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Feedback in Response to Senator Grassley and Senator Wyden's Report: The Price of Sovaldi and its Impact on the US Health Care System

Responses to question 5: What kind of tools currently exist, or should exist, to address the impact of high cost drugs and the corresponding access to restrictions, especially on low-income populations and state Medicaid programs?

Our current system of medical care in the United States will result in an unsustainable increase in drug prices. The Senate Finance Committee investigation into the pricing practices used by Gilead to establish a list price for Sovaldi and design discounts and rebates did not find a "smoking gun" of illegal activity. Each of the described actions taken by Gilead to set prices are employed by all of the for-profit pharmaceutical companies in the US. Pharmaceutical companies price drugs to maximize profits because that is their primary obligation as for-profit companies. Market research, benchmarking, and economic analyses are performed to determine the maximum price payers will bear to treat the most urgent sub-populations with an indicated disease.

Companies are allowed to determine prices based on these approaches because of capitalism, which encourages innovation, risk-taking, and investment, and where the reward is maximal financial returns. Pharmaceutical companies fulfill these criteria since drug development is highly risky (an estimated 1 out of 100 drug candidates ever reach FDA approval) and expensive (pre-clinical discovery to completion of NDA filing and marketing approval can cost \$1 billion). However, unlike many other products that compete in a market (such as cars or TVs) early drug development is often financially supported by government (taxpayer) grants, research is often performed in hospitals that receive government funding for training and care and non-profit taxpayer status, and approved drugs are paid for with taxpayer money (such as Medicare, Medicaid, state prisons and jails, and government agencies under the Federal Supply Schedule). In addition, the patent system creates monopolies that reduce the ability for competition to drive down prices. It is an uncomfortable truth that a company is fulfilling its fiduciary responsibility when it maximizes prices, and the consequences may include some patients being unable to access needed treatment.

An additional pressure on US prices is that, in general, about 50% of revenues are generated from the U.S, 30% from western Europe, Japan and Australia, and 20% from the rest of the world. Companies' market value is based on the assumption that companies can generate maximal revenue from the US because the payer system is so fragmented and there are few opportunities for large-scale negotiations like European countries can perform. The 111 countries for which Gilead provided voluntary licenses were not expected to generate significant revenue anyway.

Current trends in drug pricing may exacerbate the trend to higher prices. “Personalized medicine” allows for sub-populations or “niches” of patients to be defined who can justify premium pricing, much like orphan drugs. “Value-based medicine” has been used as another justification for maximizing prices using lifetime models that don’t account for immediate budget impact. However, proposals that threaten to over-ride the current system, such as eliminating patent protection, betray the current bargain investors have struck with pharmaceutical companies and could lead to financial distress with unknown consequences for access to new medications.

My assumptions with the following observations and suggestions include that the US medical system will remain multi-payer with a mix of public and private payers and a capitalist approach to pharmaceutical companies pricing drugs will be maintained. In general, I believe that encouraging volume-based pricing strategies is the best way to provide economic incentives for companies to reduce prices for individual patients, which will translate into more patients having access to medications. Right now, companies are caught in a vicious cycle where they are not willing to abandon premium pricing unless they are given guarantees that payers will lift restrictions and allow more patients to be treated, but payers are not willing to lift restrictions (and provide the patient volume that helps companies justify lower individual prices) without assurances that their short term budget impact will be manageable.

We have a unique opportunity to promote **volume-based pricing** for hepatitis C drugs in the US in light of the Institute of Medicine panel evaluating the feasibility of eliminating HCV in the US. In order to eliminate HCV, we would need to dramatically increase treatment rates in Medicaid populations, the incarcerated, and other groups that currently have poor access to HCV treatment because of high prices. If each state developed a comprehensive plan for eliminating HCV, they should be able to demonstrate how many patients they would need to treat, which should help facilitate volume-based pricing.

State Medicaid and Corrections:

There is justification for increased control of pricing of drugs reimbursed by public payers since the government has an obligation to use public resources efficiently and maintain the health of the population that is dependent on this care.

