Case Study

QSYMIA®

(phentermine and topiramate extended-release) capsules, for oral use, CIV

Bad Ad Case Study

Qsymia® (phentermine and topiramate extended-release) capsules, for oral use, CIV

Facilitator Guide

Approximate Time: 30 minutes

Exercise prerequisite:

Students should view the Bad Ad e-learning course located at www.fda.gov/BadAd prior to completing this exercise.

Student Materials:

Before the exercise:

- Qsymia webpage
- Prescribing Information (PI) for Qsymia

After the exercise:

- FDA Untitled Letter for Qsymia

Facilitator Materials:

- Facilitator guide (includes a detailed answer key for the case study)

Facilitator instructions:

1. Distribute the Qsymia webpage along with the PI for Qsymia.
2. Present the Background and Case Study Instructions shown below.
3. Allow students approximately 10 minutes to review the Qsymia webpage.
4. Use the discussion questions in this guide to assist students in identifying prescription drug promotion issues of concern, including false or misleading statements.
5. After discussing the issues of concern, distribute the FDA Untitled Letter for Qsymia.

Background and Case Study Instructions[1]:

This promotional piece was the homepage of the consumer website for Qsymia. Below are the indication and summary of the most serious and most common risks associated with the use of Qsymia. According to the PI:

> 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
>
> Limitations of Use
>
> - 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.

Qsymia is contraindicated in pregnancy, glaucoma, hyperthyroidism, during or within 14 days following the administration of monoamine oxidase inhibitors, and in patients with a known hypersensitivity or idiosyncrasy to the sympathomimetic amines. The PI for Qsymia contains warnings and precautions regarding fetal toxicity, increases in heart rate, suicidal behavior and ideation, acute myopia and secondary angle closure glaucoma, mood and sleep disorders, cognitive impairment, metabolic acidosis, elevation in creatinine, potential risk of hypoglycemia in patients with type 2 diabetes mellitus on anti-diabetic therapy, potential risk of hypotension in patients treated with antihypertensive medications, CNS depression with concomitant CNS depressants including alcohol, potential seizures with abrupt withdrawal of Qsymia, patients with renal impairment, patients with hepatic impairment, kidney stones, oligohidrosis and hyperthermia, hypokalemia, and monitoring laboratory tests. The most common adverse reactions associated with Qsymia are paraesthesia, dizziness, dysgeusia, insomnia, constipation, and dry mouth.

Using the PI as a reference, identify the issues of concern on the webpage. (Approximately 10 minutes)

[1] When FDA reviews a promotional piece, it determines whether the relevant legal and regulatory requirements are met, including whether the piece is truthful and not misleading, in light of the information available at that time.

Discussion Questions:

General

1. What are the key promotional messages for Qsymia on the webpage?

2. Based on your knowledge and information from the PI, which claims, if any, do you think are false or misleading?

Specific

1. Is there evidence to support the following claims on the webpage (bolded emphasis original, underlined emphasis added)?

    - "**On average, prescription Qsymia can help you lose weight 3 times <u>faster</u> than diet and exercise alone.**"

    - "**3X**
      <u>FASTER</u> WEIGHT LOSS"

    (See Detailed Answer Key #1 – False or Misleading Claims about Efficacy)

2. Is there adequate context provided in the following claims (emphasis original)?

    - "For patients with a body mass index (BMI)* of 30+† or 27 kg/mg^2 or greater (overweight) in the presence of at least one weight-related medical condition.

      Lose weight and keep it off with Qsymia
      . . . .

      12 Weeks
      Your first milestone
      15-19 Pounds of weight loss 2-3 inches off your waist

      28 Weeks
      Stay motivated
      22-29 Pounds of weight loss 3-4 inches off your waist

      56 Weeks
      Maintain progress
      24-32 Pounds of weight loss 4-5 inches off your waist"

    (See Detailed Answer Key #2 – False or Misleading Claims about Efficacy)

3. Does the webpage adequately communicate adverse events and other risks associated with Qsymia?

   (See Detailed Answer Key #3 – False or Misleading Risk Presentation)

Detailed Answer Key

1. False or Misleading Claims about Efficacy

The webpage includes the following claims (bolded emphasis original, underlined emphasis added):

- "**On average, prescription Qsymia can help you lose weight 3 times <u>faster</u> than diet and exercise alone.**"

- "**3X**
  <u>FASTER</u> WEIGHT LOSS"

These claims misleadingly suggest that Qsymia can help patients lose weight 3x faster than diet and exercise alone. According to the CLINCIAL STUDIES section of the PI, the co-primary efficacy outcomes measured the amount of weight loss after 1 year of treatment (a fixed point in time) as the percent of weight loss from baseline weight and treatment response (defined as achieving at least 5% weight loss from baseline). These studies were designed to evaluate the <u>amount</u> of weight loss and cannot be used to support claims regarding <u>rate</u> of weight loss.

The sponsor did cite data on file of calculated ratios of the amount of weight loss at specific points in time from the clinical studies. However, again, these calculations do not support claims regarding the rate of weight loss, since the clinical studies were designed to evaluate the <u>amount</u> of weight loss, rather than the <u>rate</u> of weight loss.

2. False or Misleading Claims about Efficacy

The webpage includes the following claims (emphasis original):

- "For patients with a body mass index (BMI)* of 30+† or 27 kg/mg^2 or greater (overweight) in the presence of at least one weight-related medical condition.

  Lose weight and keep it off with Qsymia
  . . . .

  12 Weeks
  Your first milestone
  15-19 Pounds of weight loss 2-3 inches off your waist

  28 Weeks
  Stay motivated
  22-29 Pounds of weight loss 3-4 inches off your waist

56 Weeks
Maintain progress
24-32 Pounds of weight loss 4-5 inches off your waist"

This presentation is misleading because it omits material information from the full indication about the relative effect of diet and exercise. Specifically, it omits that Qsymia is indicated as an adjunct to a reduced-calorie diet and increased physical activity. Note that the illustrations showing an exercise bike, a bag of groceries, and a capsule are not adequate to convey to the viewer that both exercise and diet are necessary in achieving the benefits (weight management) of Qsymia. Additionally, the webpage also omits contextual information about the placebo group results and thereby, misleadingly suggests that the results are or can be attributable to Qsymia alone.

In addition, this presentation 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 weight circumference. By failing to account for an individual's baseline weight and weight circumference and omitting this context on the webpage, this presentation misleadingly implies that all patients, no matter their baseline weight or weight circumference, should expect to see results similar to the absolute numbers presented on the webpage under the claims "Your first milestone," "Stay motivated," and "Maintain progress."

This presentation also 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 clinical trials. By selectively presenting the results for only the patients who remained on Qsymia without contextual information about patients who withdrew from the trial, the presentation overstates the efficacy of the product and misleadingly implies that all patients who received Qsymia remained on treatment.

3. 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. When looking at the risk information, it is relegated to the bottom of the webpage in paragraph format, not easily accessible to viewers; and the webpage does not present any significant signal to alert the viewer that important risk information follows the presentation of benefit information. In contrast, the benefit claims for Qsymia are presented in conjunction with colorful graphics and large bolded headlines, with significant white space. Thus, the webpage fails to present risk information in a manner that's comparable to the benefit information for Qsymia.

Discussion and Outcome

The FDA issued an Untitled Letter for this Qsymia webpage on May 22, 2019. As a result, the manufacturer for Qsymia stopped using the webpage. In addition, the manufacturer for Qsymia stopped using other promotional pieces for Qsymia that contained similar claims and presentations.