HSC 335 -- Pharmaceutical Policy (Fall 2020)

Week 6 Questions

Deadline: October 1, 2020 at 2:45pm (submit via Slack DM)

Name:

Strategies to Extend Market Exclusivity

As we've discussed, when generic drugs enter the market, the price of the once-brand-name-only drug usually falls quickly. Naturally, brand-name manufacturers use a variety of strategies to keep generic competitors from entering the market (a process sometimes called "life-cycle management"), since each extra day of delay can mean substantial revenues. In this video, we'll explore some of these strategies, and how pharmaceutical companies use them.

- What are pay-for-delay settlements, restricted distribution networks, and citizen petitions?
- How do pharmaceutical manufacturers use these strategies to delay generic entry?

Question 1

For each of the following, indicate which characteristics apply to each drug life-cycle management strategy. Indicate all that apply.

Pay for delay settlements of patent litigation:

- ☐ Delays the availability of generic drugs.
- ☐ Patients can only receive drugs through a small number of pharmacies.
- ☐ Makes it difficult for generic drug manufacturers to compare their products to the brand-name drug
- ☐ Are often denied by the FDA

Restricted distribution networks that block generic manufacturer access to samples:

- ☐ Delays the availability of generic drugs.
- ☐ Patients can only receive drugs through a small number of pharmacies.
- ☐ Makes it difficult for generic drug manufacturers to compare their products to the brand-name drug
- ☐ Are often denied by the FDA

The filing of citizen petitions claiming safety or efficacy issues with a generic version:

- [ ] Delays the availability of generic drugs.
- [ ] Patients can only receive drugs through a small number of pharmacies.
- [ ] Makes it difficult for generic drug manufacturers to compare their products to the brand-name drug
- [ ] Are often denied by the FDA

Question 2

Pay-for-delay settlements involving brand and generic manufacturer lawsuits cannot violate antitrust law.

- [ ] True
- [ ] False

Question 3

What percent of citizen petitions pertaining to pending generic drug applications were filed with the FDA by brand-name drug manufacturers?

- [ ] 10%
- [ ] 25%
- [ ] 53%
- [ ] 87%

Combatting Strategies to Extend Market Exclusivity

Now that you understand the strategies that brand-name drug manufacturers use to delay entry of generic competitors into the market, we turn our attention to how policymakers have tried to respond to these tactics. What might the government do to prevent pharmaceutical manufacturers from delaying generic entry? In the video below, we'll look at potential legislative and regulatory solutions.

Question 4

Which of the following describes a strategy that has been proposed to address problematic life-cycle management practices that delay generic drug entry?

- [ ] Create a legal presumption that pay-for-delay settlements are anticompetitive
- [ ] Set a ceiling on the prices generic drug manufacturers can charge
- [ ] Provide free generic medications for patients who cannot pay

Question 5

A recent proposal to Congress would require brand-name manufacturers to supply generic manufacturers seeking to perform bioequivalence testing with brand-name drug samples free of charge.

- [ ] True
- [ ] False

Question 6

Do you think government intervention is needed to control prescription drug prices? If so, what type of intervention do you believe would be best?

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.

The Effect of Competition on Generic Drug Prices

While we've seen that generic drugs can dramatically reduce the prices of prescription drugs, generic drugs are inexpensive because of competition. A number of factors can influence the number of generic competitors that are available for a given drug, with corresponding consequences for their prices. As you watch the video, consider:

- How does the number of generic competitors affect prices?
- What factors might cause the price of a generic drug to increase?

Question 7

How many generic manufacturers, on average, are needed to decrease drug prices 50% relative to the branded drug product?

- [ ] 1
- [ ] 3
- [ ] 5
- [ ] 10

Question 8

Generic drugs treating rare diseases are more likely to face sudden increases in price.

