# Medicamentos y precios: Pasando revista…

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Sección Farmacología Clínica

# Conflictos de interés

- No tengo conflictos de interés con esta presentación

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# Aprobaciones de fármacos 2018

# Mercado de fármacos 2019

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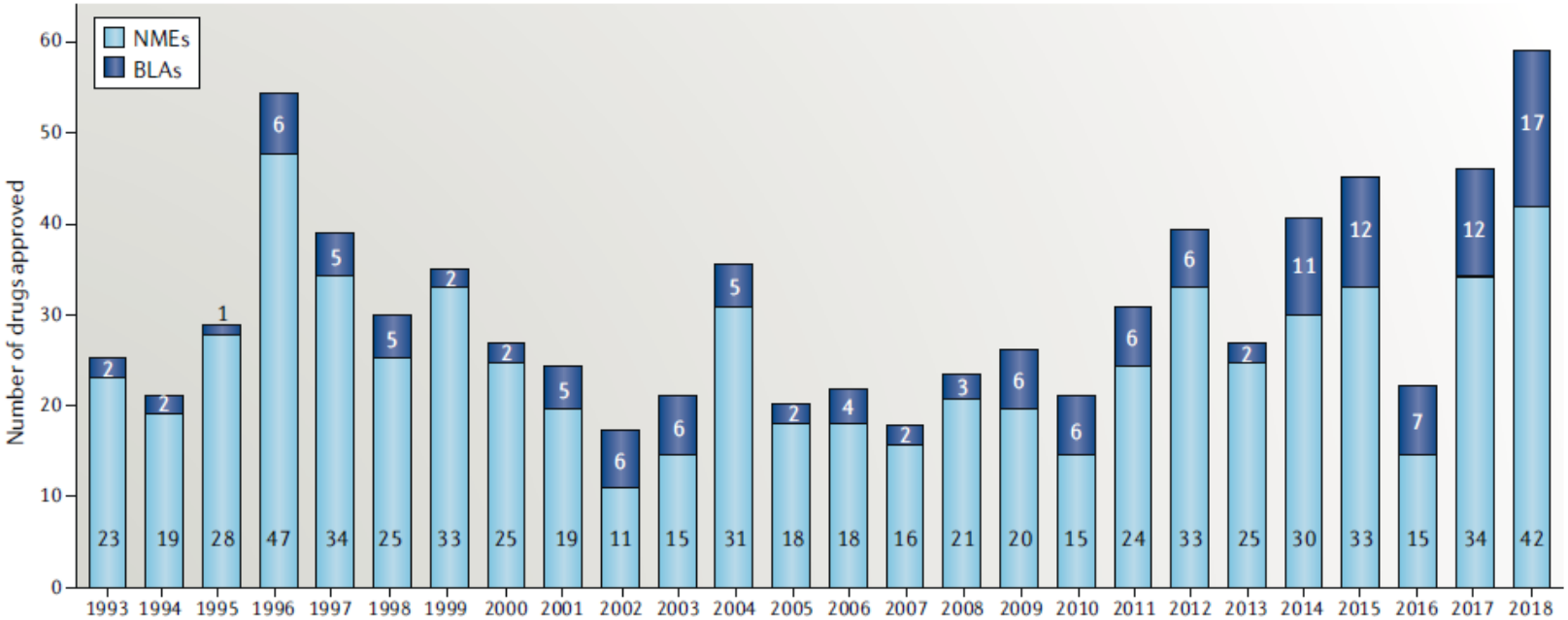
# 2018 FDA drug approvals

The FDA approved a record 59 drugs last year, but the commercial potential of these drugs is lacklustre.



