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Insulins: Managing Costs With Increasing Manufacturer Prices

Prepared by Visante on behalf of PCMA

August 2020

Executive Summary

- Insulin list prices have escalated dramatically during the past 5-10 years. This is due to only three manufacturers controlling the market, the lack of alternative insulins, and manufacturer abuse of patent extensions.
- PBMs drive competition using drug formularies and rebates. In spite of dramatic increases in list prices with total gross sales increasing from $22b in 2012 to $54b in 2019, net costs have been flat with total net sales of $13b in 2012 and remained the same $13b in 2019 due to PBM-negotiated rebates, statutory rebates, and other manufacturer discounts.
- Basaglar (a follow-on biologic insulin to the dominant brand-name Lantus) has shown how a price-competitive alternative can shift market share and reduce overall costs. Total net costs for Lantus/Basaglar decreased from $5.6b in 2014 to $2.1b in 2019.
- The Basaglar experience suggests that the seven new insulin biosimilars in the pipeline will likely create an expanded opportunity for PBMs to further reduce total insulin costs through greater formulary competition.
- PBMs are creating innovative programs that limit consumer out-of-pocket (OOP) insulin costs, to promote affordable access, as well as clinical programs that improve care and patient outcomes.

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Insulins: A World Without Competition

Primary Origins of Limited Insulin Competition

OLIGOPOLIES

- Historically, three manufacturers have made all the insulin in the United States: Eli Lilly, Novo Nordisk, and Sanofi.
- The lack of competition has led to a drastic increase in both list and launch prices of insulins.
- Evidence shows that greater competition among more manufacturers is associated with lower drug costs.

DENSE PATENT THICKETS

- Manufacturers utilize the patent system as a way to prolong market exclusivity.
- Many patents are filed after the drug has already been approved.
- Patent infringement lawsuits are commonly used by manufacturers to delay competitor entry into the market.

LACK OF ALTERNATIVES

- Insulin is considered a "biologic," which means it cannot be identically duplicated.
- Some manufacturers have released authorized generic (AG) versions of branded insulin, which merely create an illusion of generic competition.
- Two "follow-on" insulins were the first alternative products to "compete" in the market.

Sources: "Insulin Products and the Cost of Diabetes Treatment" Congressional Research Service, Nov 2018.
Generic Competition and Drug Prices: New Evidence Linking Greater Generic Competition and Lower Generic Drug Prices. FDA, Dec 2019.
"Estimating The Cost Of Delayed Generic Drug Entry To Medicaid" Health Affairs, 2020; Overpatented, Overpriced, I-MAK, 2018.

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Impacts of Limited Competition

Pricing Power

- With only three manufacturers, competition has been limited leading to uninhibited price increases.
- Manufacturer list prices have increased in lock-step with one another.

List Prices Skyrocketing

- Insulin list prices have increased more than tenfold since 1985.
- Prices for Humulin/Novolin have increased from approximately $25 per prescription in 1985 to $400+ in 2019.
- Prices for long-acting insulins have increased from about $100 per prescription in 2007 to $425+ in 2019.

Launch Prices Rising

- During the past 20 years, new insulins have entered the market, but almost always at higher prices than the existing products.
- One exception was **Basaglar**, introduced in December 2016. It was the first follow-on long-acting insulin.

Source: Visante estimates and analysis of SSR Health data, 2020.

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Lack of Alternatives Stifle Competition

Past

- Because of the molecular composition of insulin, it is not possible to create a true "generic" insulin.
- Until recently, insulin was classified as a "drug," which made it difficult to develop any alternative insulin products. Alternative insulins were classified as "follow-on" products.