- [ ] True
- [ ] False

Reasons for High Generic Drug Prices and Solutions

Brand-name drug manufacturers, consumers, and the FDA also have roles to play in maintaining a vibrant generic drug market. In particular, we'll see how advertisements by brand-name manufacturers and coupons that they provide, as well as decisions by physicians and patients, influence the use of generic drugs. We'll also see what the FDA has done and can do to increase competition in the generic drug market and help lower prices.

- How do patients' and physicians' understanding of generic drugs influence their use?
- In what circumstances might the FDA expedite generic drug applications?

Question 9

Despite a wealth of evidence on the effectiveness and safety of generic drugs approved by the FDA, about one-third of physicians and patients have been classified as being 'generic skeptics.'

- [ ] True
- [ ] False

Question 10

The FDA expedites generic drug applications in cases where the market is served by a maximum of how many manufacturers?

- [ ] 1 or fewer
- [ ] 2 or fewer
- [ ] 3 or fewer
- [ ] 4 or fewer

Question 11

A law that prevents companies from offering drug coupons if there is a generic drug available would have the greatest impact on the drug's cost if

- [ ] there is only a single generic version of the drug.
- [ ] there are numerous generic versions of the drug.
- [ ] physicians commonly write "dispense as written" on the prescription.
- [ ] there is a shortage of the drug.

Interview with Leeza Osipenko

To contrast the US drug pricing market with that of England, where the publicly-funded National Health Service (NHS) provides financial coverage of health care, we talked with Leeza Osipenko, who was the head of scientific advice for the National Institute for Health and Care Excellence (NICE). NICE is an executive body in England, and publishes guidelines relating to the use of medicines, diagnostics, and procedures by the NHS.

Question 12

What do you think about how NICE makes decisions about what products to approve? Is their approach reasonable to you?

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.

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Drug Pricing Reform -- The Approach in Germany

In the capstone activity for this module, you will put yourself into the role of an advocate for drug pricing reform in the US and consider what you think of the approach taken by two different high-income countries: Germany and England. You will consider whether or not you think the German or English system could work in the United States, or if a different approach would be more appropriate.

High prescription drug prices have been a headline issue in the US and other industrialized countries in recent years. In Germany, drug prices were found to be higher than in all but two OECD countries in 2007. Where such trends are found, they are a reflection of limited price regulation for patent-protected, brand-name drugs. For example, until earlier this decade, manufacturers in Germany could set list prices for drugs freely. Although Germany's statutory health insurers (SHIs), which insure over 90% of individuals in the country, have been able to negotiate non-disclosed rebates via a tendering process since 2007, competition via tendering has been largely limited to off-patent drugs. As a result, prices for patented brand-name drugs increased steadily.

In 2011, motivated by rising drug prices and supported by SHIs, the German parliament passed the Pharmaceutical Market Restructuring Act ("AMNOG"), which subjected new drugs to price regulation based on a formal benefit assessment. The process begins after a drug is approved by the European Medicines Agency, permitting sale within Germany. During the first year following a new