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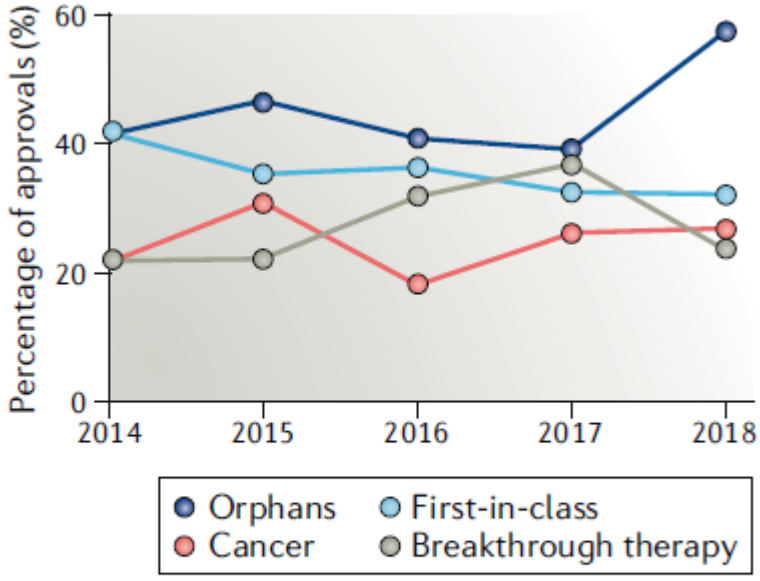



Fig. 2 | **CDER approval trends.** Source: *Nature Reviews Drug Discovery*, FDA.

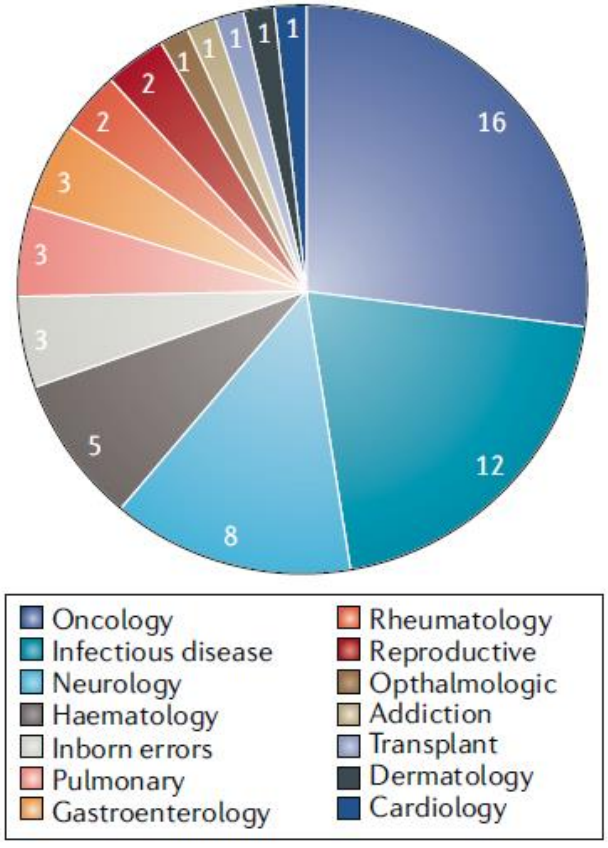
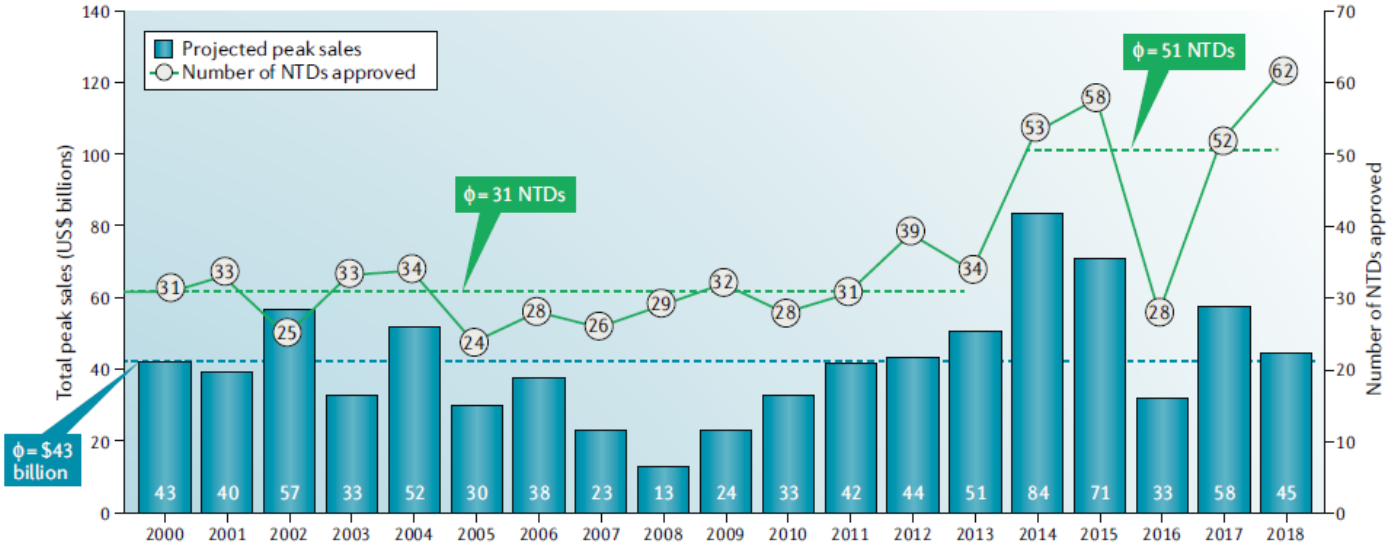