1) Publish the actual price paid for each drug by each state Medicaid taking into account all discounts and rebates. This is the public’s money and the public has a right to know how its money is being spent. This will also facilitate advocacy since state-level decisions on how much to spend for various diseases and treatments have societal, political, and public health implications. This could be updated biannually with a disclaimer that actual price determinations may lag due to the timing of rebates, etc.

- 2) Allow CMS/national Medicaid to facilitate collective negotiation by all state Medicais. The volume of patients represented by all 50 state Medicaid organizations, collectively, should allow for significant volume-based pricing.
- 3) Facilitate state carve outs that shift hepatitis C drug costs from managed care Medicaid to fee-for-service Medicaid if a state choses this option, as is being done in Washington state. Managed care Medicaid organizations do not believe that their contracts cover the cost of providing all patients access to antiviral treatment for hepatitis C. In addition, most states require that the 23.1% rebate be given back to the state. Many managed care plans are smaller and do not have strong negotiating power, so these small plans are paying high prices for HCV treatment. This leads to substantial variation in patient access to HCV treatment in each state, which is illegal per CMS.
- 4) State corrections have little negotiating ability and often pay some of the highest prices for drugs. This is our taxpayer money. Allow state and county jails and prisons to use Medicaid fee-for-service pricing (automatic and negotiated rebates) in each state or allow them to use the prices negotiated by the Veteran's Administration. Exclude them from Medicaid "best price" calculations (see below).
- 5) Encourage state department of public health to purchase drugs for conditions with high public health need such as hepatitis C under the Federal Supply Schedule for use in drug rehabilitation programs and other public health venues (and possibly state and local prisons and jails)

Payers that are impacted by Medicaid Best Price:

Pharmaceutical companies refuse to give private plans, state prisons, and other payers who are impacted by "best price" requirements substantial discounts because it will automatically lower the price they receive in all state Medicais. This ends up decreasing the ability to develop innovative payment and pricing structures.

Suggest: Allow for an exception process under "best-price" regulations. Currently, best price is calculated as a simplistic best-price-per-pill. This is meant to prevent companies from submitting high average-wholesale-producer prices (from which a 23.1% discount is applied for Medicaid) that nobody actually pays. However, it also prevents innovative pricing. For example:

The Veteran Administration (which negotiates prices for all FSS agencies) is not subject to best-price so it has substantial flexibility for innovative pricing.. It can negotiate volume-based discounting where the first patients treated pay a higher price, but once that number is exceeded, the next patients have a lower price. Another option is paying a flat fee, after which an unlimited number of patients can be treated.

Some countries negotiate "pay for cure" so they don't pay for treatment that does not work. In this case, some treatment would be free and could be considered that best-price.

Some countries negotiate the same price for treatment, regardless of duration. For example, the AbbVie regimen, Viekira Pak, can be given for 12 weeks for most patients, but this regimen does not work as well for certain patients groups, and

these need 24 weeks. It does not make sense to pay twice as much for a cure for some patients just because a particular regimen is less potent in that group. But if some patients received 24 weeks for the same price as 12 weeks, that translates into best-price being 50% less, so this offer is not offered in the US.

I suggest that companies submit a proposal for innovative pricing for review to CMS/Medicaid. If it is determined that the structure would not result in Medicaid paying a higher price in general than it otherwise would, then allow it with monitoring. A provision can be that each state Medicaid be offered the same terms.

Engaging prescribers to be part of the solution:

Currently, there is a taboo against incorporating a price discussion in decisions about health care options. The Senate Finance Committee can facilitate a cultural shift in the importance and appropriateness of factoring in price as well as safety and efficacy when recommending treatments. These needs to be instilled into every level of health care from individual health providers deciding on which prescription to write, to professional guidelines committees, to agencies that support research such as the NIH and PCORI.

