermine 15 mg/topiramate 92 mg. In these trials, it was recommended that patients eat a well-balanced diet and reduce their caloric intake by 500 kcal/day. Your weight loss may vary depending on your BMI, diet, activity, dose of Qsymia, and other factors.[1,2]

Talk to your doctor about powering your weight-loss plan with once-daily Qsymia.

False or Misleading Claims about Efficacy

- Claims that Qsymia can help patients lose weight 3x faster than diet and exercise alone are misleading.
  - The sponsor cited calculated ratios of the amount of weight loss at specific points in time from the clinical studies.
  - These calculations do not support claims regarding the rate of weight loss.
  - In addition, the clinical studies were designed to evaluate the amount of weight loss and cannot be used to support claims regarding rate of weight loss.

For patients with a body mass index (BMI)* of 30+† or 27 kg/m² or greater (overweight) in the presence of at least one weight-related medical condition.

Lose weight and keep it off with Qsymia[1,2]

Clinically proven results at 12, 28 and 56 weeks[1,2‡]

The results presented here are from the combined studies supporting FDA approval of Qsymia. The dosing schedule in those studies differ from the dosing schedule that your physician may recommend. As a result of this dosing differential, your results may vary depending on your BMI, diet, activity, dose of Qsymia, and other factors.[1] Please see additional study design information below.

False or Misleading Claims about Efficacy

- The webpage
  - Omits material information from the full indication about the relative effect of diet and exercise, as well as contextual information about weight loss results in the placebo group, and thereby suggests that the results can be attributable to Qsymia alone
  - Selectively presents the more favorable absolute amount of weight loss and reduction in waist circumference, which fails to account for an individual's baseline weight and waist circumference
  - Selectively presents the results for patients who remained on Qsymia at distinct points in time and fails to account for the substantial number of patients who withdrew from the trial

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Take control of your hunger and cravings with Qsymia

It can be frustrating coping with the daily cycle of hunger and cravings. Willpower alone is not enough. Qsymia can give you around the clock control.[1]

LEARN HOW QSYMIA WORKS

Get a FREE two-week starter dose of Qsymia

Our money-savings offer helps you get started on your plan to long-term weight loss. Restrictions apply.

Want your Qsymia Savings Card delivered to your phone via text message? Learn more.

START NOW AND SAVE

Indication

Qsymia should be used together with a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of:

- 30 kg/m² or greater (obese) or
- 27 kg/m² or greater (overweight) in the presence of at least one weight-related medical condition such as high blood pressure, type 2 diabetes, or high cholesterol

LIMITATIONS OF USE:

- It is not known if Qsymia changes your risk of heart problems or stroke or of death due to heart problems or stroke
- It is not known if Qsymia is safe and effective when taken with other prescription, over-the-counter, or herbal weight loss products
- It is not known if Qsymia is safe and effective in children under 18 years old

Important Safety Information

Do not take Qsymia if you are pregnant, planning to become pregnant, or become pregnant during Qsymia treatment; have glaucoma; have thyroid problems (hyperthyroidism); are taking certain medicines called monoamine oxidase inhibitors (MAOIs) or have taken MAOIs in the past 14 days; are allergic to topiramate, sympathomimetic amines such as phentermine, or any of the ingredients in Qsymia. See the end of the Medication Guide for a complete list of ingredients in Qsymia.

QSYMIA CAN CAUSE SERIOUS SIDE EFFECTS, INCLUDING:

Birth defects (cleft lip/cleft palate). If you take Qsymia during pregnancy, your baby has a higher risk for birth defects called cleft lip and cleft palate. These defects can begin early in pregnancy, even before you know you are pregnant. Women who are pregnant must not take Qsymia. Women who can become pregnant should have a negative pregnancy test before taking Qsymia and every month while taking Qsymia and use effective birth control (contraception) consistently while taking Qsymia. Talk to your healthcare provider about how to prevent pregnancy. If you become pregnant while taking Qsymia, stop taking Qsymia immediately, and tell your healthcare provider right away. Healthcare providers and patients should report all cases of pregnancy to FDA MedWatch at 1-800-FDA-1088, and the Qsymia Pregnancy Surveillance Program at 1-888-998-4887.