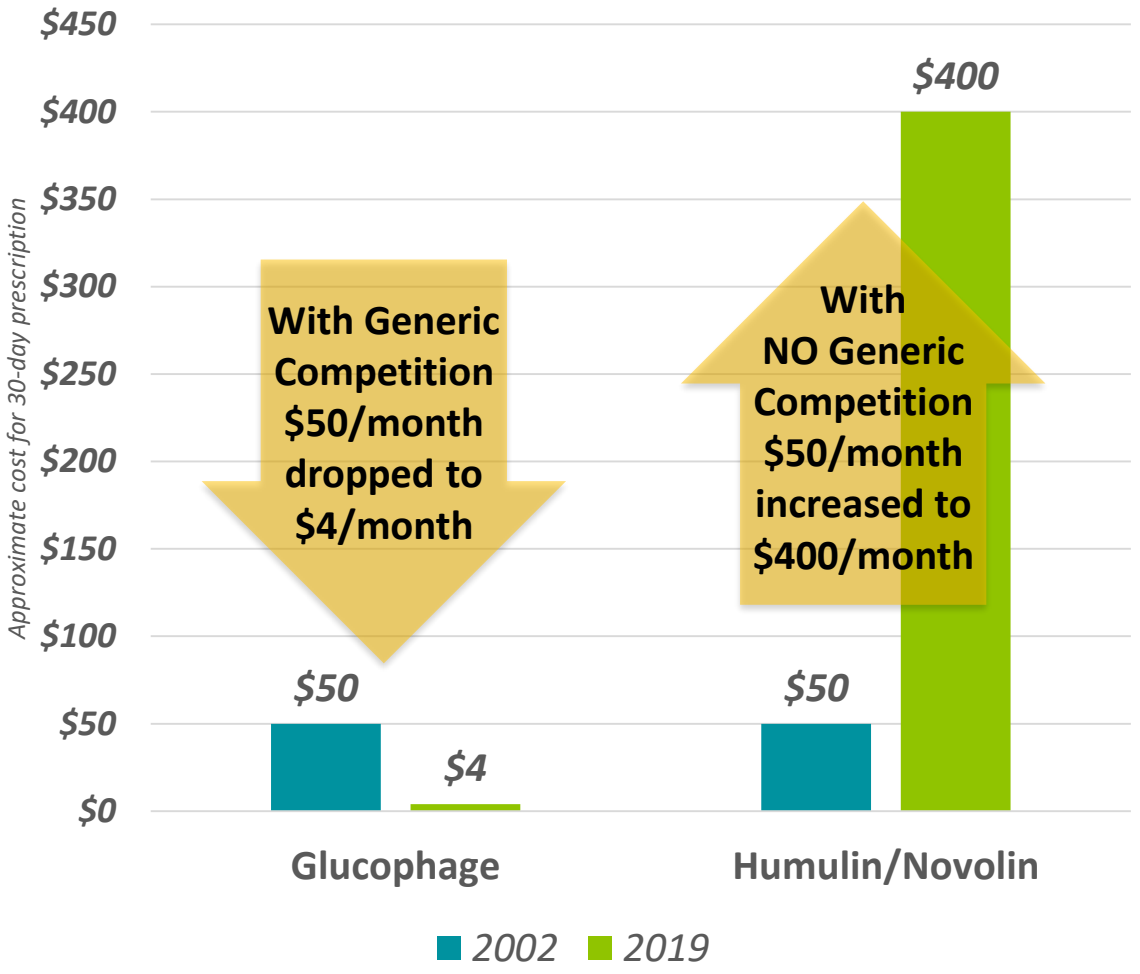
Present

- The "follow-on" biologic Basaglar is a currently-marketed direct competitor to the popular Lantus.
- As of March 2020, FDA guidance requires future alternative insulins to be licensed as "biologics;" this allows for the development of biosimilar insulins, some of which could be interchangeable with branded versions.

Future

- While none are approved yet, biosimilar insulins have the potential to create more intense competition and lower prices.
- Non-insulin biosimilars in the US typically have launch prices 15-35% below the reference product's list price.

Tale of Two Diabetes Drugs: Glucophage vs Human Insulin



Sources: Visante estimates and analysis of SSR Health data, 2020.
"Insulin Gains New Pathway to Increased Competition" FDA, Dec 2019
"Information for Patients About Regulatory Changes for Certain Biological Product Medications" FDA, Mar 2020.

