Why France Spends Less Than the United States on Drugs: A Comparative Study of Drug Pricing and Pricing Regulation

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Policy Points:

- Spending on prescription drugs is much higher per capita in the United States than in most other industrialized nations, including France.
- Lower prescription drug spending in France is due to different approaches to managing drug prices, volume of prescribing, and global health budgets.
- Linking a drug’s price to value both at the launch of the drug and over its lifetime is key to controlling spending. Regulations on prescription volume and global spending complement the interventions on prices.
- If the United States adopted the French approach to regulating drug pricing, Medicare could potentially save billions of dollars annually on prescription drug spending.

Context: Prescription drug spending per capita in the United States is higher than in most other industrialized countries. Policymakers seeking to lower drug spending often suggest benchmarking prices against other countries, including France, which spends half as much as the United States per capita on prescription drugs. Because differences in drug prices may result from how markets are
organized in each nation, we sought to directly compare drug prices and pricing regulations between the United States and France.

**Methods:** For the six brand-name drugs with the highest gross expenditures in Medicare Part D in 2017, we compared the price dynamics in France and the United States between 2010 and 2018 and analyzed associations between price changes in each country and key regulatory events. We also comprehensively reviewed US and French laws and regulations related to drug pricing.

**Findings:** Prices for the six drugs studied were higher in the United States than in France. In 2018, if Medicare had paid French prices for the brand-name drugs in our cohort, the agency would have saved $5.1 billion. We identified 12 factors that explain why the United States spends more than France on drugs, including variations in unit prices and the volume of prescriptions, driven by use of health technology assessment and value-based pricing in France.

**Conclusions:** Key drivers of lower drug spending in France compared to the United States are that the French government regulates drug prices when products are launched and prohibits substantial price increases after launch. The regulation of prescription drugs in France is governed by rules that can inform discussions of US prescription drug policy and potential Medicare price negotiations.

**Keywords:** Prescription drug prices, Medicare, drug regulation, France, United States.

Prescription drug spending in the United States has risen substantially in the past decade, contributing to adverse patient outcomes and straining the budgets of health care payers.\(^1\text{-}^5\)

As US lawmakers consider strategies to reduce spending on brand-name prescription drugs, the approaches taken in other high-income countries are frequent points of comparison. During the Trump administration, both President Donald Trump and Speaker of the US House of Representatives Nancy Pelosi proposed plans that would rely on drug prices in other countries as benchmarks for negotiations by US government payers.\(^6\text{-}^7\)

France is among the European countries often invoked as a comparator in US policy debates about drug pricing because it has lower prescription drug prices than the United States despite having a similar economy.\(^8\)

Historically, the United States and France were among the Organisation for Economic Co-operation and Development (OECD) countries with the highest spending on pharmaceuticals, with very similar levels of
spending from the mid-1980s to the mid-1990s. However, in France, the rate of spending began to slow by the mid-1990s and early 2000s with implementation of new regulations,\textsuperscript{9,10} whereas spending in the United States continued to climb. US spending per capita on prescription drugs reached $1,220 in 2017, compared to $653 in France.\textsuperscript{11}

One reason for the difference in drug spending may be how prices are negotiated by government payers in France, both when a drug is launched and over time.\textsuperscript{12–15} To determine national insurance coverage for drugs, France’s Transparency Committee rates them according to their demonstrated medical benefit (\textit{service médical rendu} [SMR]). The SMR synthesizes the benefit/risk ratio of each drug, classifying the evidence to support coverage as important, moderate, mild, or insufficient to support coverage, and the classification determines the share of the drug’s cost that national insurance will cover (between 100\% and 0\%), with the remainder becoming the patient’s responsibility.

The prices of reimbursed drugs are regulated in France through conventions negotiated between the manufacturer and the Economic Committee for Health Products (Comité économique des produits de santé [CEPS]), which includes representatives from the health and economic ministries, the national health insurer, and private complementary insurers. The negotiation is framed by a national agreement,\textsuperscript{16} and the price of a specific drug takes into account the product’s added medical benefit (\textit{amélioration du service médical rendu} [ASMR]), which synthesizes the benefit of the drug, in comparison with available alternatives. The ASMR is determined by the Transparency Committee and classified as major (ASMR I), important (II), moderate (III), mild (IV), or absent (V). Drugs with an ASMR I, II, or III classification are entitled to a European price guarantee (which ensures list prices at a level similar to those in the United Kingdom, Germany, Spain, and Italy). Since 2013, the prices of ASMR I, II, and III drugs have also depended on a cost-effectiveness evaluation conducted by the Economic and Public Health Committee. Price negotiations may further account for factors such as the price of comparators (other drugs used to treat the same or similar conditions) and the size of the population eligible for the drug (with drugs for larger populations tending to receive lower prices). The price and coverage decisions, including the ASMR and cost-effectiveness evaluations, are reviewed at least every five years.

Another consideration that may help explain drug spending differences between the United States and France is the volume of
prescriptions per capita, which is in part due to varying approved indications for drugs.\textsuperscript{17}

There have been a limited number of studies on drug pricing in France,\textsuperscript{18–23} and, to our knowledge, no studies directly comparing US and French prices over time. We therefore sought to describe drug price dynamics in France compared to those in the United States. To do so, we identified the six brand-name drugs with the highest gross Medicare Part D spending in 2017 and then compared their French prices to those paid by Medicare, the largest US government payer. Next, we identified key regulatory events in the two countries and reviewed how drug pricing laws and regulations might account for observed differences in brand-name drug prices between France and the United States.