Increases in heart rate. Qsymia can increase your heart rate at rest. Your healthcare provider should check your heart rate while you take Qsymia. Tell your healthcare provider if you experience, while at rest, a racing or pounding feeling in your chest lasting several minutes when taking Qsymia.

Suicidal thoughts or actions. Topiramate, an ingredient in Qsymia, may cause you to have suicidal thoughts or actions. Call your healthcare provider right away if you have any of these symptoms, especially if they are new, worse, or worry you: thoughts about suicide or dying; attempts to commit suicide; new or worse depression; new or worse anxiety; feeling agitated or restless; panic

False or Misleading Risk Presentation

- The webpage
  - Fails to present information relating to contraindications, warnings, precautions, and adverse reactions for Qsymia with a prominence and readability reasonably comparable to the presentation of information relating to benefits for Qsymia

ParaGard Untitled Letter

- Direct-to-consumer television advertisement (TV ad)
- Indication:
  - ParaGard is indicated for intrauterine contraception for up to 10 years.
- Contraindications include:
  - Pregnancy or suspicion of pregnancy
  - Abnormalities of the uterus resulting in distortion of the uterine cavity
  - Acute pelvic inflammatory disease, or current behavior suggesting a high risk for pelvic inflammatory disease
  - Postpartum endometritis or postabortal endometritis in the past 3 months
  - Known or suspected uterine or cervical malignancy
  - Genital bleeding of unknown etiology

Warnings and Precautions for ParaGard

- Warnings include:
  - Intrauterine pregnancy
  - Ectopic pregnancy
  - Pelvic infection
  - Immunocompromise
  - Embedment
  - Perforation
  - Expulsion
  - Wilson's Disease (a rare genetic disease affecting copper excretion)
- Precautions include:
  - Vaginal bleeding
  - Vasovagal reactions, including fainting
  - Expulsion following placement after a birth or abortion

ParaGard TV Ad

False or Misleading Risk Presentation

- The TV ad:
  - Presents claims and/or representations about the uses and benefits of ParaGard
  - Fails to include important risk information associated with ParaGard
  - Misleadingly suggests that ParaGard is safer than has been demonstrated

False or Misleading Risk Presentation

- The TV ad also includes the following claims and presentations (emphasis original):
  - "No hormones! I found a birth control with no hormones! ParaGard's 100% hormone-free…!"
  - "No hormones not an ounce! With an ingredient I can pronounce."
  - "100% HORMONE FREE"
  - "1 SIMPLE ACTIVE INGREDIENT"

Stendra Warning Letter

- Direct-to-consumer print advertisement (ad) and banners
- Indication:
  - Stendra is a phosphodiesterase 5 (PDE5) inhibitor for the treatment of erectile dysfunction (ED).
- Contraindications:
  - Using any form of organic nitrate or a guanylate cyclase stimulator
  - Known hypersensitivity to any component of the tablet
- Warnings and precautions include:
  - Cardiovascular risks
  - Concomitant use of CYP3A4 inhibitors, alpha-blockers and other antihypertensives, alcohol, and other PDE5 inhibitors or ED therapies
  - Prolonged erection
  - Sudden vision or hearing loss
  - Effects on bleeding
  - Counseling patients about sexually transmitted diseases


STENDRA
(avanafil) tablets
Treat ED and Reduce Risk of Heart Failure with a PDE-5 Inhibitor
Stendra is the next-generation, PDE-5 inhibitor that improves erectile function.
Stendra (Avanafil) is FDA-approved, safe and effective for those with heart disease and diabetes, becomes effective in as little as 15 minutes, and flexible with food and alcohol intake.
Learn more at
BIT.LY/STENDRA
Drinking too much alcohol when taking Stendra can increase heart rate, lower blood pressure, and increase chances of getting a headache. The most common side effects of Stendra include headache, flushing, and nasal congestion. Please report negative side effects of prescription drugs to the FDA. Visit MedWatch or call 1-800-FDA-1088.