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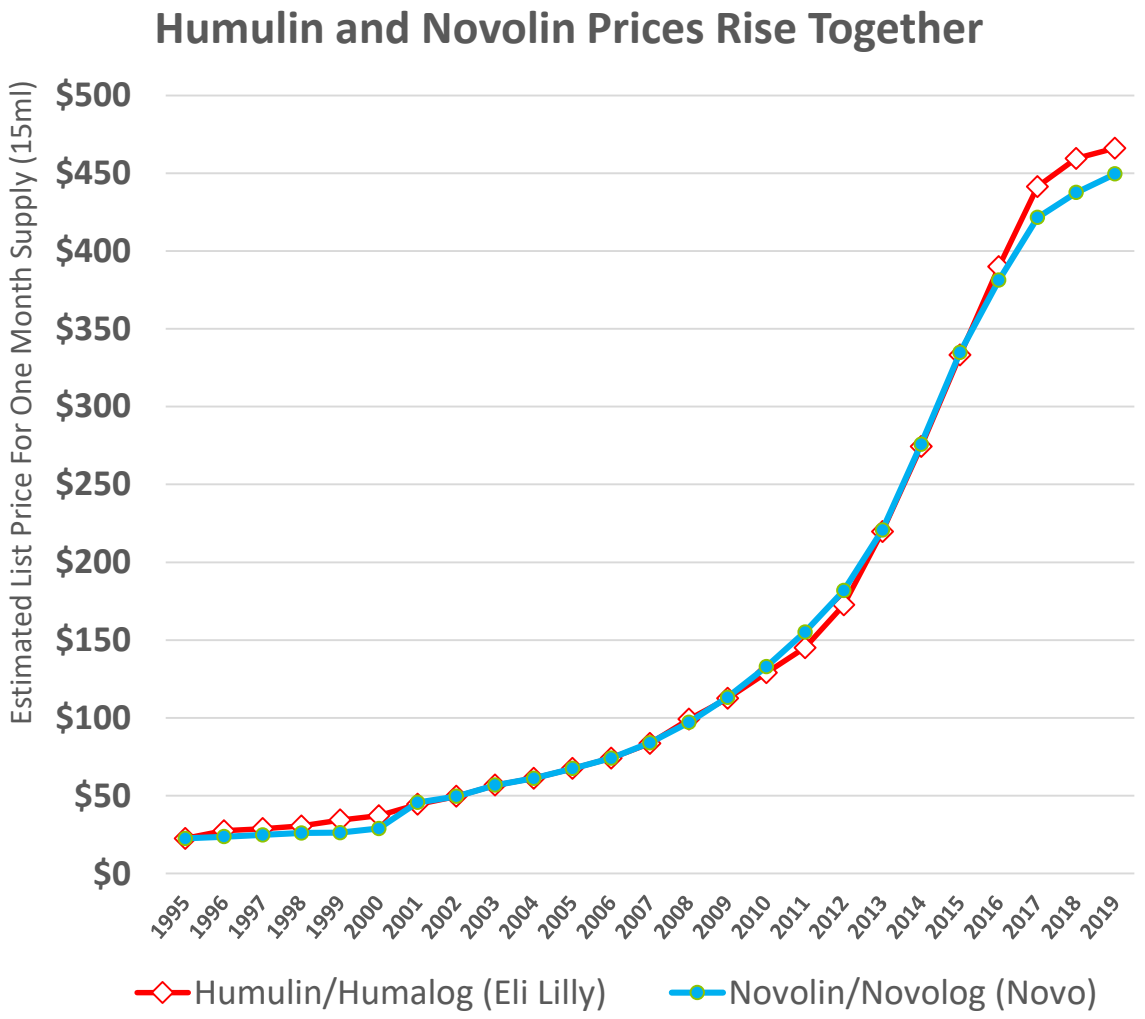
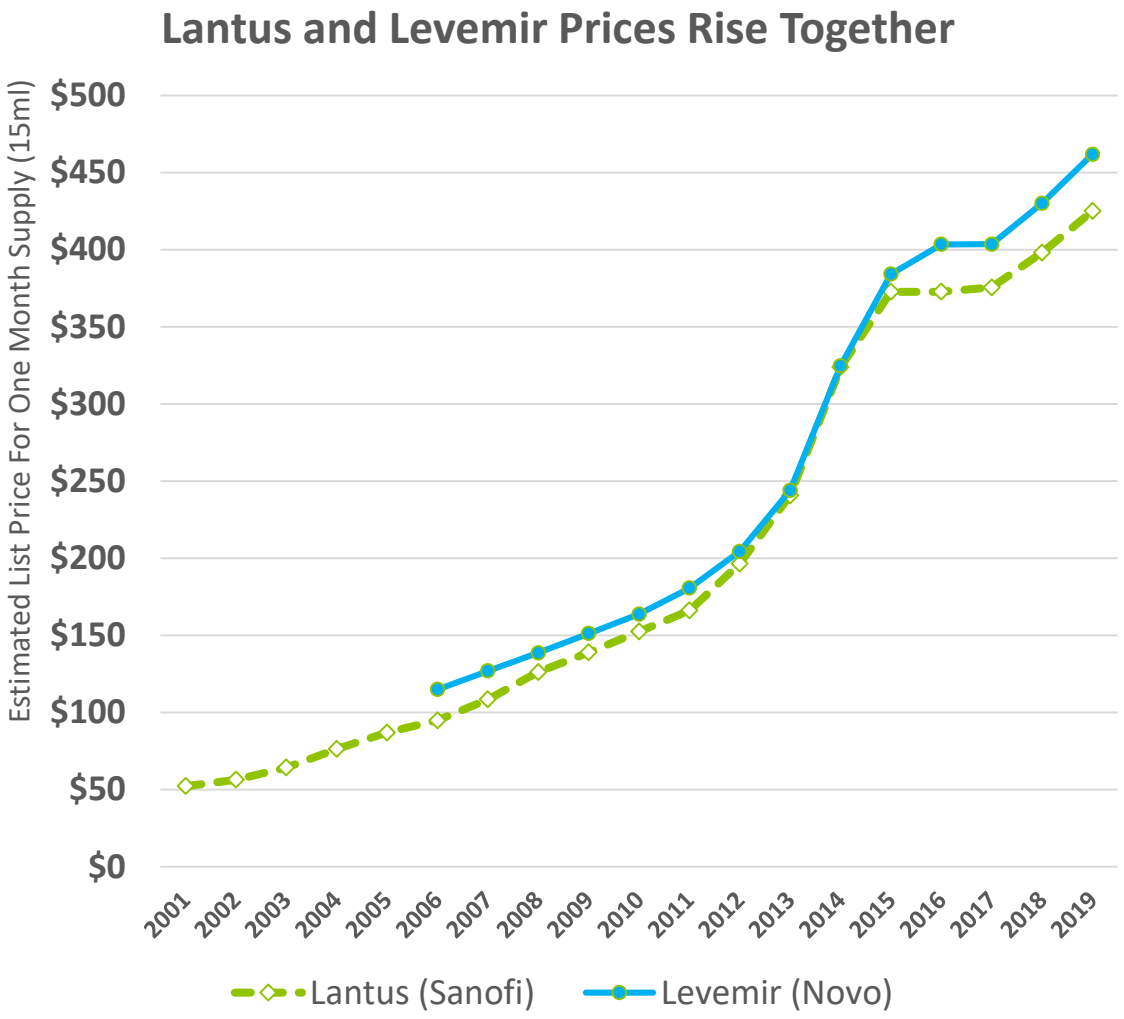
Stifled Competition as Prices for Two Manufacturers Increase in Lock-Step





Source: Visante estimates and analysis of SSR Health data, 2020.

