HSC 335 -- Pharmaceutical Policy (Fall 2020)

Week 8 Questions

Deadline: October 15, 2020 at 2:45pm (submit via Slack DM)

Name:

Evolution and Scope of Direct-to-Consumer Advertising

Though pharmaceutical manufacturers spend the bulk of their advertising budgets on marketing to physicians, outreach directly to patients is often another substantial facet of their promotional strategies. If you are in the US (or New Zealand, the other industrialized nation that broadly permits advertising of specific drugs to patients), you have probably seen advertisements for drugs to treat depression, cancer, erectile dysfunction, and other conditions. You may also have seen advertisements about different ailments such as restless leg syndrome that do not mention specific drugs, or social media posts promoting various products. Taken together, these direct-to-consumer advertising strategies increase drug sales by affecting patients' interactions with their physicians.

- How do branded and unbranded advertisements differ?
- What information must be included in branded advertisements?
- How have pharmaceutical manufacturers used social media to promote their products?

Question 1

Which of the following **are FALSE** regarding unbranded advertisements? (Select **all that apply**)

- ☐ Unbranded advertisements are required to disclose drug side effects.
- ☐ Unbranded advertisements are intended to raise awareness of a disease or medical condition.
- ☐ Unbranded advertisements are advertisements for generic drugs.
- ☐ Unbranded advertisements are advertisements of drug products without explicit mention of a brand-name drug.

Question 2

Instagram posts can be subject to FDA drug advertisement regulations.

- ☐ True
- ☐ False

The Case for and against Direct-to-Consumer Advertising

What are the consequences of direct-to-consumer advertising? This practice has a significant effect on consumer behavior, which can lead to problematic outcomes, but also some social positives. In this video, we will take a look at some of the ways that these ads can present drug information in unbalanced ways as well as the results of some studies analyzing the effects of direct-to-consumer advertising.

Question 3

Which of the following **are TRUE** about direct-to-consumer advertising? (Select **all that apply**)

- ☐ Direct-to-consumer advertising raises brand recognition for a drug.
- ☐ Direct-to-consumer advertising presents a balanced assessment of drug benefits and risks.
- ☐ Direct-to-consumer advertising increases the use of the drugs being advertised.
- ☐ Direct-to-consumer advertising does not cover generic drugs.

Question 4

Which of the following are examples of "implicit content" in a direct-to-consumer advertisement? (Select **all that apply**)

- ☐ Children playing on a grass field
- ☐ A photogenic person stating the side effects of a drug
- ☐ A drug container in the background of an advertisement
- ☐ Mention of the clinical symptoms associated with a disease

Question 5

What kinds of drug marketing have you observed? Which of the drug sales strategies have you observed?

Please also cut and paste your answer to this question into the appropriate section of the #discussion channel on Slack and comment on at least one other student response.

- ☐ Click the checkbox to confirm you've posted and commented on Slack.

Interview with Lisa Schwartz and Steve Woloshin

In the activity for this module, you will evaluate three drug advertisements to further your understanding of the strategies used and their effect. You will also hear the perspectives of two leading experts in the field of medical communication, Dr. Lisa Schwartz and Dr. Steven Woloshin. In the interview below, they share their thoughts on the role of direct-to-consumer advertising in the pharmaceutical market, as well as how this type of advertising is regulated.

Question 6

Identify **three** new things you learned from the conversation with Drs. Lisa Schwartz and Steven Woloshin:

Please also cut and paste your answer to this question into the appropriate section of the #discussion channel on Slack and comment on at least one other student response.

☐ Click the checkbox to confirm you've posted and commented on Slack.

Other Types of DTCA

Not all marketing is as easy to spot as the physician and direct-to-consumer advertising campaigns we have seen so far. Drug companies use a number of other strategies to promote their drugs and increase their share of the pharmaceutical market. We will next take a look at some of these approaches.

- How do drug samples affect physician prescribing practices?
- What are the effects of drug coupons on patient behaviors and health care spending?
- What is the role of funding from drug manufacturers in supporting patient assistance programs? How do these "donations" make their way back to the manufacturer?