Methods

Study Design

We used data from the 2017 Medicare Part D drug spending dashboard to identify the six brand-name drugs with the highest gross expenditures.\textsuperscript{24} The drugs, by decreasing order of spending, were lenalidomide (Revlimid), an antineoplastic agent; apixaban (Eliquis), an anticoagulant; sitagliptin (Januvia), an antidiabetic; insulin glargine (Lantus solostar), an antidiabetic; rivaroxaban (Xarelto), an anticoagulant; and ledipasvir/sofosbuvir (Harvoni), a hepatitis C antiviral. We then compared the price per unit for each drug in France and the United States from 2010 to 2018 in the United States (Medicare released 2018 data while this study was being conducted) and from 2010 to 2019 in France. We explored potential explanations for pricing differences by identifying important regulatory events and relevant laws and regulations in France and the United States. We also reviewed other regulatory events unrelated to drug pricing that might affect drug spending, such as measures to limit the volume of use.

Data Sources

Our key measure was drug price per unit for Medicare and in France, including spending by both payers and patients (i.e., cost sharing). We extracted Medicare spending per unit from the Part D Drug spending
dashboard, using the most recent data set for each year. The unit represents the form in which the drug is marketed for use, such as the number of tablets, grams, milliliters, or other units, as defined in the methodology for the Medicare Part D drug spending dashboard. Medicare spending per unit was adjusted for inflation using the annual Consumer Price Index for All Urban Consumers and expressed in 2018 US dollars.

The gross spending per unit reported by Medicare excludes confidential rebates negotiated by individual Medicare Part D plans or their pharmacy benefit managers (PBMs). We also estimated "net price" after rebates and price concessions by using drug-specific rebate data from SSR Health, which relies on a proprietary algorithm to calculate net prices based on publicly reported manufacturer revenues. The rebate is calculated as follows: \(1 - \frac{\text{SSR net price per unit}}{\text{Medicare spending per unit}}\).

For one drug, lenalidomide, the SSR estimates of net price per unit were unrealistically higher than gross Medicare spending per unit, so we instead used an estimate of total Medicare price concessions for antineoplastic agents in a July 2019 US Government Accountability Office (GAO) report to estimate the net price. The GAO-reported price concessions for antineoplastic agents were $170 million on $8.4 billion of spending (2.03%). We applied this rate constantly throughout the study to the gross Medicare spending per unit of lenalidomide to estimate the net price.

French prices were extracted from a publicly available national insurance database of drug claims, Médic'am annuel labellisé, which registers the amount spent on drugs in retail pharmacies (for apixaban, sitagliptin, insulin glargine, rivaroxaban), and from Rétrocéd'am, which registers the amount spent on drugs in hospital pharmacies (for lenalidomide and ledipasvir/sofosbuvir). Médic'am annuel labellisé data were available from January 1, 2010 through June 30, 2019 and Rétrocéd'am data were available from January 1, 2010 to December 31, 2018. Data from tous régimes (all insured patients) were preferred if available. When these data were not available (i.e., 2010-2011 for retail pharmacies, 2010-2016 for hospital pharmacies), we used data from the régime général, which covers the largest proportion of the salaried and retired population. Ledipasvir/sofosbuvir distribution was transitioned from hospital to retail pharmacies in 2018, so 2018-2019 prices for that product are from Médic'am annuel labellisé. For each drug, the price per unit was
computed by dividing the total amount spent by the number of units delivered. Prior to 2015, the unit cost also included the distribution fee. Beginning in 2015, this fee was billed separately and we therefore manually added it to the reported prices ($1.01 per pack in 2015, $1.28 in 2016, $1.31 in 2017, $1.32 in 2018, and $1.97 in 2019). If several dosages were available, we calculated the price per unit of each dosage and computed a weighted mean according to the relative number of units reimbursed for each dosage, similar to the methodology of the Medicare Part D drug spending dashboard.\textsuperscript{25} The study includes the unregulated price of ledipasvir/sofosbuvir during its temporary authorization for use in 2014 (i.e., $59,406 for 12 weeks treatment).\textsuperscript{31} We converted French prices in Euros to US dollars using the OECD annual purchase power parity estimate\textsuperscript{32} and adjusted these prices for inflation to 2018 dollar values using the annual convertor from the French National Institute of Statistics and Economic Studies (Institut national de la statistique et des études économiques).\textsuperscript{33} Drugs prices in France are subject to confidential rebates, but these data are unavailable on the product level and tend to be much smaller than rebates offered in the United States (the overall rebate reached 8% in France in 2018,\textsuperscript{34} compared to 25% for Medicare drugs).\textsuperscript{35(p140)}

Quantitative Data Analysis

We tracked annual prices in the United States and France for the six drugs of interest. To understand why prices changed at certain time points, we collected relevant decisions and milestones in published reports from (1) the US Food and Drug Administration (FDA) and European Medicines Agency (EMA) on the regulatory history and approvals for each drug (and their associated generics or biosimilars when applicable), (2) the health technology assessment conducted by the Transparency Committee and the cost-effectiveness analysis conducted by the Economic and Public Health Committee, both within France’s National Authority for Health (Haute Autorité de santé), and (3) pricing decisions from the CEPS in France. We charted the milestones along with the evolution of prices to identify concurrent changes.

We estimated the potential savings for Medicare by applying the French unit price in place of the net (post-rebate) Medicare unit price for total Medicare spending on these six drugs in 2018. In a
sensitivity analysis, we estimated potential savings accounting for rebates on French prices, based on drug-class-specific average rebates published by the CEPS for 2018.35

Qualitative Data Collection

To interpret the potential significance of milestones identified in the quantitative analysis, we reviewed the regulations and laws related to prescription drug regulatory approval and pricing that have been implemented in France and the United States. Our goal was to identify factors that could account for differences in brand-name drug pricing trends observed for the six drugs of interest related to price negotiation, price setting, or price caps. We also examined how regulations might impact the volume of prescriptions or the global spending to provide a more complete account of drug expenditures.