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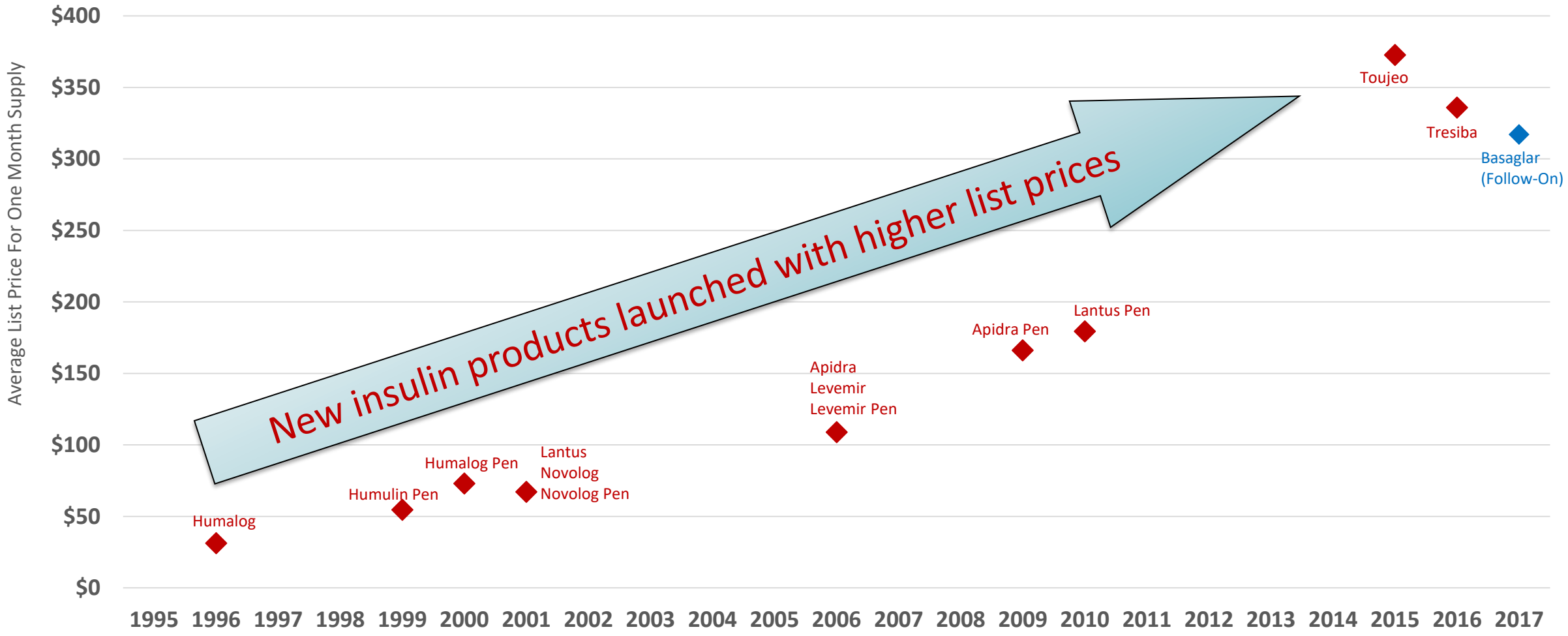
Cost Driver: Higher Launch Prices for New Insulin Products



Source: Visante estimates and analysis of SSR Health data, 2020.

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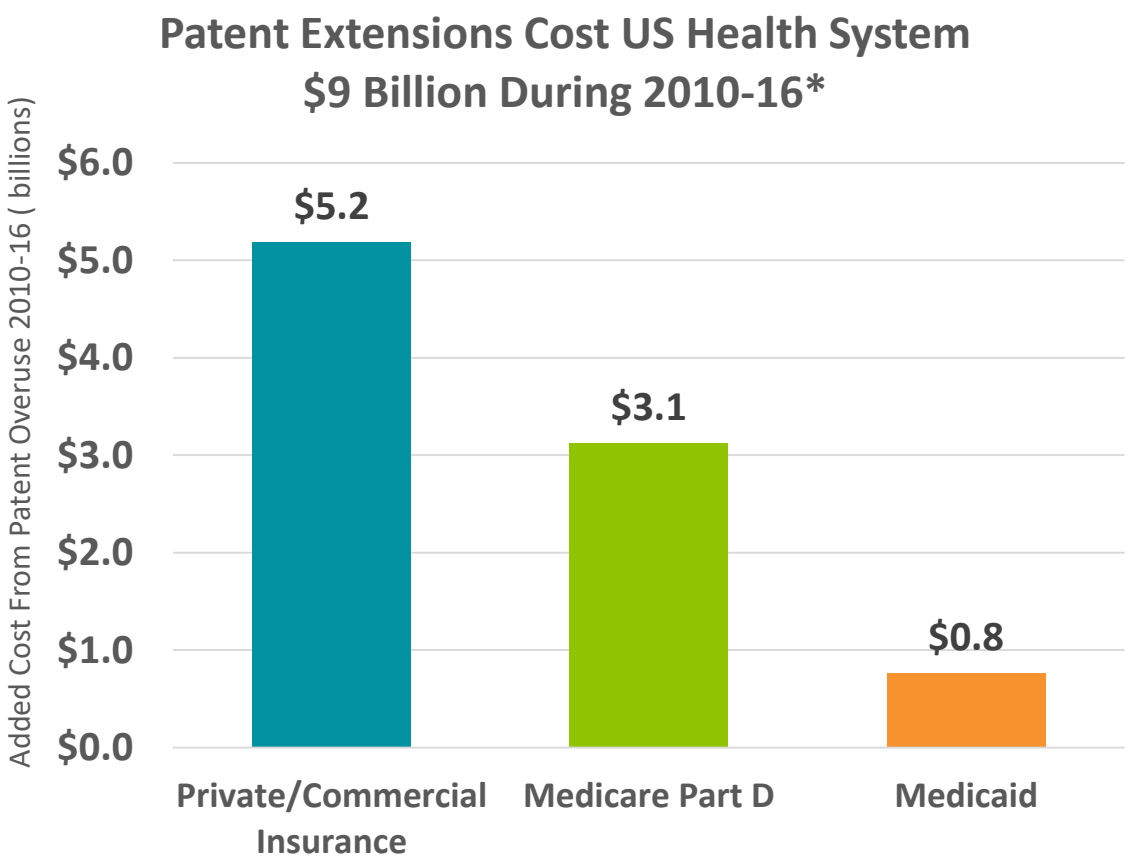
Dense Patent Thickets Delay Competition