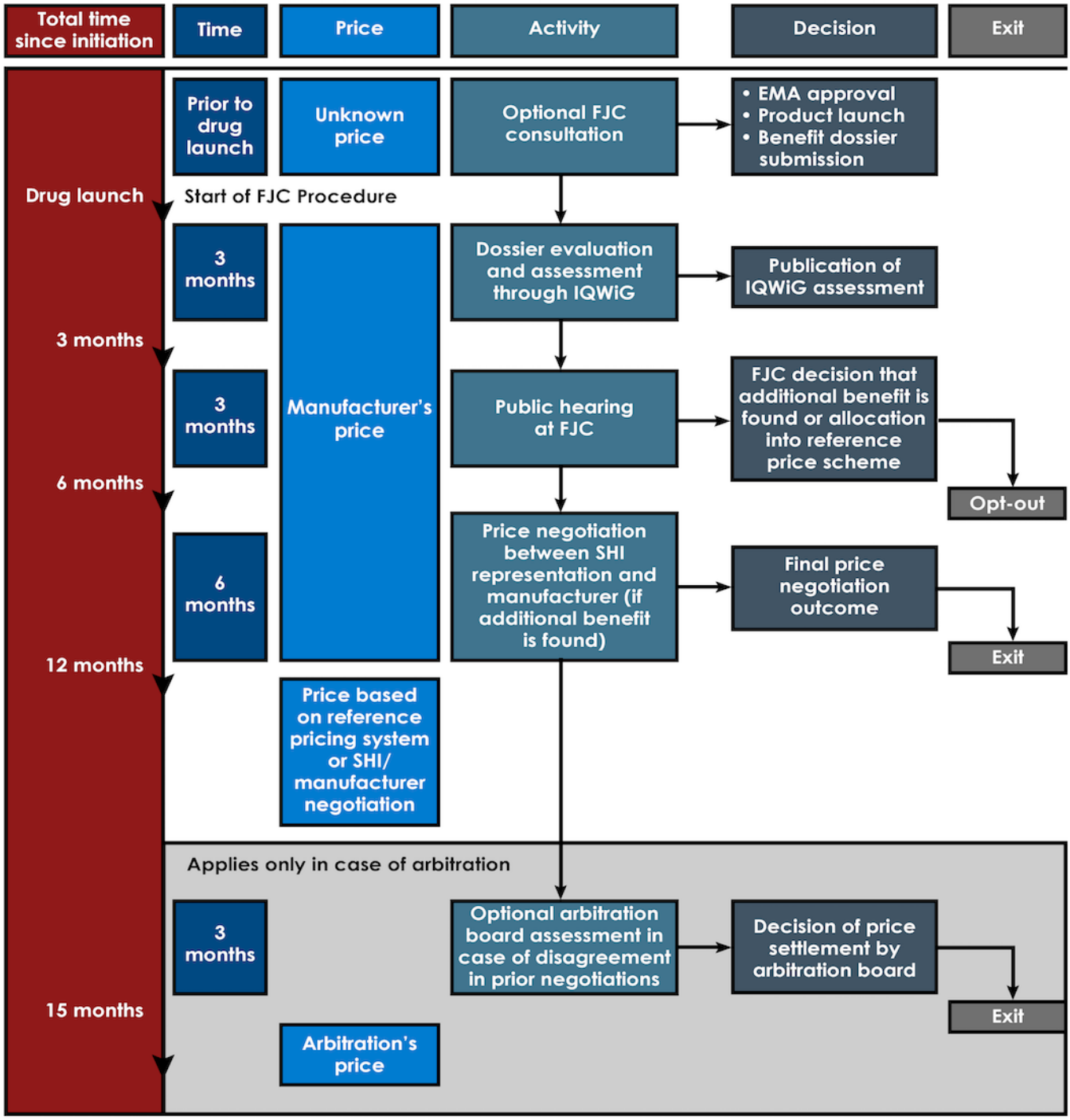
drug's launch, the manufacturer sets the drug's price and must submit a report summarizing the product's benefit to the Federal Joint Committee, the highest decision-making body of the joint self-government of physicians, dentists, hospitals, and health insurance funds in Germany.

The Federal Joint Committee forwards the report to the Institute for Quality and Efficiency in Health Care (IQWiG), an independent, non-profit institute that researches the value of medical interventions. The IQWiG must then complete a benefit assessment within three months. The evaluation is designed to take into account clinical evidence of the drug's effectiveness and follows transparent and standardized procedures. The IQWiG process includes external experts and patients' perspectives, and there is ongoing monitoring to ensure that staff members and external experts have no conflicts of interest. (You can read more about IQWiG's methods at https://www.iqwig.de.)