Question 7

Free drug samples would be expected to (select all that apply)

☐ Make patients more likely to continue with that drug in the future

☐ Be frequently used by higher-income patients

☐ Increase use of generic drugs

☐ Help enhance a detailer's sales pitch

Question 8

Prescription drug coupons do which of the following:

- [ ] Lower patient out-of-pocket costs without affecting insurers' drug costs
- [ ] Lower patient out-of-pocket costs and lower insurers' drug costs
- [ ] Increase patient out-of-pocket costs and lower insurers' drug costs costs
- [ ] Increase patient out-of-pocket costs without affecting costs for insurers

Question 9

Evaluate the following statements about drug manufacturers' support of patient assistance programs and indicate if each is True or False.

Patient assistance programs offer need-based copay support.

- [ ] True
- [ ] False

Patient assistance programs reduce drug spending for insurers.

- [ ] True
- [ ] False

Question 10

Do you think allowing pharmaceutical companies to market **directly to patients** is a good idea?

- [ ] Yes
- [ ] No

Explain your answer:

Please also cut and paste your answer to this question into the appropriate section of the #discussion channel on Slack and comment on at least one other student response.

- [ ] Click the checkbox to confirm you've posted and commented on Slack.

Extent and Significance of Off-Label Marketing

After the FDA approves a drug, it can be prescribed for unapproved ("off-label") purposes. Although off-label prescribing is legal and can be an essential part of medical practice, it is difficult for physicians and patients to assess the risks and benefits of off-label uses of drugs, especially in the face of advertisements and other promotional materials that promote the benefits of such use in unbalanced ways. For this reason, the FDA limits off-label marketing of prescription drugs. Nonetheless, the potential financial incentives for pharmaceutical manufacturers are so great that every major drug company has engaged in illegal off-label promotion, leading to patient harm and substantial criminal and civil fines. As we think about the extent and significance of off-label marketing, consider:

- What are the benefits and risks of off-label use?
- What restrictions does the FDA place on off-label marketing?
- What are the consequences if a pharmaceutical company does not follow the regulations and promotes off-label use of their drug in a prohibited manner?

Question 11

Which of the following strategies can manufacturers use to communicate about off-label use of prescription drugs? (Select all that apply)

- [ ] Sponsor continuing medical education programs that discuss off-label drug uses and have certain characteristics demonstrating their independence from the manufacturer
- [ ] Highlight off-label use in print advertisements
- [ ] Engage in unsolicited discussion of the merits of off-label use in detailing visits with physicians
- [ ] Distribute reprints of peer-reviewed medical journal articles that discuss off-label uses

Question 12

Most off-label drug prescribing is not supported by the same level of evidence as would be required for FDA drug approval.

- [ ] True
- [ ] False

Question 13

What penalty do manufacturers usually face when found to have engaged in off-label promotion?

- [ ] Fines
- [ ] Loss of marketing privileges
- [ ] Imposition of risk evaluation and mitigation strategies (REMS)

Marketing as Commercial Speech

The concept of "commercial speech" – that communications proposing business transactions may have some protections under the First Amendment to the US Constitution – emerged through a series of court cases in the 1970s. Restrictions on such speech were found to be constitutional only if they pass all four components of what became known as the Central Hudson test.

As you'll see, this modern-era change in Constitutional interpretation has threatened the FDA's ability to regulate off-label promotion of drugs. In this video, we'll review the Central Hudson test and see how it was applied to the case of a pharmaceutical sales representative who made outrageous, potentially dangerous claims about off-label use of the product that he was promoting. We'll also consider the rationale for the court's decision and the strengths and weaknesses of the reasoning used.

Question 14

In the Caronia case, the court of appeals found that restrictions on truthful, non-misleading drug promotion are not permissible if there are other effective ways of preventing unsafe off-label drug use.

- ☐ True
- ☐ False

Question 15

Which are considerations in evaluating a restriction on commercial speech—like current rules relating to off-label marketing—as described in the Central Hudson case? (Select all that apply)

- ☐ The commercial speech must not be false or misleading
- ☐ The government must have a substantial interest in restricting the commercial speech at issue
- ☐ The government's restriction must directly and materially advance the government's substantial interest
- ☐ The restriction must not be more restrictive than necessary to achieve the interest.