For example, the AASLD/IDSA/IAS HCV guidance specifically chose not to incorporate price into treatment recommendations, as is typical of guidelines committees. One barrier to doing so (besides tradition) was the lack of available true prices and the recognition that few payers were actually paying the published wholesale acquisition costs. I co-led the cost effectiveness section of the guidance, and we tried to provide a high level overview of cost-effectiveness of HCV treatment, but it did not provide clinicians with the level of information that would allow them to help incorporate price into their decisions. For example, the guidance recommends four different regimens, which have roughly similar safety and efficacy:

Recommended regimens for patients with HCV genotype 1a infection who have compensated cirrhosis, in whom prior PEG-IFN and RBV treatment has failed

Daily fixed-dose combination of ledipasvir/sofosbuvir for 24 weeks

WAC price = \$189,000

Daily fixed-dose combination of ledipasvir/sofosbuvir plus weight-based RBV for 12 weeks

WAC price = \$97,500

Daily fixed-dose combination of paritaprevir/ritonavir/ombitasvir plus twice-daily dosed dasabuvir and weight-based RBV for 24 weeks

WAC price = \$171,635

Daily sofosbuvir plus simeprevir with or without weight-based RBV for 24 weeks

WAC price = \$300,000 (without RBV)

There is no indication in the guidance that one regimen costs three times as much as another, and there are no data suggesting that the higher priced regimens are superior in any way.

In another example, the combination of sofosbuvir plus ledipasvir (Harvoni) had a suggestion in the product label that patients with no cirrhosis and HCV RNA levels less than 6 million IU/mL could receive 8 weeks of Harvoni instead of 12 weeks. In a study of real-world registries of patients being treated for hepatitis C, investigators found that of 323 patients who qualified for 8 weeks, only 41% actually received 8 weeks, and the rest received 12 weeks (Tsai, HepDart 2015). The SVR (cure) rates in patients who received 8 weeks of Harvoni was 97% compared to 97% in those who were treated for 12 weeks.. If Harvoni for 12 weeks costs \$95,000 and 8 weeks costs \$63,333, then treating everyone in this cohort for 8 weeks instead of 59% receiving 12 weeks would have saved \$6 million with no decrease in safety or efficacy.

FDA and price of drugs:

Physicians should be encouraged to consider price as well as efficacy, safety, tolerability, convenience, and other factors we currently take into account when selecting regimens. This means we need to know how much each regimen costs. The FDA is prohibited from taking the price of drugs into account when it recommends drug approvals. In the case above for Harvoni, the FDA provided a weak recommendation for 8 weeks in a specific group and contributed to distrust of this shorter duration regimen, which *contributed to the waste of millions of dollars*. Drug regimens risk not being approved if the FDA believes there are inadequate data supporting safety or efficacy. If the FDA were allowed to take price into account, they could recommend that data are inadequate to determine the optimal duration of treatment for specific groups, which would have significant implications for total price paid, and would be able to require additional post-approval studies to clarify how to optimally use a regimen for resource allocation.

Indian Health Services

The per capita health care spending for Native Americans that are covered by IHS is \$2849 compared to \$9816 in the US overall. Drug prices are negotiated by the Veterans Administration (where per capita health spending costs are somewhat higher than the US average). The VA is able to negotiate substantial discounts on drugs, including HCV drugs. However, the VA still required an infusion of \$1.5 billion to cover the (discounted) costs of HCV treatment. IHS is burdened by high rates of HCV and complications from this infection. It is unable to pay for HCV treatment that was priced for US health systems with much higher per capita spend and with no additional infusion of funds. Mandate discounts of 80% or more since the health economy of these sovereign nations is more like middle income countries (if they were able to negotiate as separate nations they would be paying far lower prices like elsewhere in the world).

Generic medications:

Differ from originator medications because little research is required to bring them to market. Price controls or other regulation won't risk limiting innovation, since this already occurred (and society paid) with the originator drug. However, without competition generics can end up not much less expensive than branded alternatives. Examples include doxycycline, buprenorphine, entecavir. As has been shown recently with pyrimethamine, one company can create a monopoly on a generic, raise prices, and take advantage of the slow FDA process for approving generic medications that would prevent a competitor from entering the market for about four years.

Suggestions:

Accelerate the FDA approval process for generic equivalents.

Allow the FDA to take price into account for accelerating the evaluation of generics, since this is the key "innovation" present with generics.

Have a lower threshold to seize drugs by imminent domain for important health crises because the risk of patent override on future innovation is not present.

Please email me with any questions: 

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