Following the presentation of the IQWiG's benefit assessment, the Federal Joint Committee reaches a final decision regarding the level of benefit of the new drug relative to pre-defined comparable therapies, which are identified by the committee prior to assessment. A drug is assigned to one of six benefit levels: major added benefit; considerable added benefit; minor added benefit; non-quantifiable added benefit; no evidence of added benefit; and less benefit than the appropriate comparator. If the benefit assessment falls into any of the first four categories for any patient subgroup, the Federal Joint Committee gives a positive benefit rating for the indication as a whole, and price negotiations begin.

After the Federal Joint Committee's decision, a manufacturer must decide how to proceed with the German market. If the manufacturer is unsatisfied with the outcome of the Federal Joint Committee's evaluation (e.g., after receiving a negative benefit assessment, which puts the manufacturer in a weak position for price negotiations), it can choose to opt-out and withdraw its drug from Germany within four weeks. An opt-out at this point prevents a negotiated price from being published in the official German drug price list, which can be referenced by other countries' price-setting bodies.

If the manufacturer decides to keep its product in the German market, the AMNOG process proceeds to price negotiations with the SHI umbrella organization. Over the course of six months, the parties are expected to come to an agreement regarding the drug's price. If there is no proof of additional benefit relative to the pre-selected comparator drug(s), the new drug can be directly placed into a reference price group, in which the price cannot be set higher than the other reference group members. If the reference group includes low-cost generics, this could mean quite a low price. However, if a reference price group is not available (because the new drug provides some benefit over comparable therapies), price negotiations begin from the point at which the annual cost of therapy with the new drug is no higher than the annual cost of therapy with its comparator(s). If the SHI umbrella organization and the manufacturer cannot agree on a fair price, an arbitration board is assigned to set a price within three months. Following arbitration, a manufacturer can decide again to exit the German market. The figure below summarizes the major steps in the AMNOG process over the 15-month period immediately following a drug's market entry and indicates potential market exit points for manufacturers during the process.



Key to abbreviations: FJC (Federal Joint Committee), EMA (European Medicines Agency), IQWiG (German institute for quality and economics in Health Affairs)

Question 13

Compare the German system described here with the American pharmaceutical market and how manufacturers establish prices. Which system do you prefer? Describe your reasoning below and post it to the #discussion forum on Slack.

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.

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It was initially feared that important new drugs would be driven from the German market by this system. However, a recent study (Pietrulla et al., Health Affairs, 2019, which also serves as the source of this exercise) found that in the early years of the new legislative framework, only a minority of new drugs subsequently exited the German market. A positive clinical benefit assessment predicted a higher likelihood of remaining on the market, while a negative clinical benefit assessment was a strong predictor of subsequent market exit.

Question 14

Discuss why you think the early fears have not materialized thus far.

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.

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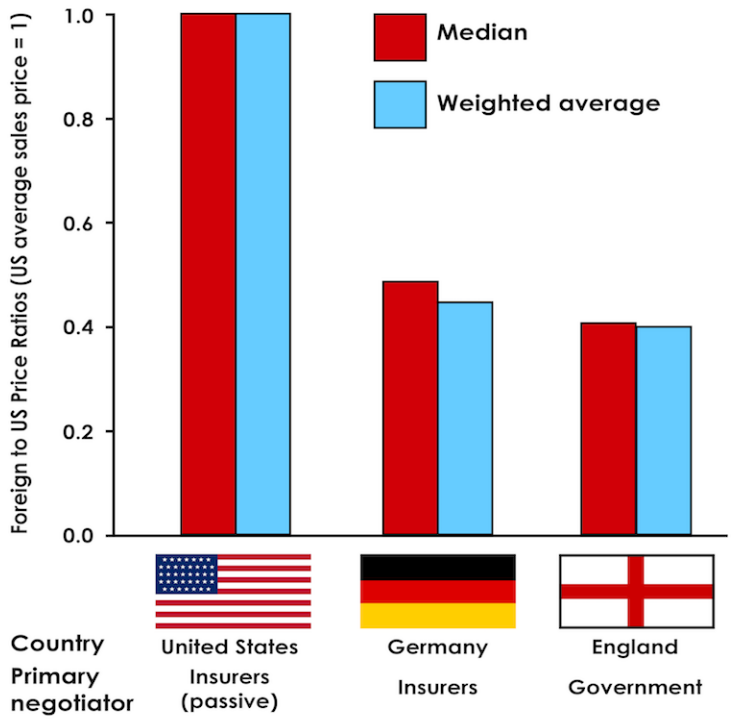
Drug Pricing Reform -- The Approach in England