Manufacturers exploit patent system to block competition

- Manufacturers rely on obtaining additional patents for their drug products to delay competition.
- These additional patents are often for incremental improvements such as delivery mechanisms (e.g., insulin pens) and alternative formulations (e.g., multi-drug combination products).
- The length of protection is extended by keeping cheaper alternatives off the market while new manufacturers of insulin challenge the patents.
- One study estimated the excess Medicaid spending on drugs predicted to lose market exclusivity to be $761 million over a seven-year period (2010-2016). For 80 percent of the drugs with delayed generics, patent litigation on later-issued patents was the most common reason associated with delays in generic entry.



Sources: "Estimating The Cost Of Delayed Generic Drug Entry To Medicaid" Health Affairs, 2020.
"Overpatented, Overpriced", I-MAK, 2018

*Visante estimate assuming patent extensions affect Private Health Insurance, Medicare and Medicaid equally.

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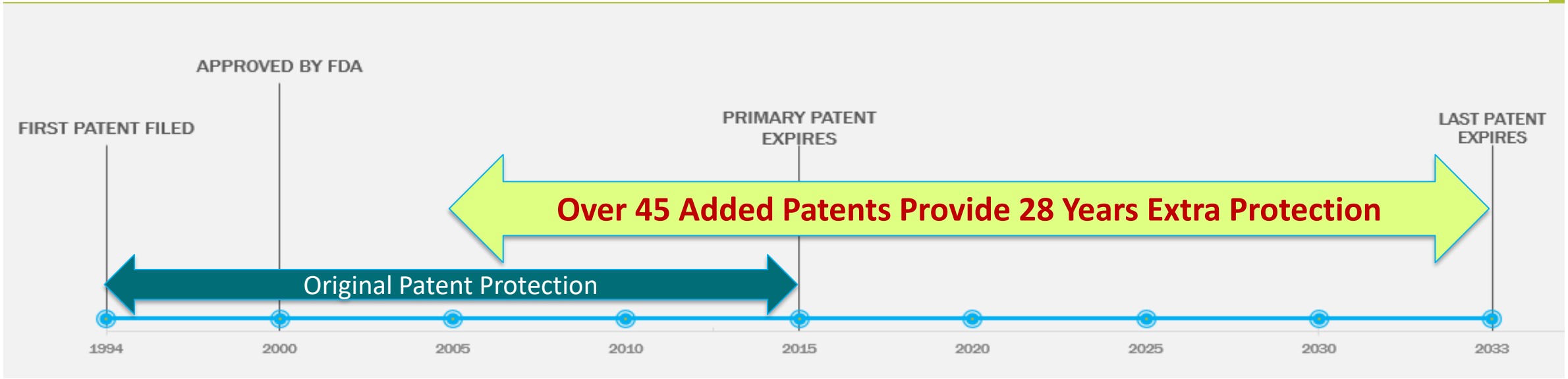
Insulin Patent Thickets Delay Competition

The Lantus Patent Thicket (more than 45 additional patents)



- More than 80% of the active patents for Lantus are not about the drug itself, but the delivery device.
- For example, there are patents related to the delivery mechanism such as the injector, cartridge holder, drive mechanism, dispensing apparatus, housing for dispensing apparatus, and snap fastening connections.
- The last of these active patents expires 33 years after the drug was originally approved.

Sources: Overpatented, Overpriced Special Edition, Lantus. I-MAK, Oct 2018.
Form 20-F. Sanofi, 2019.
United States Patent and Trademark Offices. July 2020.

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The Future is Looking Brighter for Insulin Competition

Seven insulin competitors – and four new manufacturers – in the pipeline to increase competition

Four new manufacturers/ manufacturer alliances are entering the market to penetrate the oligopoly.

Biosimilar Manufacturer	Reference Product		
	Humalog	Novolog	Lantus
Mylan/Biocon	X	X	X
Gan&Lee/Sandoz			X
Lannett			X
Diasome	X		
Sanofi		X	

Lantus competitors approvable as early as mid-2020 and could also compete against other long-acting insulins.

Sources: Biosimilars Pipeline Report. Amerisource Bergen, June 2020.
IPD Analytics Experts Discuss the Insulin Pipeline. AJMC's Center for Biosimilars, April 2020.