Fig. 3 | **CDER approvals by therapeutic area in 2018.** Source: *Nature Reviews Drug Discovery*.

# 2018 FDA approvals hit all time high — but average value slips again




| | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Average peak sales per NTD (US$ billions) | 1.4 | 1.2 | 2.3 | 1.0 | 1.5 | 1.3 | 1.4 | 0.9 | 0.5 | 0.7 | 1.2 | 1.4 | 1.1 | 1.5 | 1.6 | 1.2 | 1.2 | 1.1 | 0.7 | ϕ = $1.2 billion |
| Median peak sales per NTD (US$ billions) | 0.5 | 0.7 | 0.9 | 0.3 | 0.7 | 0.6 | 0.8 | 0.5 | 0.3 | 0.3 | 0.4 | 0.5 | 0.3 | 0.5 | 0.4 | 0.4 | 0.6 | 0.5 | 0.4 | ϕ = $0.5 billion |

Table 1 | **Top product forecasts for 2019**

| Rank | Product | Company | Pharmacological class | 2019 worldwide sales (US$ millions) |
|---|---|---|---|---|
| 1 | Humira | AbbVie | Anti-TNF mAb | 19,604 |
| 2 | Revlimid | Celgene | Immunomodulator | 10,918 |
| 3 | Keytruda | Merck & Co. | Anti-PD1 mAb | 9,801 |
| 4 | Eliquis | Bristol-Myers Squibb | Factor Xa inhibitor | 7,666 |
| 5 | Opdivo | Bristol-Myers Squibb | Anti-PD1 mAb | 7,341 |
| 6 | Avastin | Roche | Anti-VEGF mAb | 6,151 |
| 7 | Stelara | Johnson & Johnson | Anti-IL-12/IL-23 mAb | 5,874 |
| 8 | Prevnar 13 | Pfizer | Pneumococcal vaccine | 5,806 |
| 9 | Herceptin | Roche | Anti-HER2 mAb | 5,599 |
| 10 | Rituxan | Roche | Anti-CD20 mAb | 5,358 |

HER2, human epidermal growth factor receptor 2; IL, interleukin; mAb, monoclonal antibody; TNF, tumour necrosis factor; VEGF, vascular endothelial growth factor. Source: EvaluatePharma, January 2019.

- 2010- 2014 : 70% de las aprobaciones fueron por big pharma
- 2018: 63% aprobaciones por start ups o laboratorios pequeños
- Drogas para mercados pequeños (pocos pacientes y alto precio)

# A Delicate Balance — Pharmaceutical Innovation and Access

William W. Chin, M.D.

It's possible to deliver so many new medications to patients while still managing costs because the United States relies on competitive markets to set prices and encourage innovation — a system that, as I see it, is working well.