Limitations

This is a case study of the six drugs with the highest gross Medicare spending and may not be generalizable to all drugs in Medicare Part D. In addition, we may not have identified all reasons for differential pricing between the United States and France.

Though we identify events that were temporally associated with price changes in France and the United States, we cannot prove that these events caused price changes. In France, the range of factors affecting drug price negotiations is complex and includes added medical benefit, cost-effectiveness evaluation, the price of other medications in the same class, expected volumes of sales, agreements between the CEPS and the industry, as well as other variables. The design of the study does not permit us to estimate the share of a price change that correlates with a given regulatory event. We cannot exclude the possibility that other factors, such as competition with other brand-name or generic/biosimilar drugs in the same class, might have driven price dynamics for a given product. We are unable to draw conclusions about the extent to which regulations targeting drug prices versus those targeting prescribing practices might lead to differences in overall spending in the United States and France.

The certainty of our estimates of what Medicare might save overall by adopting French drug prices is limited by the confidentiality of
rebates provided by manufacturers to both the French national insurance program and Medicare Part D. The US net prices from SSR Health are derived from publicly reported manufacturer revenues and likely underestimate total net spending by Medicare plans by excluding administrative costs, dispensing fees and taxes, and fees paid to PBMs. Additionally, net prices from SSR Health reflect averages across all payers (not just Medicare). As noted earlier, we did not use SSR Health data to estimate rebates for lenalidomide; instead, we used drug-class-specific data for Medicare alone, where oncologic drugs are a protected class, and this estimate might therefore be lower than the prices paid by US commercial payers. We may have underestimated net US prices and therefore the potential for savings using French prices for the six drugs of our sample.

To be conservative, we did not apply any rebates to French prices in our primary analysis because rebate data are not available at the product level or over time. We used the limited drug-class-specific rebate data from 2018 in a sensitivity analysis. This analysis should be considered with caution as we have no guarantee that the products in our analysis were effectively subject to rebates and, if so, at the average level. Class-level rebates were not disclosed for the other years considered in our study.

Results

Potential Medicare Savings

The six drugs in our cohort accounted for a total of $19.7 billion in gross spending by Medicare in 2018, with spending per product ranging from approximately $1.7 billion to approximately $5.0 billion (Table 1). Assuming Medicare had paid French prices for the same number of units, we estimate that Medicare’s 2018 savings would have totaled $5.1 billion for the six drugs.

We observed that in 2018, more than 90% of Medicare Part D patients treated for hepatitis C received ledipasvir/sofosbuvir, whereas more than 90% of patients in France treated for hepatitis C received velpatasvir/sofosbuvir (Epclusa). To overcome the risk of structural bias in the comparison, we estimated, in a complementary analysis, the overall savings Medicare could have achieved in 2018 using
<table>
<thead>
<tr>
<th>Active Ingredient (Brand Name)</th>
<th>Gross Medicare Spending, M$</th>
<th>Net Medicare Spending After Estimated Rebates, M$(^a) (A)</th>
<th>Estimated Net US Price per Unit, $(^b) (B)</th>
<th>French Unit Price, $(^b) (C)</th>
<th>Estimated Medicare Spending Using French Prices, M$(^d) (D)</th>
<th>Potential Medicare Savings, M$(^d) (E)</th>
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<tbody>
<tr>
<td>lenalidomide (Revlimid)</td>
<td>4,065</td>
<td>3,983</td>
<td>683.21</td>
<td>202.53</td>
<td>1,181</td>
<td>2,802</td>
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<td>apixaban (Eliquis)</td>
<td>4,992</td>
<td>2,535</td>
<td>3.55</td>
<td>1.50</td>
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<td>1,468</td>
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<td>sitagliptin (Januvia)</td>
<td>3,229</td>
<td>906</td>
<td>4.16</td>
<td>1.40</td>
<td>304</td>
<td>602</td>
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<tr>
<td>insulin glargine (Lantus solostar)</td>
<td>2,370</td>
<td>608</td>
<td>6.81</td>
<td>4.69</td>
<td>419</td>
<td>189</td>
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<tr>
<td>rivaroxaban (Xarelto)</td>
<td>3,359</td>
<td>1,442</td>
<td>6.00</td>
<td>3.08</td>
<td>739</td>
<td>703</td>
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<tr>
<td>ledipasvir/sofosbuvir (Harvoni)</td>
<td>1,726</td>
<td>358</td>
<td>234.70</td>
<td>663.66</td>
<td>1,013</td>
<td>-655</td>
</tr>
<tr>
<td>Total</td>
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<td>9,831</td>
<td>N/A</td>
<td>N/A</td>
<td>4,722</td>
<td>5,109</td>
</tr>
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</table>

Abbreviations: M$, million US dollars; N/A, not applicable.

Spending and prices per unit are rounded for readability; all calculations in the table have been made on exact numbers.

\(^a\)Medicare spending using average rebates is estimated as follows, based on data from reference 24: (A) = (Medicare total gross spending/Medicare list spending per unit) × Unit price with rebate at the product level.

\(^b\)Prices per unit are expressed in 2018 US dollars. The unit represents the form in which the drug is marketed for use (e.g., number of tablets, grams, milliliters, or other units) as defined in the methodology for the Medicare Part D drug spending dashboard.

\(^c\)(D) = [(A)/(B)] × (C).