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PBMs Drive Competition To Lower Costs

- PBMs and health plans use formularies and formulary exclusions to drive competition between manufacturers, minimize overall medical costs, improve patient access to more affordable care, and provide patients with an improved quality of life.
- Rebates are used to drive competition to the lowest "net price."
- Specific to insulin, generally accepted clinical guidelines for treatment of both type 1 and type 2 diabetes suggest when and how to use insulins, but do NOT favor one brand over another.
- Physicians, pharmacists, and other clinicians on P&T committees for PBMs, health plans, hospitals, and health systems have universally determined:
  - Humulin/Humalog and Novolin/Novolog are therapeutically similar and can compete for preferred status on formularies.
  - Likewise, long-acting insulins are therapeutically similar and can compete for preferred status on formularies.

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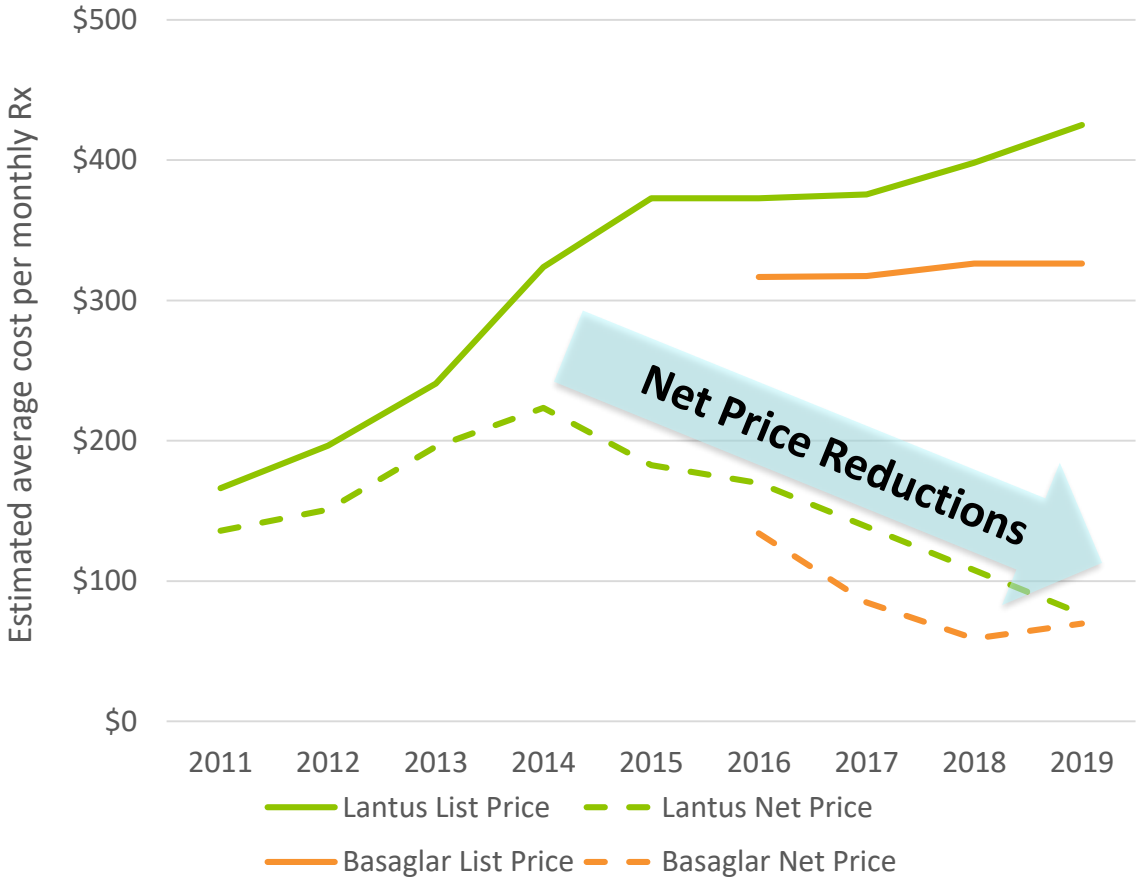
What Works: PBMs Pit Basaglar Against Lantus On Formularies

- Basaglar was introduced in late 2016, as a follow-on competitor to Lantus. Follow-on insulins are FDA-approved copies of a biologic product, but don't meet the definition of a "generic."
- Prior to Basaglar, Lantus was continuously increasing in both list price and net price (i.e., "net-of-rebate" price).
- PBMs used Basaglar to drive competition with Lantus. As a result, the net price of Lantus decreased by almost 55% since Basaglar was introduced.
- In 2019, even though Basaglar had a lower list price than Lantus, the net-of-rebate price of Basaglar and Lantus were almost equal.
- CONCLUSION: Basaglar competition had a dramatic impact on Lantus pricing.

PBMs used Basaglar competition to drive significant reductions in net price



Source: Visante estimates and analysis of SSR Health data, 2020.

"Biosimilar and Follow-on Insulin: The Ins, Outs, and Interchangeability." *J Pharm Technol, Feb 2019.*