Question 16

Disclaimers relating off-label marketing that would be included on drug labeling would likely be effective at reducing inappropriate overuse of the drug being promoted.

- ☐ True
- ☐ False

Interview with Maragret Hamburg -- Off-Label Promotion

Recent Cases

Decisions like that in the Caronia case directly threaten the FDA's ability to protect the public from misleading or exaggerated claims of benefits relating to off-label uses of prescription drugs. With the Caronia precedent, courts have taken different approaches to weighing lawsuits related to illegal off-label marketing. Let's take a look at a couple of these more recent cases, and where things currently stand.

- How did the Caronia decision affect FDA's approach to regulating off-label drug promotion?
- How have courts responded to more recent cases involving misleading advertising by drug manufacturers?
- What effects could the Caronia case have on manufacturers' decisions relating to seeking approval from the FDA for their drugs?

Question 17

In the first year after the Caronia decision, the FDA fundamentally revised its approach to regulating off-label drug promotion.

- ☐ True
- ☐ False

Question 18

If the reasoning in the Caronia case is followed, one outcome could be that drug manufacturers seek FDA approval of a new drug for the narrowest indication possible and then use information to sell their drug for unapproved purposes that would not meet the FDA's standards for determining efficacy and safety.

- ☐ True
- ☐ False

Question 19

Do you think allowing **off-label marketing** by pharmaceutical companies is a good idea?

- ☐ Yes
- ☐ No

Explain your answer:

Please also cut and paste your answer to this question into the appropriate section of the #discussion channel on Slack and comment on at least one other student response.

- ☐ Click the checkbox to confirm you've posted and commented on Slack.

Interview with Commissioner Hamburg -- DTCA

Advertisement Analysis

In the capstone activity for this module, you will analyze advertisements for three different prescription drugs.

Using what you've learned about how pharmaceutical manufacturers promote their products in direct-to-consumer advertising, you will look at a print ad, a video ad, and an online ad from the perspective of an informed consumer to discover the strategies that these advertisements use to promote their products. Then, you will compare your observations with those of your peers as well as the experts, Dr. Steven Woloshin and Dr. Lisa Schwartz.

The first advertisement in our activity is a print advertisement for the brand-name testosterone product AndroGel. Take a few minutes to study the ad. As you do, think about what medical conditions you think AndroGel is meant to treat, and how the use of imagery and text could affect patients' assessment of its benefits and risks.

(see advertisement on the next page)

For something that's clear and odorless, the effects are surprisingly noticeable.

RESTORE YOUR ENERGY. RECHARGE YOUR LIFE. **VISIT WWW.ANDROGEL.COM**

Indication: AndroGel is indicated for replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.

Safety information: AndroGel must not be used if you have known or suspected prostate cancer or breast cancer (a rare condition for men). AndroGel must not be used by women who are pregnant, may become pregnant, or breastfeeding, as testosterone may cause fetal harm.

The major risks of AndroGel include prostate enlargement, prostate cancer, and transfer of testosterone to others (including women and children). Transference can occur when vigorous skin-to-skin contact is made with the application site and can be minimized by washing your hands after application and covering the application site with clothing.

The most common adverse events reported are skin irritation where gel is applied, breast development or tenderness, acne, prostate enlargement, changes in lab test results, and changes in urinary habits.

Remember, the information in this ad does not take the place of the advice you get from your doctor or other health care professional. Always talk with your doctor if you have questions about AndroGel.

Please see Patient Information on next page.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.FDA.gov/medwatch or call 1-800-FDA-1088.

AndroGel is a registered trademark of Unimed Pharmaceuticals, LLC, a Solvay Pharmaceuticals, Inc. Company.

Marketed by Solvay Pharmaceuticals

Partnership for Prescription Assistance

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Question 20

Based on the ad, which of the following conditions do you think AndroGel is intended to treat? In the second part of this activity, briefly describe how the ad's imagery and/or text support your choice.