\(^d\)(E) = (A)−(D).
French prices and French utilization patterns: using the French price of velpatasvir/sofosbuvir ($474.78) instead of the French price of ledipasvir/sofosbuvir ($663.66), the overall savings for Medicare for all six drugs in the study would have been $5.4 billion instead of $5.1 billion.

In a sensitivity analysis, we applied average class-specific French rebates disclosed by CEPS for 2018. This analysis changes the potential 2018 savings for Medicare from $5.1 billion to $6.5 billion (Table 2).

Concordance of Drug Prices and Regulatory Events

Figures 1 through 6 plot prices in the United States and France and identify significant regulatory events for the six drugs in this study. Figure 1 shows that the US and French prices for lenalidomide remained relatively steady early in the study period. US prices then increased, whereas French prices began to decrease in 2013, the year in which the cost of the drug was included in the hospital stay tariff (i.e., hospitals became responsible for negotiating the inpatient cost of lenalidomide rather than the government). As explained later, this event may have exerted downward pressure on prices.

Between 2017 and 2018, a sharper decline in the French price for lenalidomide coincided with the end of the rare disease drug special market exclusivity period for this product in France. Though French regulators do not require price decreases at the end of exclusivity, exclusivity status is associated with more favorable negotiating conditions for the manufacturer. For example, at the end of the rare disease market exclusivity period, lenalidomide was registered in the generic index, opening the French market to generics. The French regulation stipulates that when the first generic is launched on the market, the price of the originator drug is reduced by 20%. Therefore, the observed price decrease could be a result of the loss of exclusivity. In the United States, lenalidomide has received ten overlapping seven-year periods of exclusivity via the Orphan Drug Act—the first for the treatment of multiple myeloma in 2001, and the most recent for the treatment of splenic marginal zone lymphoma, which will last until 2024. The mandatory Medicare coverage for protected-class drugs prevents Medicare from negotiating substantial rebates for most oncology drugs.
Table 2. Medicare and French Spending on Medicare’s Six Most Expensive Brand-Name Drugs in 2018, Using Discounted Prices in France

<table>
<thead>
<tr>
<th>Active Ingredient (French Rebate Rate)</th>
<th>Gross Medicare Spending, M$</th>
<th>Net Medicare Spending After Estimated Rebates, M$&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Estimated Net US Price per Unit, $&lt;sup&gt;b&lt;/sup&gt;</th>
<th>French Unit Price After Estimated Rebates, $</th>
<th>Estimated Medicare Spending Using French Prices, M$&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Potential Savings, M$&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>lenalidomide (27.8%)</td>
<td>4,065</td>
<td>3,983</td>
<td>683.21</td>
<td>146.23</td>
<td>852</td>
<td>3,130</td>
</tr>
<tr>
<td>apixaban (37.4%)</td>
<td>4,992</td>
<td>2,535</td>
<td>3.55</td>
<td>0.94</td>
<td>668</td>
<td>1,867</td>
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<tr>
<td>sitagliptin (12.9%)</td>
<td>3,229</td>
<td>906</td>
<td>4.16</td>
<td>1.22</td>
<td>265</td>
<td>641</td>
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<tr>
<td>insulin glargine (12.9%)</td>
<td>2,370</td>
<td>608</td>
<td>6.81</td>
<td>4.08</td>
<td>365</td>
<td>243</td>
</tr>
<tr>
<td>rivaroxaban (37.4%)</td>
<td>3,359</td>
<td>1,442</td>
<td>6.00</td>
<td>1.93</td>
<td>463</td>
<td>979</td>
</tr>
<tr>
<td>ledipasvir/sofosbuvir (29.6%)</td>
<td>1,726</td>
<td>358</td>
<td>234.70</td>
<td>467.22</td>
<td>713</td>
<td>−355</td>
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<tr>
<td>Total</td>
<td>19,742</td>
<td>9,831</td>
<td>N/A</td>
<td>N/A</td>
<td>3,326</td>
<td>6,506</td>
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</table>

Abbreviations: M$, million US dollars; N/A, not applicable.

Spending and prices per unit are rounded for readability; all calculations in the table have been made on exact numbers.

<sup>a</sup>Medicare spending using average rebates is estimated as follows, based on data from reference 24: (A) = (Medicare total gross spending/Medicare list spending per unit) × Unit price with rebate at the product level.

<sup>b</sup>Prices per unit are expressed in 2018 US dollars. The unit represents the form in which the drug is marketed for use (e.g., number of tablets, grams, milliliters or other units) as defined in the methodology for the Medicare Part D drug spending dashboard.

<sup>c</sup>(D) = (A)/(B) × (C).

<sup>d</sup>(E) = (A) − (D).
Figure 1. Changes in Lenalidomide Unit Prices in the United States and France, 2010-2018

Abbreviations: ASMR, amélioration du service médical rendu (added medical benefit); FR, France.
Legend: The arrows represent the regulatory events that coincide with marked price changes. The US list curve shows spending per unit reported in the Medicare Part D drug spending dashboard. The US net curve shows the price per unit discounted with the rebate estimated by the Government Accounting Office for oncology-class drugs. Year labels and annual costs are displayed in the middle of the year for clarity of presentation.