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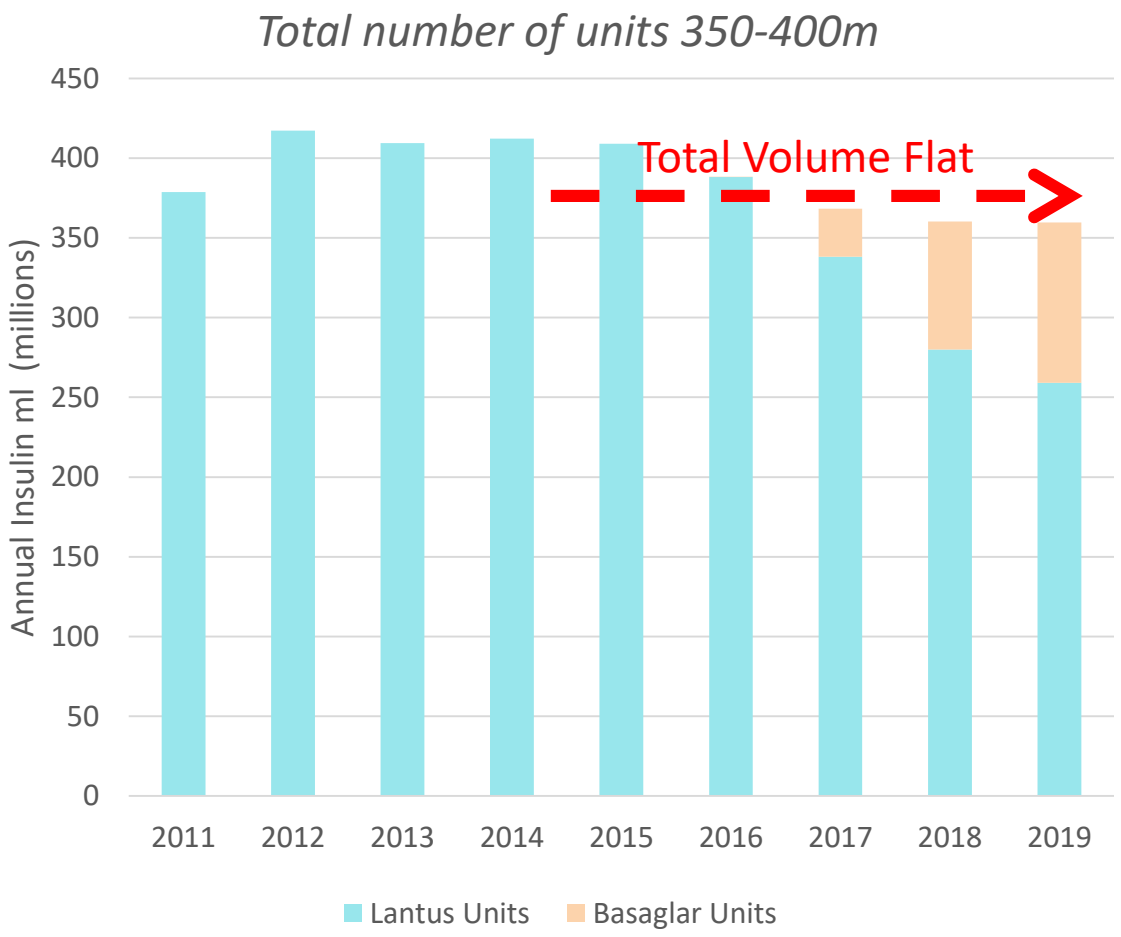
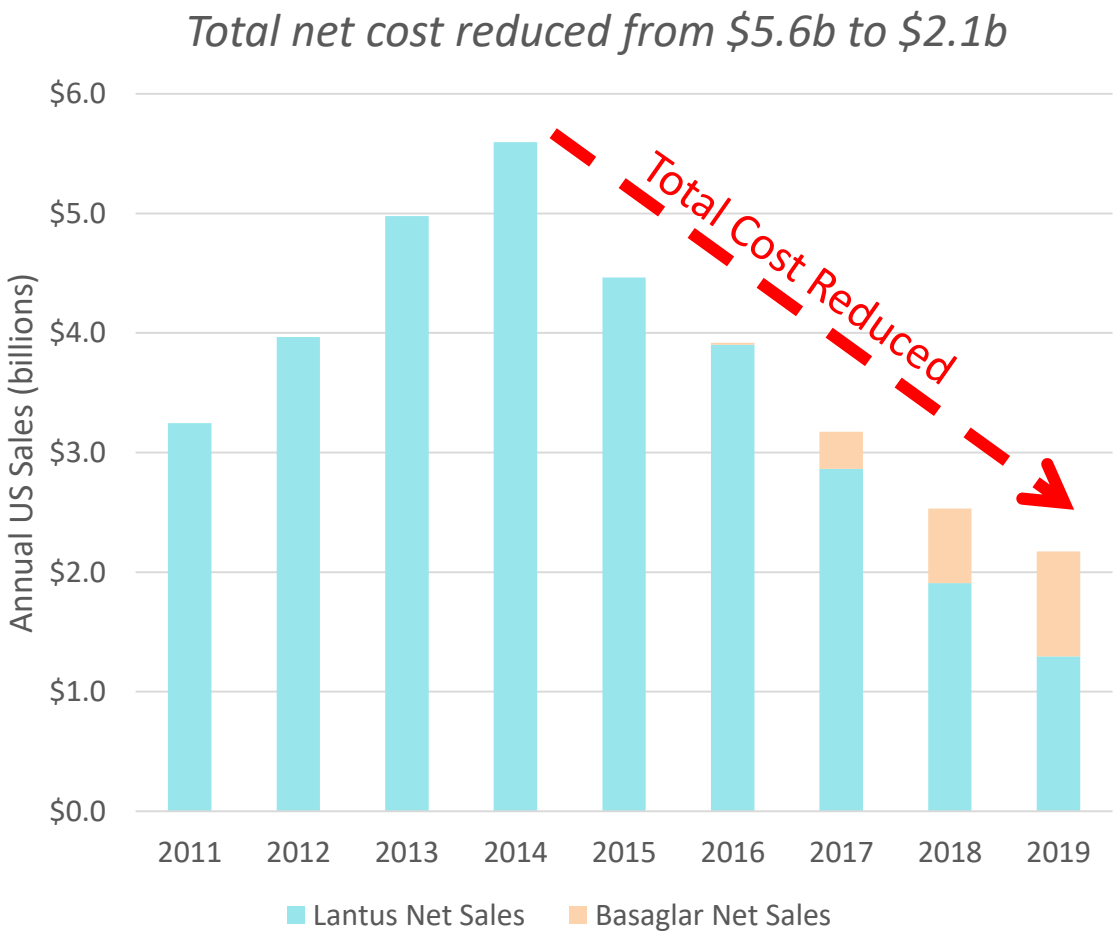
What Works: PBMs Pit Basaglar Against Lantus On Formularies… Competition Leads to Massive Cost Reductions