## New Math on Drug Cost-Effectiveness

Peter B. Bach, M.D., M.A.P.P.

*The rate of introduction of new and expensive drugs has accelerated; the pace of conversion to generics is slowing; the prices of many generics are rising; and expensive drugs are now being introduced for conditions that affect millions of people rather than thousands.*

N ENGL J MED 373;19 NEJM.ORG NOVEMBER 5, 2015

# Cuanto cuesta desarrollar un fármaco?

JAMA Internal Medicine | Original Investigation

Sección Farmacología Clínica

# Research and Development Spending to Bring a Single Cancer Drug to Market and Revenues After Approval

Vinay Prasad, MD, MPH; Sham Mailankody, MBBS

## Key Points

**Question** What is the estimated research and development spending for developing a cancer drug?

**Findings** In this analysis of US Securities and Exchange Commission filings for 10 cancer drugs, the median cost of developing a single cancer drug was $648.0 million. The median revenue after approval for such a drug was $1658.4 million.

**Meaning** These results provide a transparent estimate of research and development spending on cancer drugs and show that the revenue since approval is substantially higher than the preapproval research and development spending.

*JAMA Intern Med*. 2017;177(11):1569-1575. doi:10.1001/jamainternmed.2017.3601
Published online September 11, 2017. Last corrected on August 13, 2018.

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Original Investigation | Health Policy

# Comparison of Sales Income and Research and Development Costs for FDA-Approved Cancer Drugs Sold by Originator Drug Companies

Kiu Tay-Teo, PhD; André Ilbawi, MD; Suzanne R. Hill, PhD

## Key Points

**Question** How does income from the sales of cancer drugs compare with the costs of research and development?

**Findings** In this observational study of 99 cancer drugs approved by the FDA from 1989 to 2017, the median income return by the end of 2017 was found to be $14.50 (range, $3.30-$55.10) for every $1 research and development spending. Many drugs, particularly biologics, continued to generate high-sales incomes for the originator companies after expiry of patents and exclusive marketing rights.

**Meaning** Cancer drugs, through high prices, have generated incomes for the companies far in excess of research and development costs; lowering prices of cancer drugs and facilitating greater competition are essential for improving patient access, health system's financial sustainability, and future innovation.

*JAMA Network Open*. 2019;2(1):e186875. doi:10.1001/jamanetworkopen.2018.6875 January 4, 2019

Sección Farmacología Clínica

# Genéricos y Biosimilares pueden bajar los precios?

# La competencia entre varios medicamentos para la misma indicación ayuda a disminuir el precio?

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Sección Farmacología Clínica

# Assessment of Price Changes of Existing Tumor Necrosis Factor Inhibitors After the Market Entry of Competitors

Alvaro San-Juan-Rodriguez, PharmD
Max V. Prokopovich, BS
William H. Shrank, MD, MSHS
Chester B. Good, MD, MPH
Inmaculada Hernandez, PharmD, PhD

**Discussion** | Annual treatment costs with existing TNF inhibitors increased after the entry of 3 new agents. If cost trends had not changed after the entry of new products, costs of etanercept, infliximab, and adalimumab in December 2016 would have been 40% to 45% lower than they actually were.



JAMA Internal Medicine Published online February 18, 2019

# Deflazacort—New Costs of an Old Medicine

VIEWPOINT

**Stephen Mark Chrzanowski, PhD**
Department of Physiology and Functional Genomics, University of Florida, Gainesville.

**Rosha Poudyal, PhD**
Department of Biochemistry and Molecular Biology, University of Florida, Gainesville.

Two thousand dollars vs $89 000. That is the cost of deflazacort per year before and after the recent US Food and Drug Administration (FDA) approval for symptomatic treatment in Duchenne muscular dystrophy (DMD).[1] On February 9, 2017, the FDA granted approval for labeled use of deflazacort to mitigate DMD symptoms.[2] Prior to its approval in the United States, deflazacort had been available overseas for decades; in accordance to the Federal Food, Drug, and Cosmetic Act,[3] it was then legal to obtain it overseas. (Briefly, this law states that patients are allowed to import foreign drugs if several criteria are met, including an absence of commercialization in the United States.) After the domestic approval and commercialization of deflazacort, it is now illegal to purchase foreign deflazacort, which was previously affordably priced.