- ☐ Low energy due to aging
- ☐ Lack of libido due to low testosterone
- ☐ Low testosterone due to aging
- ☐ Low testosterone due to a disorder or injury
- ☐ Another condition

Explain why you chose this answer:

Now let's see what Drs. Schwartz and Woloshin have to say about the ad for AndroGel. Did you notice everything that they did?

Rising Tide

For our second ad, let's take a look at a television commercial. This one is an unbranded advertisement about heart failure. How does this ad make you feel? If you compare this ad to TV ads that you've seen for specific drugs, or to the AndroGel ad that we just reviewed, what information is missing from this "unbranded" ad that is present in other advertisements?

Question 21

Share your response and observations about this ad below.

How did the ad make you feel? Why? What information is missing from this ad that is present in branded advertisements?

Please also cut and paste your answer to this question into the appropriate section of the #discussion channel on Slack and comment on at least one other student response.

☐ Click the checkbox to confirm you've posted and commented on Slack.

Now, we'll hear what Drs. Schwartz and Woloshin had to say about this ad.

(No questions associated with this video.)

Dry Eye Quiz

Finally, we have an Internet advertisement. Restasis is a prescription eye drop that is FDA approved "to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca," otherwise known as dry eye. Visit this site, review the information there, and take the dry-eye quiz. Try taking the quiz more than once, changing your answers to see what happens – you may be surprised!

Question 22

Below (and in the #discussion channel on Slack), share your observations about the Restasis ad. Briefly describe something that you found interesting or surprising about the ad.

Please also cut and paste your answer to this question into the appropriate section of the #discussion channel on Slack and comment on at least one other student response.

☐ Click the checkbox to confirm you've posted and commented on Slack.

Now, we'll hear what Drs. Schwartz and Woloshin had to say about this ad.

(No questions associated with this video.)

Case 1: Lampytinib

Use the information below, and your understanding of the course material, to answer the questions that follow. If you have questions about the quiz or need clarification, you can post to the discussion forum at the bottom of the page, but do NOT post answers or ask for the answers to the quiz questions on the forum. Any posts that specifically discuss answers to the quiz questions will be deleted by the discussion forum moderators.

Assume that the hypothetical drug lampytinib is FDA-approved to treat Merkle Cell carcinoma, a rare form of skin cancer, and is manufactured by the fictional pharmaceutical manufacturer OLP Pharma. OLP organizes another clinical trial of lampytinib for a rare form of bone cancer called osteosarcoma. The primary endpoint of the trial showed no change in overall survival. However, when they re-analyzed the data in a different way, focusing on only patients with osteosarcoma in the long bones of the extremities, there did appear to be a statistically significant increase in overall survival of 4 months.

Shortly after the osteosarcoma trial ended, OLP Pharma sent out its marketing representatives to physicians' offices with a copy of the publication of the trial and other promotional materials in which the re-analyzed data were prominently presented. Sales of the drug doubled over the next three years due to increased use of lampytinib among osteosarcoma patients.

However, this sort of data re-analysis of trial results is not definitive and is generally understood to be useful as a hypothesis-generating exercise only. In fact, a follow-up study organized by OLP Pharma that sought to prospectively evaluate the efficacy of lampytinib specifically in long-bone osteosarcoma—which involved 182 patients in 12 centers across the world—showed no survival difference between patients receiving the drug and placebo (median survival of 14 months vs 15 months). In other words, the results from the post-hoc analysis of the earlier trial were not supported by the new study.

Question 23

Other marketing strategies used by OLP Pharma to generate prescriptions of lampytinib for osteosarcoma might have included

- ☐ large displays at oncology medical conferences in which sales representatives seek to engage conference attendees.
- ☐ setting up a website featuring a celebrity survivor of osteosarcoma to promote screening for the disease among at-risk patients.
- ☐ coupons for physicians to give their non-Medicare patients for 50% off their copayment for a lampytinib prescription.
- ☐ All of the above.