Lack of Adequate Directions for Use

- The headline claim “Treat ED and Reduce Risk of Heart Failure with a PDE-5 Inhibitor”
  - Provides evidence that Stendra is intended for a new use for which it lacks approval, and for which its labeling does not provide adequate directions for use

False or Misleading Risk Presentation

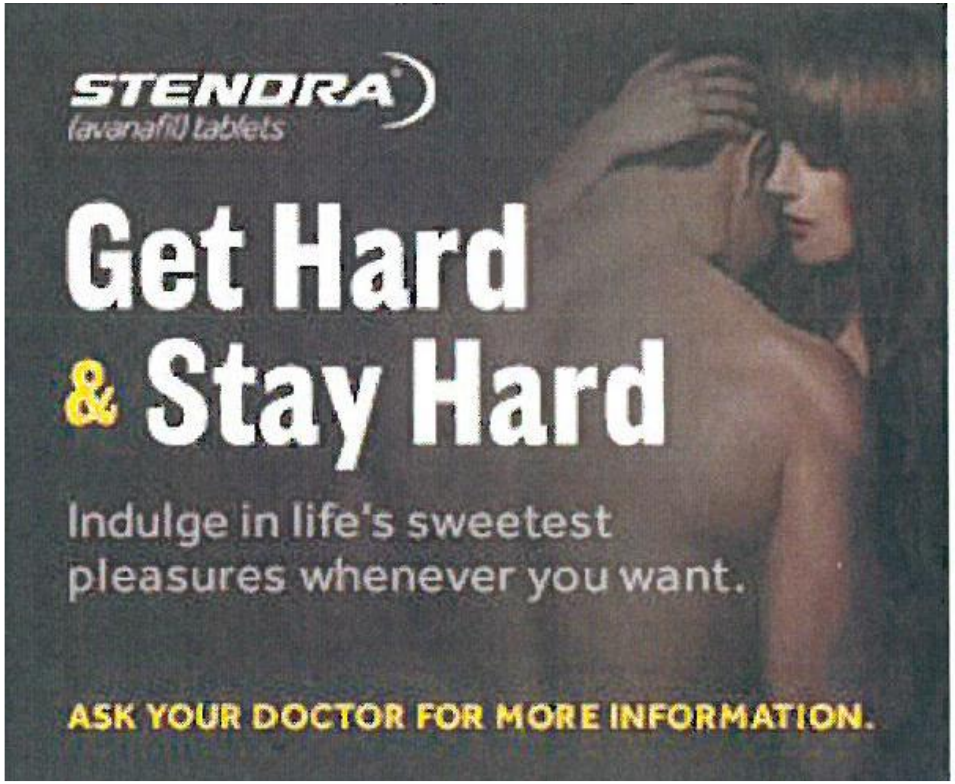
- The print ad
  - Omits serious risks associated with Stendra and fails to provide material information about the consequences that may result from its use
  - Fails to present information about risks with a prominence and readability reasonably comparable with the presentation of information related to the effectiveness, thus minimizing the risks associated with Stendra

False or Misleading Risk Presentation

- The print ad includes the following claims (underlined emphasis added)
  - "Treat ED and Reduce Risk of Heart Failure with a PDE-5 Inhibitor"
  - "Stendra (Avanafil) is … safe and effective for those with heart disease …."
  - "Stendra is the next-generation PDE-5 inhibitor that improves erectile dysfunction."