VIEWPOINT

# Obstacles to the Adoption of Biosimilars for Chronic Diseases

**Aaron Hakim, MS**
Yale University School of Medicine, New Haven, Connecticut.

**Joseph S. Ross, MD, MHS**
Section of General Internal Medicine and Robert Wood Johnson Foundation Clinical Scholars Program, Yale University School of Medicine, New Haven, Connecticut; and Center for Outcomes Research and Evaluation, Yale–New Haven Hospital, New Haven, Connecticut.

Primer biosimilar aprobado por FDA 2015
22 biosimilares aprobados por EMA 2006-2015
Intercambiabilidad
Problema del descuento
400 millones de días/pacientes con biosimilares (EMA): seguridad y eficacia

JAMA June 6, 2017 Volume 317, Number 21

Sección Farmacología Clínica

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# Switching to biosimilar infliximab (CT-P13): Evidence of clinical safety, effectiveness and impact on public health

Jürgen Brown [a], Alex Kudrin [b, *]

[a] Rheumazentrum Ruhrgebiet, Claudiusstr. 45, 44649 Herne, Germany
[b] Celltrion Inc, Celltrion, 23 Academy-ro, Yeonsu-gu, Incheon 406-840, South Korea

**Table 3**
Stance of regulatory authorities on interchange and substitution of biosimilars

| Regulatory authority | Interchange | Substitution | Ref |
|---|---|---|---|
| EU (EMA) | Leaving it to each member country to decide | Not permitted at the pharmacy level, and the decision is left to the prescribing physician | [5,8] |
| Finland (Fimea) | Allowed under supervision of a health care professional | No comment | [13] |
| Portugal (Infarmed) | Allowed under supervision of a health care professional | No comment | [13] |
| Netherland (MEB) | Allowed under supervision of a health care professional | No comment | [14] |
| France (ANSM) | Not recommended | Allowed when initiating a course of treatment and only if the prescribing physician has not marked the prescription as 'non-substitutable' | [15,16] |
| Australia (PBAC) | Allowed | Allowed | [17] |
| Italy (AIFA) | Allowed under supervision of a health care professional | Not recommended | [18] |

Biologicals (2016), http://dx.doi.org/10.1016/j.biologicals.2016.03.006

# Como enfrentan otros países el problema de costos en medicamentos

Sección Farmacología Clínica

JAMA | Special Communication

# The High Cost of Prescription Drugs in the United States
## Origins and Prospects for Reform

Aaron S. Kesselheim, MD, JD, MPH; Jerry Avorn, MD; Ameet Sarpatwari, JD, PhD

*JAMA*. 2016;316(8):858-871. doi:10.1001/jama.2016.11237

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## Figure 1. Per Capita Spending on Prescription Pharmaceuticals