As previously described by Dr. Leeza Osipenko, England's system of pharmaceutical price determination is highly centralized and very effective at controlling drug prices. One single agency – the National Institute for Health and Care Excellence (NICE) – is responsible for drug reimbursement decisions for the entire National Health Service (NHS). If NICE recommends a new drug, the constitution of the NHS states that it must be made available within 3 months.

As part of this process, an independent academic center evaluates a manufacturer's evidence submission and completes an evidence report that considers both the clinical and cost-effectiveness of a new drug product, using metrics like QALYs (quality-adjusted life-years External link External link, which can be used to determine how great a benefit is provided by a drug). An advisory committee then produces a final recommendation. In general, NICE is unlikely to recommend any new treatment with a cost-effectiveness ratio above £20,000 – £30,000 per QALY gained. However, some high-cost cancer drugs that are not recommended by NICE for cost-effectiveness reasons may still be made available to patients through a federally-funded Cancer Drugs Fund.

England also engages in risk sharing agreements with manufacturers. For example, in exchange for a positive recommendation for the use of lenalidomide (Revlimid) in multiple myeloma, the manufacturer agreed to pay the drug costs for patients who remain on treatment beyond 2 years (Luo and Kesselheim, Harvard Health Policy Report, 2016).

The figure below shows relative prices of a sample of drugs covered in the US by Medicare Part B, as well as comparative prices in Germany and England. As demonstrated, non-US pricing strategies lead to substantial (>46%) cost savings (Hwang et al, JAMA Internal Medicine, 2019).



Question 15

Compare the English system to the German system described earlier. Which system do you prefer? Explain your reasoning in 100 words or less.

- ☐ I prefer the German system.
- ☐ I prefer the English system.
- ☐ I think that both systems are equally good.
- ☐ I think that both systems are equally problematic.

In 2014, NICE declared eculizumab (Soliris) to be a cost-effective use of NHS resources. Eculizumab treats a rare and potentially fatal condition called atypical haemolytic uremic syndrome (aHUS), which is thought to affect just 200 people per year in England. aHUS causes inflammation of the blood vessels and formation of blood clots throughout the body, which can lead to multiorgan failure. Eculizumab has an annual price tag of around £340,000 per patient and coverage was predicted to cost the national health service up to £58m in the first year, rising to £82m after five years. In response, NICE added some additional requirements, such as that treatment with the drug must be coordinated through an expert center and eculizumab patients be followed in a registry. There would also need to be created a national protocol for starting and stopping eculizumab for clinical reasons.

The case of Soliris

Question 16

Do you think it is reasonable for the English National Health Service to spend almost £100m in a single year on a drug indicated for just 200 patients?

- ☐ Yes
- ☐ No

Case 1: Asparzanab

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.

It is well-known that US brand-name drug prices are far higher than those in other high-income countries around the world. In 2018, the US presidential administration unveiled an international price reference proposal for some Medicare drugs in which drug prices would be determined based on the average or lowest price paid by comparable non-US payers. Asparzanab is a drug approved in the US and the UK for advanced pancreatic cancer, which has a poor survival prognosis. Pivotal trial results show a small and statistically significant median overall survival gain of 1.8 months for asparzanab (5.8 months) compared with best supportive care (4.0 months). Asparzanab is sold in the US at a list price of $30,000 for a course of therapy, and sold in the UK for $8,500 for a course of therapy.