False or Misleading Risk Presentation

- The print ad
  - Omits important serious risk information for Stendra
  - Fails to present information about the risks with a prominence and readability reasonably comparable with the presentation of information related to the effectiveness
  - Implies that Stendra is safe for all patients with heart disease
  - Suggests that Stendra is safer or more effective than its competitors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(avanafil) tablets
Get Hard
& Stay Hard
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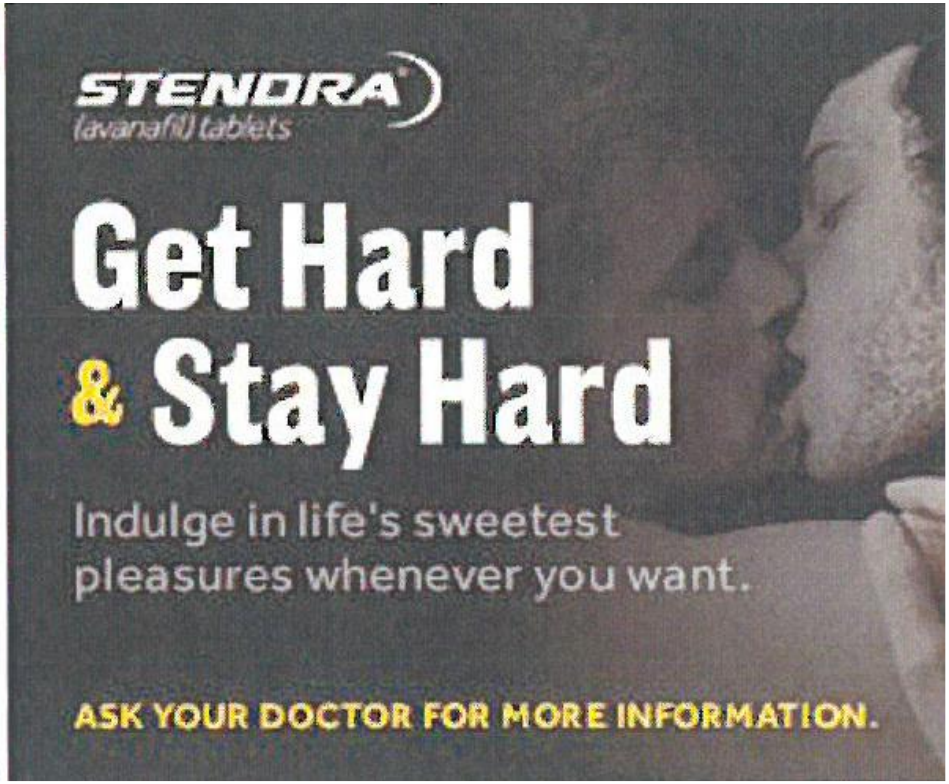
STENDRA
(avanafil) tablets
Get Hard
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Indulge in life's sweetest
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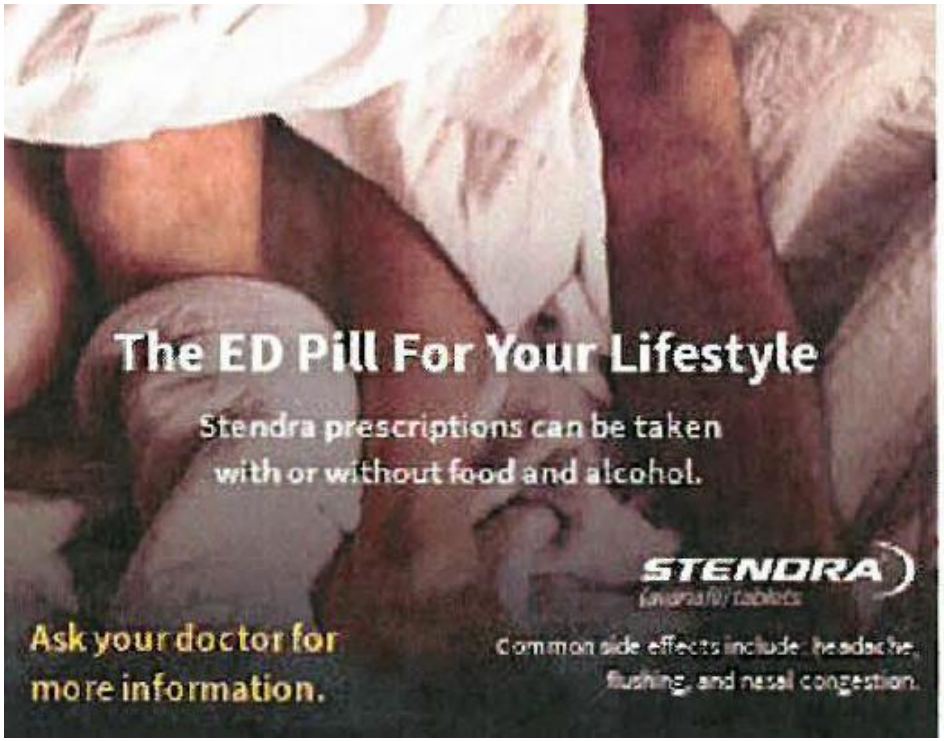
ASK YOUR DOCTOR FOR MORE INFORMATION.