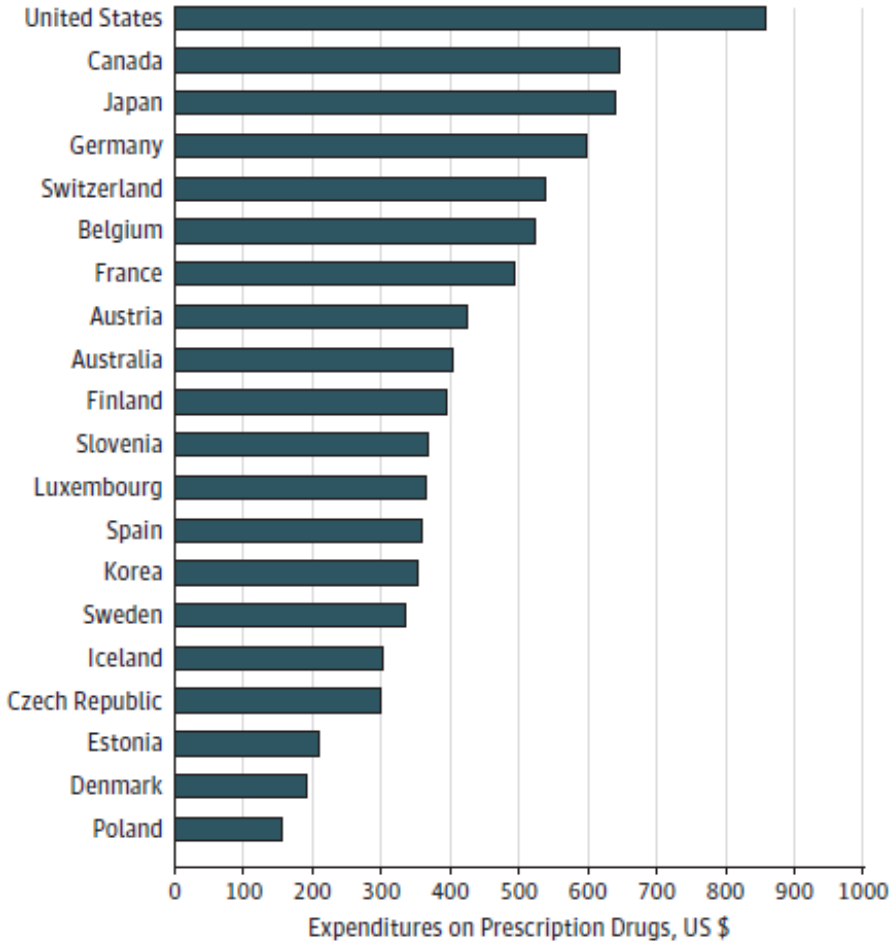

Table 1. Examples of Country-Specific Average Drug Prices for Top-Selling Drugs in 2015

| Drug | Monthly Price, US $ | | | | |
|---|---|---|---|---|---|
| | United States | | | | |
| | Nondiscounted Price | Estimated Discounted Price | Canada | France | Germany |
| Adalimumab (Humira), 40 mg biweekly | 3430.82 | 2504.50 | 1164.32 | 981.79 | 1749.26 |
| Fluticasone/salmeterol (Advair), 250 µg, 50 µg daily | 309.60 | 154.80 | 74.12 | 34.52 | 37.71 |
| Insulin glargine (Lantus), 50 insulin units daily | 372.75 | 186.38 | 67.00 | 46.60 | 60.90 |
| Rosuvastatin (Crestor), 10 mg daily | 216.00 | 86.40 | 32.10 | 19.80 | 40.50 |
| Sitagliptin (Januvia), 100 mg daily | 330.60 | 168.61 | 68.10 | 35.40 | 39.00 |
| Sofosbuvir (Sovaldi), 400 mg daily | 30 000.00 | 17 700.00 | 14 943.30 | 16 088.40 | 17 093.70 |
| Trastuzumab (Herceptin), 450 mg every 3 wk | 5593.47 | 4754.45 | | 2527.97 | 3185.87 |

VIEWPOINT

# FDA Approval of Tisagenlecleucel
## Promise and Complexities of a $475 000 Cancer Drug

**Peter B. Bach, MD**
Memorial Sloan Kettering Cancer Center, New York, New York.

**Sergio A. Giralt, MD**
Memorial Sloan Kettering Cancer Center, New York, New York.

**Leonard B. Saltz, MD**
Memorial Sloan Kettering Cancer Center, New York, New York.

In this case, one clear comparator treatment will be Amgen's blinatumomab, which at $178 000 for a typical treatment course of 6 weeks is also priced outside the normal range of cancer treatments. Thus, comparison to high-cost alternatives can be misleading (this is the same mechanism that allows a BMW to look like a bargain when the only other car on the lot is a Ferrari).

JAMA November 21, 2017 Volume 318, Number 19

Sección Farmacología Clínica

# Que se puede hacer para evitar esta catástrofe?

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# Drug Regulation and Pricing — Can Regulators Influence Affordability?