Figure 2 shows that launch prices for ledipasvir/sofosbuvir were far lower in France than list prices in the United States in the same year; however, after estimated price concessions, the US and French prices were similar. When the drug was initially covered in France, the Transparency Committee recognized an additional minor medical benefit provided by the drug compared to other sofosbuvir-based treatments. However, the cost-effectiveness evaluation was invalidated by the Economic and Public Health Committee because the evaluation did not include a relevant comparator, and because the clinical evidence supporting the cost-effectiveness evaluation was limited. According to the French negotiation framework, the invalidation of cost-effectiveness
evaluation limits the negotiation power of the pharmaceutical company. Prices for ledipasvir/sofosbuvir decreased in France in 2017, coinciding with the introduction of sofosbuvir/velpatasvir (Epclusa), a new, lower-priced drug in the firm’s portfolio. A 2017 change in the ledipasvir/sofosbuvir distribution channels in France from hospital pharmacies to retail pharmacies, which have a different negotiation framework giving more power to the CEPS, also coincided with lower prices for that product. By 2018, spending on sofosbuvir/velpatasvir constituted 88% of all sofosbuvir-based spending in France’s retail pharmacies, lowering the actual cost of sofosbuvir-based treatment of hepatitis C below the price of ledipasvir/sofosbuvir. Medicare’s estimated net ledipasvir/sofosbuvir prices also fell over time. However, we may have underestimated those net prices because of a limitation in SSR methodology; the rebate data used in the estimation are not exclusive.
Figure 3. Changes in Apixaban Unit Prices in the United States (2013-2018) and France (2012-2019)

Abbreviations: ASMR, amélioration du service médical rendu (added medical benefit); DVT, deep vein thrombosis; FR, France; NAF, nonvalvular atrial fibrillation; PE, pulmonary embolism; TC, Transparency Committee; VTE, venous thromboembolic events.

Legend: The arrows represent the regulation events that coincide with marked price changes. The US list curve shows spending per unit reported in the Medicare Part D drug spending dashboard. The US net curve shows the price per unit discounted with the rebate reported by SSR Health at the product level. Year labels and annual costs are displayed in the middle of the year for clarity of presentation.

to Medicare but apply to all “non-Medicaid” payers. SSR systematically underestimates Medicaid rebates by excluding “best price” discounts. This methodological limitation is particularly important for drugs like ledipasvir/sofosbuvir with high Medicaid utilization. Figure 2 suggests that, despite the different regulation processes in France and the United States, within-class competition seems to explain the substantial price reductions in both countries.

Figures 3 and 4 show price dynamics for two anticoagulant drugs, apixaban and rivaroxaban, respectively. Although the launch prices for both products were similar in France and the United States, subsequent
price declines were sharper in France. The drop in French apixaban prices from 2013 to 2014 coincided with coverage for a new indication: the prevention of stroke and systemic embolism in patients with nonvalvular atrial fibrillation. Prior to this, French insurance only covered apixaban prescribed for the prevention of venous thromboembolic events following hip or knee replacement surgery. When the new indication was covered, the Transparency Committee concluded that neither apixaban nor rivaroxaban provided any improvement compared to alternative atrial fibrillation treatments. In addition, atrial fibrillation was far more prevalent than the initial indication covered, and the expanded size of the patient population for apixaban provided an opportunity for the
French payer to negotiate a lower price. The price decrease in France for rivaroxaban also coincided with the market approval of apixaban, and within-class competition may have played a role in the negotiation that lowered the rivaroxaban price.

The second, more moderate price decrease observed in France for both apixaban and rivaroxaban from 2017 to 2018 followed a routine reevaluation requested by the Transparency Committee of all anticoagulant drugs, which created a new opportunity for the French CEPS to negotiate lower prices. In addition, the price of rivaroxaban decreased in France following approval of generic alternatives in 2018. Under French regulations, when the first generic is launched on the market, the price of the originator drug is reduced by 20%; therefore, the observed price decrease might be interpreted as a result of loss of exclusivity.

Figure 5 shows that in 2010 sitagliptin was priced much higher in the United States than in France, even after estimated US rebates. Prices in both countries then steadily decreased. There were two noteworthy sharp declines in the price of sitagliptin in France: the first followed a routine reevaluation for coverage renewal in 2015, without major changes in the evaluation of the benefit provided by the drug. The second occurred when a generic entered the market in 2018. In contrast, no generic version of sitagliptin has been approved in the United States. However, net US prices did decline after 2016, possibly in response to competition from new classes of antidiabetic drugs.

Figure 6 shows that the price of insulin glargine in the United States at the start of the study period was higher than in France. The US price increased substantially from 2010 to 2014, and the US net price decreased from 2015 to 2018. The US net price decrease coincided with FDA approval of a concentrated form of insulin glargine (Toujeo) and another product with a clinically comparable active ingredient, also called a follow-on biologic (Basaglar). The French price steadily decreased in conjunction with (1) routine reevaluations by the Transparency Committee in 2011, 2014, and 2018 that concluded there was no benefit for insulin glargine over insulin NPH or detemir, and (2) competition from concentrated (2015) and biosimilar (2017) forms of insulin glargine.

To summarize, Figures 1–6 show that, for five of the six drugs in this study (all except ledipasvir/sofosbuvir), the US list prices increased by the end of the study period whereas the French prices decreased. The US net prices declined for those five drugs over the study period. However,
Figure 5. Changes in Sitagliptin Unit Prices in the United States (2010-2018) and France (2010-2019)

Abbreviations: ASMR, amélioration du service médical rendu (added medical benefit); FR, France.

Legend: The arrows represent noteworthy regulatory events that occurred during the study period. The US list curve shows spending per unit reported in the Medicare Part D drug spending dashboard. The US net curve shows the price per unit discounted with the rebate reported by SSR Health at the product level. Year labels and annual costs are displayed in the middle of the year for clarity of presentation.
Figure 6. Changes in Insulin Glargine Unit Prices in the United States (2010-2018) and France (2010-2019)

Abbreviations: ASMR, amélioration du service médical rendu (added medical benefit); EMA, European Medicines Agency; FDA, US Food and Drug Administration; FR, France.