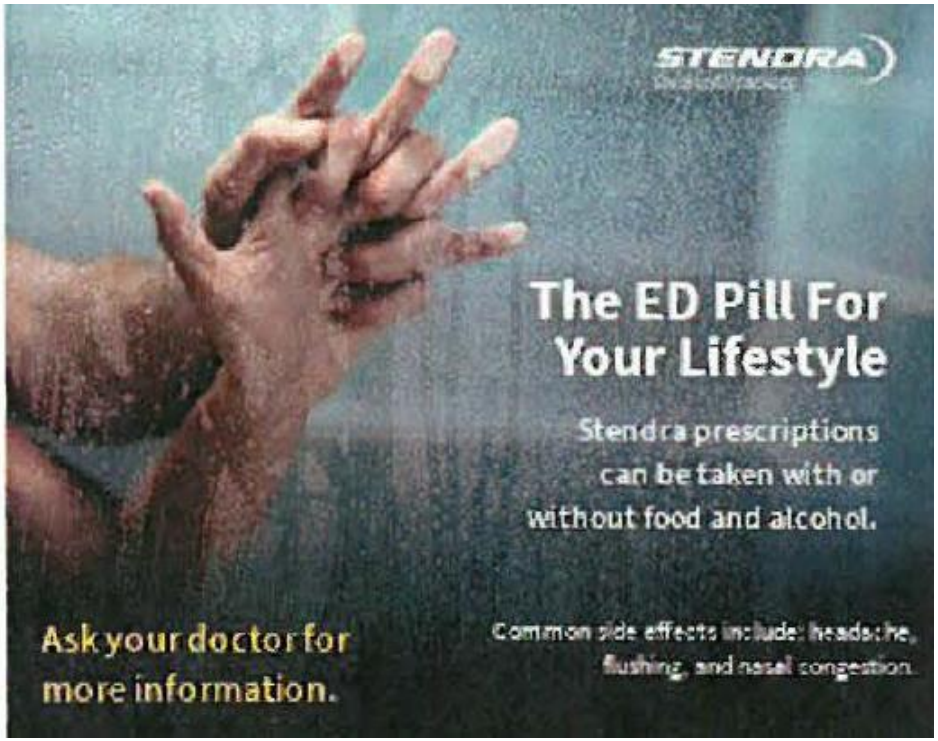
False or Misleading Risk Presentation

- The banners include the following statements but fail to communicate any risk information about Stendra:
  - "Get Hard & Stay Hard"
  - "Indulge in life's sweetest pleasures whenever you want"
  - "Ask your doctor for more information"

False or Misleading Claims about Efficacy

- The banners also fail to communicate material information regarding the indication for Stendra (underlined emphasis added):
  - Stendra is a PDE5 inhibitor indicated <u>for the treatment of erectile dysfunction</u>.


The ED Pill For Your Lifestyle
Stendra prescriptions can be taken with or without food and alcohol.
STENDRA
Ask your doctor for more information.
Common side effects include: headache, flushing, and nasal congestion.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Stendra prescriptions can be taken with or without food and alcohol.
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Common side effects include: headache, flushing, and nasal congestion.

False or Misleading Risk Presentation

- The banners include the following statements but fail to include any of the contraindications or warnings:
  - "The ED Pill For Your Lifestyle"
  - "Stendra prescriptions can be taken with or without food and alcohol"
  - "The Fast-Acting ED Prescription"
  - "Common side effects include: headache, flushing, and nasal congestion"
  - "Ask your doctor for more information"

OPDP Web Resources

- OPDP Home Page
  - http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm090142.htm
- Guidances
  - http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm109905.htm#Guidances
- Social Science Research
  - https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm090276.htm
- Warning and Untitled Letters
  - www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCcompanies/default.htm

OPDP Contact Information

- **Telephone Number**
  - 301-796-1200
- **Fax Numbers**
  - 301-847-8444
  - 301-847-8445
- **Submission Address**
  - Food and Drug Administration
    Center for Drug Evaluation and Research
    Office of Prescription Drug Promotion
    5901-B Ammendale Road
    Beltsville, MD 20705-1266


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ADMINISTRATION