Hans-Georg Eichler, M.D., Hugo Hurts, M.Sc., Karl Broich, M.D., and Guido Rasi, M.D.

However, we fail to comprehend prices that, like Sovaldi's, recoup the entire investment within the first few months after a product's launch but are so unaffordable that patients in need are denied access.[1] We are committed to doing our part to facilitate continued access to effective and safe treatments.

# The High Cost of Prescription Drugs in the United States
## Origins and Prospects for Reform

Aaron S. Kesselheim, MD, JD, MPH; Jerry Avorn, MD; Ameet Sarpatwari, JD, PhD



**Table 3. Approaches to Drug Pricing in Selected Countries**

| | Australia | Canada | | Germany | United Kingdom |
|---|---|---|---|---|---|
| National organization | Pharmaceutical Benefits Advisory Committee | Patented Medicines Prices Review Board | Canadian Agency for Drugs and Technology in Healthcare | Federal Joint Committee or Institute for Quality and Efficiency in Healthcare | National Institute for Health and Clinical Excellence |
| Remit | Public payers | All payers | Public payers except in Quebec (noncancer drugs) | All insurers | National Health Service |
| Review criteria | Comparative effectiveness, safety, and cost-effectiveness; projected usage and overall costs to the health care system | Therapeutic innovation; comparative pricing with respect to France, Germany, Italy, Sweden, United Kingdom, and United States | Comparative effectiveness, safety, and cost-effectiveness; patient experiences | Comparative benefit | Clinical effectiveness and cost-effectiveness |
| Decision | Coverage (yes, no, limited) | Price reductions or rebates | Coverage | Price setting after first year on the market | Coverage |
| Binding | Yes | Yes | No | Yes | Yes |

JAMA | Special Communication

# The High Cost of Prescription Drugs in the United States
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### State

**Drug product selection laws:** Convert permissive generic substitution policies to mandatory substitution policies; eliminate patient consent requirements for generic substitution; limit "carve-outs" that make it more difficult to substitute in certain clinical categories (eg, antiepileptics, follow-on biologics)

**Price negotiation:** Test value-based drug pricing and rational prescribing reimbursement models for Medicaid

### Health Care Organizations

**Price negotiation:** Develop value-based formularies and co-payment plans that encourage patients to make better choices but do not penalize them and hamper adherence

**Information dissemination:** Initiate academic detailing programs to market the best comparative evidence to prescribers and policy makers

### Federal

**Patenting:** Limit secondary patents for trivial changes of a patented molecule (eg, heightening patenting standards to require showing enhanced safety or effectiveness over previously patented version of the molecule)

**Anticompetitive strategies:** Aggressively police anticompetitive business practices (eg, pay for delay, product hopping)

**Price negotiation:** Enable Medicare to negotiate drug prices for individual Part D plans and to exclude coverage for expensive products that add limited clinical benefit; experiment with value-based drug pricing and rational prescribing reimbursement models for Medicare

**Addressing extraordinary shortage or pricing problems:** Invoke "march-in" rights or government royalty-free license rights on excessively costly products that were developed in large part with government funding

**Generic drug policies:** Allocate greater resources at the FDA for reviewing generic drug applications to facilitate competition; in the event of a shortage of manufacturers, accelerate review of drug applications and authorize temporary drug importation from well-regulated pharmaceutical markets; mandate brand-name drug sample sharing with generic manufacturers