Legend: The arrows represent noteworthy regulatory events that occurred during the study period. The US list curve shows spending per unit reported in the Medicare Part D drug spending dashboard. The US net curve shows the price per unit discounted with the rebate reported by SSR Health at the product level. Year labels and annual costs are displayed in the middle of the year for clarity of presentation.

the US net prices for those drugs remained substantially higher than prices in France.

Factors Contributing to Drug Pricing Differences

We have identified seven factors contributing to the differences in prices between France and the United States for these six drugs; two related to prescription volume; and three related to overall spending (Table 3).

Price-Related Factors. France had lower launch prices than Medicare Part D for several drugs in our study. The CEPS has the authority
to negotiate the prices of new drugs covered by the national health insurance.\textsuperscript{41,42} In the United States, Medicare Part D cannot engage in direct price negotiation with manufacturers, but negotiation happens at the individual plan level, typically via PBMs that represent both Part D plans and commercial payers. The rebates negotiated by individual Part D plans through this structure tend to be less effective and lead to prices higher than those achieved by the French centralized federal negotiation.\textsuperscript{43}

In France, price negotiation occurs based on evidence from a health technology assessment, with more clinical benefit translating into higher permitted prices. The Transparency Committee then ranks drugs based on comparative effectiveness at five levels of medical added benefit (ASMR). By law, drugs providing no additional clinical benefit compared to other available therapies (i.e., ranked ASMR V) must be priced to provide savings in the cost of treatment.\textsuperscript{44} More broadly, stronger therapeutic benefits tend to reduce the negotiating power of CEPS. By contrast, CEPS has substantial negotiating power when a drug is found to provide marginal or no improvement compared to others on the market. In France, when ledipasvir/sofosbuvir was launched as a hepatitis C therapy, it was graded as a “minor improvement” over other sofosbuvir-based combination drugs already on the market and was thus priced approximately 35\% below the sofosbuvir/daclatasvir and sofosbuvir/simeprevir combinations that were then the reference drugs.\textsuperscript{45} In the United States, the manufacturer of ledipasvir/sofosbuvir, Gilead, set the drug’s list launch price at a higher level than the prices for other sofosbuvir products already on the market. Although US net prices for ledipasvir/sofosbuvir were lower than US list prices, how much lower is unknown due to limitations in estimating confidential rebates. Despite lower net prices, high list prices remain a concern for US patients, impacting the cost of drugs for uninsured patients and the out-of-pocket costs for insured patients.\textsuperscript{46}

According to the European price guarantee defined in the price negotiation framework in France,\textsuperscript{16} drugs granted a major (ASMR I), important (ASMR II), or moderate (ASMR III) clinical added benefit can claim list prices similar to the prices offered in the United Kingdom, Germany, Italy, and Spain.\textsuperscript{16} Drugs that lack robust cost-effectiveness evidence lose this right to rely on higher European prices, increasing the negotiating power of the CEPS.
In France, the health technology and cost-effectiveness assessments take place at the indication level. Thus, a given drug may theoretically be priced differently for different indications, depending on the disease-specific clinical benefit. In practice, drugs used for multiple indications in France have uniform prices that are based on the average price weighted by use for each indication. Apixaban and rivaroxaban (Figures 3 and 4) decreased in price after France began covering the drugs for a new, highly prevalent indication (atrial fibrillation). Compared to vitamin K antagonists already used for this indication, apixaban and rivaroxaban were considered to provide “no improvement” in treating the condition. In this case, the approval of a new indication did not increase the value of the drugs; rather, the new indication contributed to decreased prices as the relative value of the new indication is lower than the relative value of the first indication approved.

The negotiated launch price acts as a cap throughout France. By contrast, US drug prices vary considerably across government and private payers. The launch price also constrains future prices in France because year-over-year price increases are prohibited in the absence of new regulatory action. In the United States, list prices for five of the six drugs in our cohort increased at a rate greater than the rate of inflation.

Two other types of regulation in France affect the prices of certain high-cost drugs. First, in the United States and France, reimbursement for hospital stays depends on the diagnosis-related group (DRG) assigned on admission. In France, expensive hospital-administered drugs are covered separately in the period immediately after approval but later integrated into the bundled hospital payment. This transition incentivizes hospitals to negotiate lower prices as the pharmaceutical industry may fear a lower use if the drug cannot be funded through the bundled payment. This incentive may lead to a spillover effect on the negotiation of prices for outpatients. For example, the transition of lenalidomide from the special list to bundled DRG payment in 2013 correlated with price declines.

In the United States, Medicare Part A and other payers may have very little leverage to negotiate inpatient brand-name drug prices. Most expensive drugs are included in the bundled DRG payment. If drugs that are new and costly compared to the DRG rate provide a substantial clinical improvement over existing services or technologies, an add-on payment can be implemented. However, the add-on payment may take
several years to go into effect. All the drugs in our sample were Medicare Part D drugs, so we could not observe any add-on payment.

Second, the French framework for price negotiation stipulates that prices automatically decline by 20% with expiration of a patent or other market exclusivity. The price for generic versions of the drug are then set 60% below the price of the originator. More broadly, the general logic of the regulation is to fund new drugs through cost reductions of older ones. Thus, French lenalidomide and sitagliptin prices decreased in 2018, before any reimbursement decisions relating to the generic drugs were made (see Figures 1 and 5). The French price of lenalidomide was also lowered when its rare disease drug status ended. In the United States, brand-name drug list prices usually decrease after generic competition begins, but the reductions in price are variable and only occur if there is sufficient market competition from available generic drugs.

There have been recent concerns that generic competition in the United States may not substantially lower prices for some specialty drugs.