Question 17

The price of asparzanab in the US

- [ ] is set at a level at which it will earn back its cost of development, plus a 20% profit margin, by the expected date of generic entry.
- [ ] is more likely to be closer to the "value-based" price of the drug than the price offered in the UK.
- [ ] was approved by the FDA at the same time the FDA approved the drug for use in US patients.
- [ ] reflects manufacturers' estimates of what it believes the US market will bear.

Question 18

The efficacy of asparzanab as noted in its pivotal trials

- [ ] is likely reflected in its US price.
- [ ] is likely reflected in its UK price.
- [ ] is irrelevant in determining a "value-based" price for the drug.
- [ ] is so small as to be clinically insignificant for all patients.

Question 19

Implementing an international reference price for US drug prices, in the case of asparzanab, would

- ☐ not have an effect in this case since the prices in the US and UK are close enough.
- ☐ not affect the price of asparzanab, since this price is likely close to the cost of manufacturing and cannot be reduced any further.
- ☐ likely reduce the price of asparzanab in the US, but also might collaterally affect the price being offered in the UK.
- ☐ not be relevant since the clinical efficacy of asparzanab is too slight.

Case 2: Reducing Generic Competition

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.

As a brand-name manufacturer selling a capsule version of a cholesterol-lowering medication approaches the end of its market exclusivity, the manufacturer issues a tablet version of its product at all the same doses. The tablet has a patented coating to protect against excessive disintegration by saliva. The secondary patent (on the coating of the pill) lasts for an additional 10 years. About 1 year before the generic version of the capsule is supposed to be introduced, the manufacturer pulls its capsule off the market and starts selling only the tablet version.

Two generic manufacturers challenge the brand-name manufacturer's tablet coating patent in court, arguing that the patent was improperly granted for being too obvious in light of other tablet coatings in widespread use. While the patent challenge litigation is underway, the brand-name manufacturer issues its own 'authorized generic' version of the tablet at a 25% discount to the brand-name product. It also settles the case with the 2 generic manufacturers and agrees to let these manufacturers sell their generic products in another 5 years and to let them share in the overseas marketing rights to the coated tablet in exchange for their dropping their lawsuits.

Five years later, as the generic entry date approaches, the brand-name manufacturer issues coupons to patients taking the drug. The coupons suggest that patients tell their physicians to write "dispense as written" so that they can receive the original version of the product and provide a full refund of their copayment amount for the brand-name version.

Question 20

From the brand-name manufacturer's point of view, pulling its capsule version off the market 1 year before generic entry

- ☐ was a bad idea because the manufacturer lost 1 year of revenue from this successful product.
- ☐ was inconsequential because a generic manufacturer could have still come on the market with the capsule anyway.
- ☐ was a strategic move to switch current patients onto the coated tablet version, which had many years remaining on its market exclusivity.
- ☐ was unnecessary since pharmacists are allowed to automatically dispense tablets in place of capsules as long as both are the same dosage strength.

Question 21

The patent litigation settlement between the brand-name and generic manufacturers

- ☐ was a positive outcome for patients because the generic manufacturers entered the market 5 years sooner than they would have in the absence of the litigation.
- ☐ was a positive outcome for overseas patients, which balances out any possible harms to US patients.
- ☐ was a negative outcome for patients since challenges by generic manufacturers to "secondary" patents such as the ones on the coating of the pill often lead to the patent being overturned and rapid generic entry.
- ☐ was legal as long as no cash was exchanged between the brand-name and generic manufacturer.

Question 22

The drug coupons employed in this case

- ☐ are unlikely to work because "dispense as written" requests are rarely permitted by state pharmacy laws.
- ☐ reduce out-of-pocket costs for patients but drive up health care costs overall since the majority of a brand-name drug's price is often covered by the insurer.
- ☐ are illegal in all but 2 states.
- ☐ represent an antitrust violation that puts the manufacturer at risk of investigation by the Federal Trade Commission.