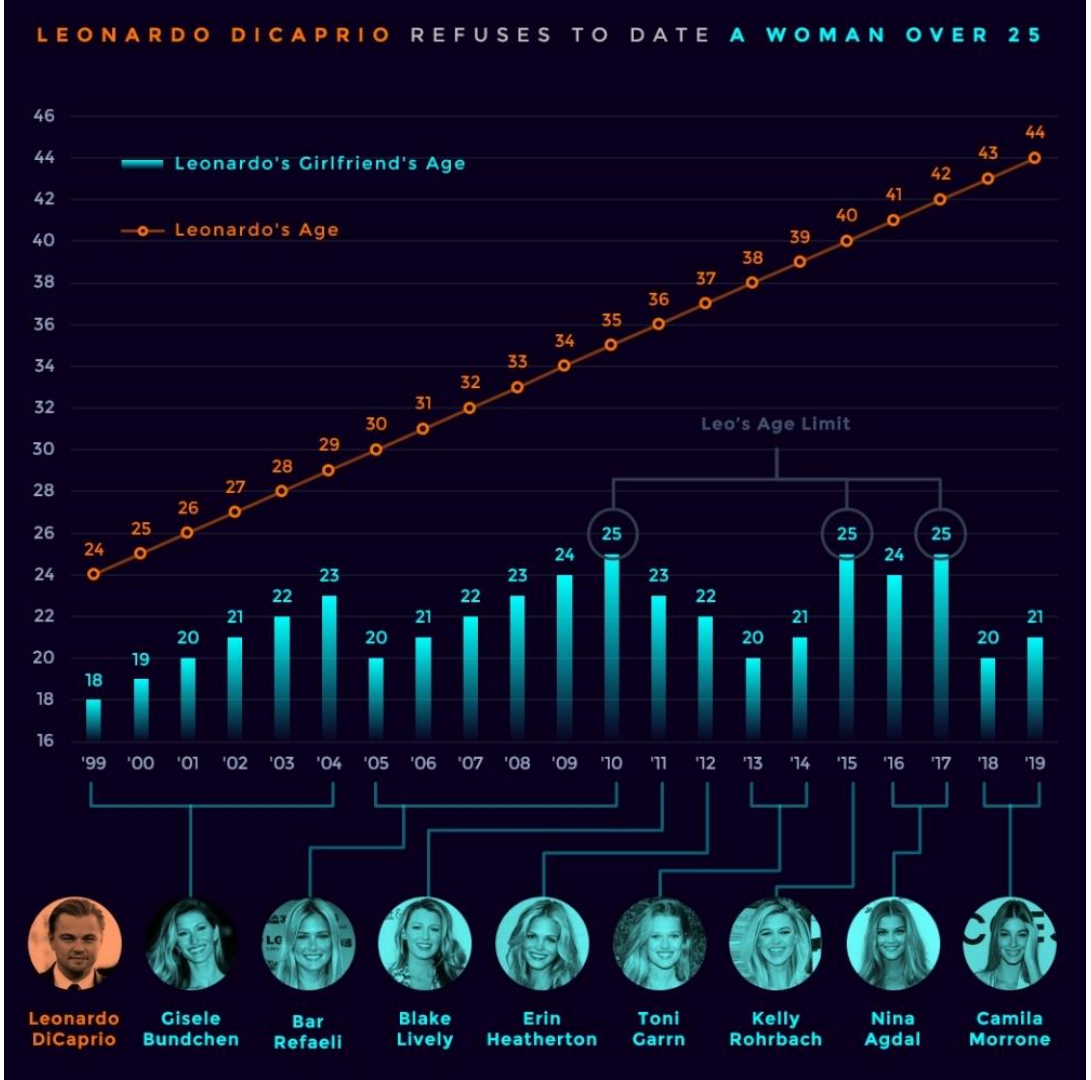
**Follow-on biologic policies:** Allocate greater resources to the FDA for reviewing follow-on biologic applications; promulgate product-specific guidance on demonstrating interchangeability; conduct rigorous postapproval surveillance of follow-on biologics to ensure the safety and effectiveness of these products

# La paradoja Di Caprio

**1.** adj. desus. **paradójico.**

**2.** f. Hecho o expresión aparentemente contrarios a la lógica.

**3.** f. Ret. Empleo de expresiones o frases que encierran una aparente c
ontradicción entre sí, como en *mira*
*al avaro, en sus riquezas, pobre.*


LEONARDO DICAPRIO REFUSES TO DATE A WOMAN OVER 25
Leonardo's Girlfriend's Age
Leonardo's Age
Leo's Age Limit
Leonardo DiCaprio
Gisele Bundchen
Bar Refaeli
Blake Lively
Erin Heatherton
Toni Garrn
Kelly Rohrbach
Nina Agdal
Camila Morrone