Prescription Volume–Related Factors. Spending on high-priced prescription drugs in France may be lower than in the United States because of differences in prescription volumes. Several factors, including marketing, early adoption of new drugs, and off-label use, may explain differences in the volume of use between the countries. Our study highlights that divergence may also occur when the approved indication is more restrictive in the European Union than in the United States. For example, the EMA approved lenalidomide for certain myelodysplastic syndromes in the European Union only “when other therapeutic options” were “insufficient or inadequate.” Such restrictions do not apply in the United States. Similarly, apixaban is indicated in France for patients with non-valvular atrial fibrillation who possess certain heightened risk factors. By contrast, the FDA has approved the drug for all patients with non-valvular atrial fibrillation.

Because national approved uses in France are based on the Transparency Committee’s health technology assessment, they may be even more limited than approved EMA uses. For example, the Transparency Opinion deemed the evidence insufficient to support sitagliptin as monotherapy, and thus, the national insurance did not cover this use.

Global Spending–Related Factors. Three aspects of the annual pharmaceutical budgeting process in France help explain why France spends less
than the United States on drugs. First, in France, Parliament votes on the budget of the national insurance and regulation provisions annually. The main mechanism of budget control is a contribution—called “contribution Lv” for drugs in retail pharmacies and “contribution Lh” for drugs delivered in hospitals—that must be paid by the pharmaceutical companies if the evolution of spending exceeds the annual “L-rate”—the maximum spending increase set by the Parliament. In addition to this general provision, a supplemental regulation called the “W-mechanism” has been defined to require pharmaceutical companies to return the portion of their revenues exceeding a fixed budget. The W-mechanism was implemented for hepatitis C treatments in the 2015, 2016, and 2017 budgets, which helped contain overall spending.

Second, the French national health insurance may set reimbursement rates at different levels according to the actual benefit of the drug. For example, only 35% of the price of sitagliptin was covered by the national insurance from 2008 to 2013, while both more effective and less expensive agents for diabetes were covered at 70%. This helps France direct the allocation of public resources toward more effective drugs.

Finally, the French government offers various incentives to encourage the use of generic drugs when available. For example, patients may request brand-name versions, but the national insurance only covers the price of the cheapest generic. In addition, physicians receive pay-for-performance incentives based on the prescription in international nonproprietary names. Though many US states mandate generic substitutions unless providers or patients request otherwise, individual plans make coverage and cost-sharing decisions between brand-name and generics, with brand-name rebates complicating this calculus.

Discussion

For the six brand-name drugs in our cohort, all but one had lower initial prices in France than in the United States; prices for these drugs in France then declined at rates that typically exceeded those in the United States. In 2018, the gap between French and Medicare prices was wide: we estimated that Medicare would have saved $5.1 billion on the six drugs in our cohort if it had paid French prices.
### Table 3. Factors Contributing to the Differences in Drug Prices and Spending between France and the United States

<table>
<thead>
<tr>
<th>Reason</th>
<th>Details (Case Examples)</th>
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<td><strong>Price-related factors</strong></td>
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<td>Launch prices negotiated by the government</td>
<td>France’s Transparency Committee ranks all new drugs based on comparative effectiveness at five levels: no improvement (ASMR V), minor improvement (ASMR IV), moderate improvement (ASMR III), important improvement (ASMR II), and major improvement (ASMR I). The CEPS then negotiates launch prices commensurate to ranking. Drugs classified as ASMR I, II, or III are entitled to the European price guarantee (i.e., a list price similar to the price in the UK, Germany, Italy, and Spain) (e.g., ledipasvir/sofosbuvir).</td>
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<td>Cost-effectiveness evidence used in health technology assessment</td>
<td>The CEPS uses cost-effectiveness evidence when negotiating prices for products in ASMR categories I-III. If robust evidence of cost-effectiveness is provided, the price is set based on reference to other European prices. If robust evidence is not provided, a price lower than other European prices can be set (e.g., ledipasvir/sofosbuvir).</td>
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<tr>
<td>Blended pricing in France for drugs with multiple indications</td>
<td>The Transparency Committee assesses each indication for a drug separately, and the ASMR rank can vary across indications. The CEPS then defines an average price (weighted by indication). If a drug is given a lower ASMR rank for a new indication relating to a larger population of users, CEPS lowers the average price for that drug (e.g., apixaban, sitagliptin, rivaroxaban).</td>
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<td>Regulation of prices</td>
<td>The CEPS’s decision caps a drug’s list price throughout France; charging more than list price is prohibited. In the United States, list prices are freely set by the manufacturers and net prices can vary substantially depending on agreements between the payer and the manufacturer.</td>
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<td>Prices stay stable or decrease over time</td>
<td>Drug prices in France do not increase routinely over time; in the United States, there are no limits to annual drug price increases. If France’s Transparency Committee lowers a drug’s effectiveness rating, the price for that drug decreases (e.g., the ASMR rating for insulin glargine was changed from “moderate improvement” to “minor improvement” and then to “no improvement” as new safety data were documented and market competitors emerged).</td>
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### Table 3. (Continued)