Question 24

Distributing the peer-reviewed publication of the clinical trial discussing the off-label use of lampytinib for long-bone osteosarcoma would be permitted as an exception to FDA's marketing rules; another such exception would cover distribution of

- ☐ the promotional materials, since osteosarcoma is a life-threatening disease.
- ☐ clinical practice guidelines that recommend lampytinib as treatment for osteosarcoma.
- ☐ television advertisements describing results of the published study.
- ☐ vouchers for free cruises to physicians who prescribed the most lampytinib for osteosarcoma.

Question 25

If an OLP Pharma marketing representative decided set up a session in which a group of local oncologists would get together for dinner to talk about lampytinib's use in osteosarcoma with a regional osteosarcoma clinical expert

- ☐ the payment would have to be listed in the Open Payments Database.
- ☐ FDA rules require that alcohol not be served at the event.
- ☐ such an event cannot qualify for Continuing Medical Education credits.
- ☐ the price of lampytinib is off-limits for discussion.

Question 26

The government sought to charge OLP Pharma with improper off-label marketing. Under the Caronia standard, OLP Pharma's lawyers cited that the abstract was true and non-misleading. How could government lawyers have tried to rebut this claim?

- ☐ By describing how the abstract did not present both the positive and negative conclusions of the trial.
- ☐ By pointing out that post-hoc subgroup analyses are not reliable and are hypothesis-generating exercises at best.
- ☐ By arguing that if OLP Pharma had a definitive prospective trial underway, it would have only been true and non-misleading if they had disclosed that as well.
- ☐ By contending that OLP Pharma should have also disclosed that the primary endpoints of the trial were negative.
- ☐ All of the above.

Case 2: Disease Awareness

Disease Awareness Campaigns

Use the information below, and your understanding of the course material, to answer the questions that follow. If you have questions about the quiz or need clarification, you can post to the discussion forum at the bottom of the page, but do NOT post answers or ask for the answers to the quiz questions on the forum. Any posts that specifically discuss answers to the quiz questions will be deleted by the discussion forum moderators.

Disease awareness campaigns are intended to influence how physicians and the public think about what constitutes disease and when drugs are needed. They can involve celebrity endorsers, television and magazine ads, and mobilizing industry-funded advocacy groups. The campaigns also target physicians through special journal supplements and continuing medical education.

A manufacturer of a new formulation of testosterone develops a website with a "Low T Question Quiz." The quiz consists of 10 questions including whether a person is experiencing lower libido, worse sexual performance, and changes in energy, mood, and fatigue. It ends by suggesting that patients who score 3 or higher ask their physicians about "Low T" (low testosterone level). The manufacturer's new formulation of testosterone is FDA-approved to treat hypogonadism, which causes low testosterone levels and the symptoms described. The Low T website does not mention the manufacturer's formulation of testosterone, does not link to the manufacturer's other websites that mention the drug, and does not mention the manufacturer. The website does direct patients to an online coupon repository in which they can download coupons for the new testosterone formulation (as well as other drugs).

Question 27

Disease awareness campaigns funded by brand-name manufacturers

- [ ] are useful because they bring attention to conditions that patients may not recognize.
- [ ] are misleading because in describing the condition, they neglect to mention other possible explanations for the symptoms (such as stress or depression in the case of the symptoms linked to "Low T").
- [ ] are not subject to the requirements of the Food, Drug, and Cosmetic Act relating to prescription drug promotion.
- [ ] All of the above

Question 28

Drug promotion online

- [ ] is not subject to the same basic rules and regulations as other forms of drug promotion.
- [ ] can make it challenging for consumers to recognize the influence of manufacturers on the content.
- [ ] represents the largest share of drug manufacturer's advertising budgets.
- [ ] is unlikely to reach many potential customers.

Question 29

Disease awareness campaign instruments like the “Low T” quiz

- [ ] effectively lower the bar for diagnosis, turning ordinary life experiences into conditions that require medical diagnoses.
- [ ] are often rigorously evaluated before they are released to ensure that they have appropriate sensitivity and specificity.
- [ ] cannot be fashioned to spin the evidence about drug benefits and harms.
- [ ] would have been valid if the cutoff for having the condition was a score of 5 or above on the quiz, encompassing at least a majority of the symptoms.
- [ ] are unlikely to spur patients to ask their physicians about the condition at issue.