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<td>Hospital incentives to negotiate lower drug prices</td>
<td>In France, expensive in-hospital drugs are covered by a special budget rather than via standard DRG payments to hospitals. When drugs leave the special budget list, which occurs with the passage of time or introduction of alternative treatments, hospitals are incentivized to negotiate lower prices (e.g., lenalidomide's removal from the special budget list in 2013 corresponded with an overall price drop).</td>
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<td>Expiration of market exclusivity</td>
<td>The CEPS lowers the price of drugs as soon as patents end and comparable products are included in the generic index (e.g., rivaroxaban and lenalidomide in 2018). Price decreases may also follow other types of lost exclusivity (e.g., prices declined for lenalidomide in 2018 when its rare disease exclusivity ended, and for insulin glargine following the introduction of Basaglar in 2019).</td>
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**Prescription volume–related factors**

| Narrower indications for use | The EMA or ANSM may approve a more limited indication for use than the FDA for a particular drug, and therefore the health insurer in France covers that drug for the limited indications (e.g., in the European Union, lenalidomide is approved as a monotherapy for certain myelodysplastic syndromes only “when other therapeutic options are insufficient or inadequate,” whereas such restrictions are not made in the United States). |

| Coverage decisions based on health technology assessments | Payer coverage in France may be limited to certain patients (e.g., those receiving second-line therapy) or certain indications based on the health technology assessment of indications for which the drug provides value (e.g., sitagliptin, ledipasvir/sofosbuvir, rivaroxaban low-dose). |

**Global spending–related factors**

| Spending caps at the therapeutic area level | Each year, the French Parliament votes to determine the target increases allowed at the therapeutic area level for drug spending by the national insurance. The CEPS is mandated to uphold the budget cap. A special law for hepatitis C drugs capped overall spending, leading to additional rebates for ledipasvir/sofosbuvir. |
Table 3. (Continued)

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<td>Modulation of insurance coverage according to actual benefit</td>
<td>France’s national insurance determines the level of coverage for a given drug depending on clinical benefit, which drives overall spending by affecting patient medication choices. For irreplaceable and costly drugs, coverage levels are at 100% (ledipasvir/sofosbuvir). For other drugs, insurance covers 65% of the cost if the clinical benefit is substantial (e.g., insulin glargine); 30% if the benefit is moderate (e.g., sitagliptin 50 mg); and 15% if the benefit is low. A lower rate of coverage can indicate to prescribers and patients a lower benefit and may reduce the use of the drug.</td>
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<td>Physician and patient incentives to choose less-expensive drugs</td>
<td>Pay-for-performance programs for physicians based on extent of prescribing generic products promote prescribing of less-expensive, equally effective drugs. Also, if a generic is available, the brand-name drug will have a higher co-pay to discourage patients from requesting the brand-name product.</td>
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Abbreviations: ANSM, Agence nationale de sécurité du médicament et des produits de santé (National Agency of Pharmaceutical and Health Product Security); CEPS, Comité économique des produits de santé (Economic Committee for Health Products); DRG, diagnosis-related group; EMA: European Medicines Agency; FDA, US Food and Drug Administration.

Although manufacturer rebates lowered actual US spending on the six drugs, even the Medicare net prices were higher than French prices in most cases. US net prices are driven by negotiations between PBMs, hospitals, and insurers, but these negotiations remain confidential, without a central framework or guiding principles. By contrast, regulations in France help structure negotiations and narrow the opportunities for drug manufacturers to charge high prices unrelated to value. Understanding how these rules work could inspire a more explicit framework for price and spending regulation in the United States.

Three main aspects of brand-name prescription market dynamics in France have important effects on prices. First, launch prices are heavily influenced by health technology assessment, whereas the United States does not have such a centralized process. Second, when new brand-name competitors come onto the market in France, regulators use these
occasions to reevaluate comparative effectiveness and relative prices within a drug class. By contrast, brand-brand competition in the United States rarely lowers list prices,\textsuperscript{55} and the changes in net prices associated with brand-brand competition are variable.\textsuperscript{5} The evidence for brand-brand competition lowering prices in the United States is limited,\textsuperscript{55} and the lack of data on confidential rebates further complicates assessments of temporal changes in response to competition.

Third, even in the absence of new competitors, French regulators periodically reassess prices after initial price negotiation. Such reassessments occur routinely, but they can also be driven by new evidence or the expansion of a drug’s indication. However, in recent years, French policymakers have suggested that they limit the extent of systematic reassessments to the first years of the commercialization of a limited number of drugs, which might diminish the opportunity to reconsider prices during a drug’s time on the market.\textsuperscript{56}

The French government restrains drug prices, in part, because its taxpayer-funded national health insurance provides an important justification for implementing value-based regulation. That is, the government perceives itself as accountable for the allocation of limited collective resources. In addition, political campaign funding in France is strictly regulated,\textsuperscript{57} limiting the power of private companies to influence policy decisions. Conversely, in the United States, the pharmaceutical lobby, which provides substantial funding to legislators at the national and state levels, has been successful at blocking meaningful drug pricing reform.\textsuperscript{58}

The regulation of drug prices in France may have drawbacks. For example, the process of evaluation and price negotiation may delay access to drugs in France,\textsuperscript{15} although France has a temporary use authorization system to help address unmet medical need while negotiations are underway. Also, the restrictions in drug approval and coverage may prevent patients from accessing a given drug, especially when a drug is approved by the FDA but eventually not covered by the French insurance. All the drugs in our sample were covered by the French national health insurance, though in some cases with a delay compared to the United States. Further study of these trade-offs in the French system are needed.

US drug pricing policy also has important trade-offs. Specifically, high drug prices may lead to adverse outcomes such as patient nonadherence and strains on health care budgets that prevent spending on other evidence-based care.
Conclusion

In 2018, Medicare could have saved at least $5.1 billion on just six high-priced drugs if it had paid the prices charged for the same drugs in France. Key drivers of lower drug spending per capita in France seem to be that drug prices are regulated at launch and substantial annual price increases are not allowed. Differences in prescription volumes and national health budgeting regulations may also help explain why France spends less on brand-name drugs than the United States does. The effects of these differences can help inform discussions of US policy changes related to prescription drug price negotiation in Medicare.

References


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