Total number of units flat



Savings to health system of $3.5 billion in 2019



Source: Visante estimates and analysis of SSR Health data, 2020.

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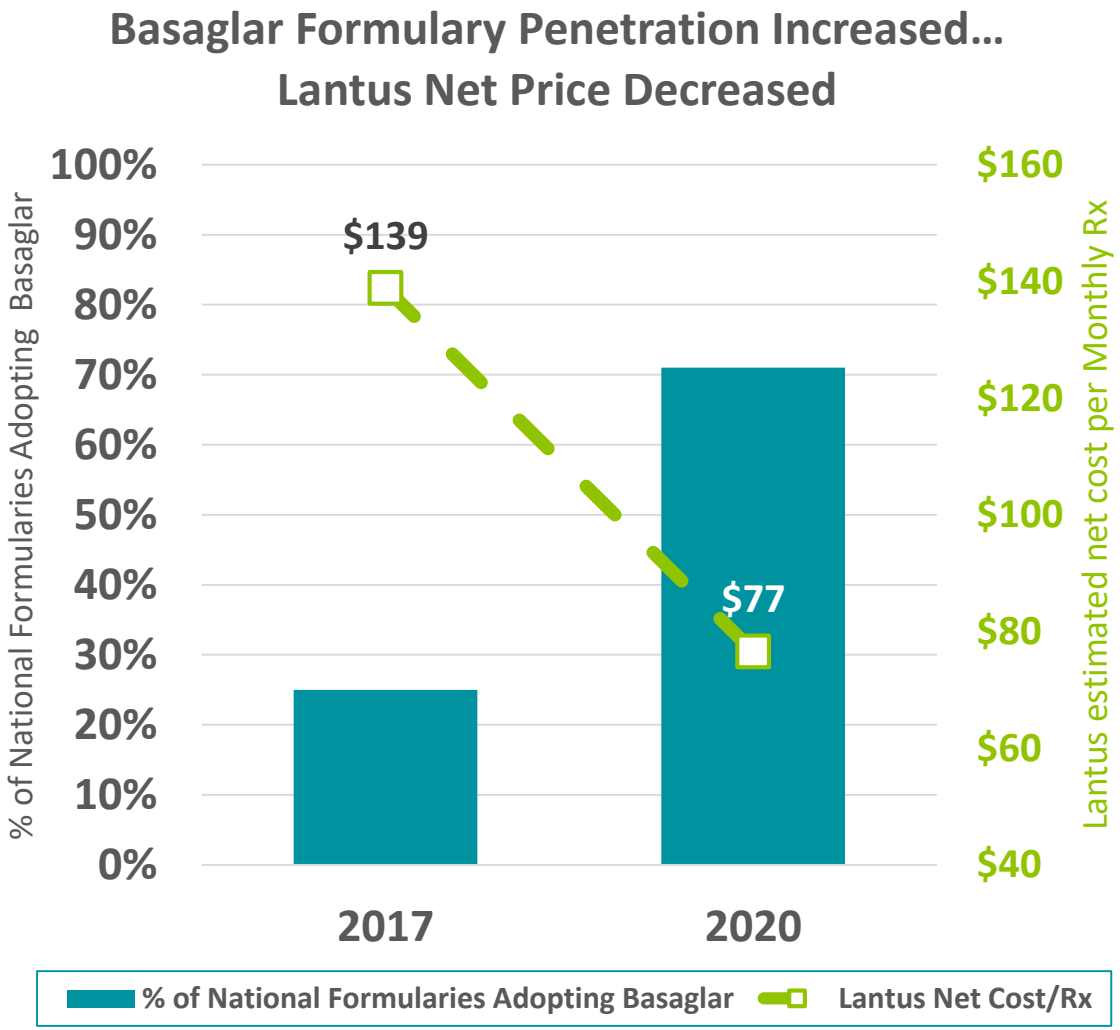
PBMs Respond to Cost-Effective Insulins

- Basaglar entered as an alternative to Lantus in 2016.
- PBMs and health plans recognized the value of cost-effective alternative insulins and reacted accordingly.
- As Basaglar gained market share and reduced price, PBMs added it to more formularies.
- Adoption of Basaglar on top commercial plan formularies has steadily increased since it was first released in late 2016.



Sources: Visante analysis of SSR Health Data.
Visante analysis of large plans with national formularies, including CVS Caremark, Express Scripts, Humana, United Health Group/Optum Rx, Cigna, Prime Therapeutics, and MagellanRx.

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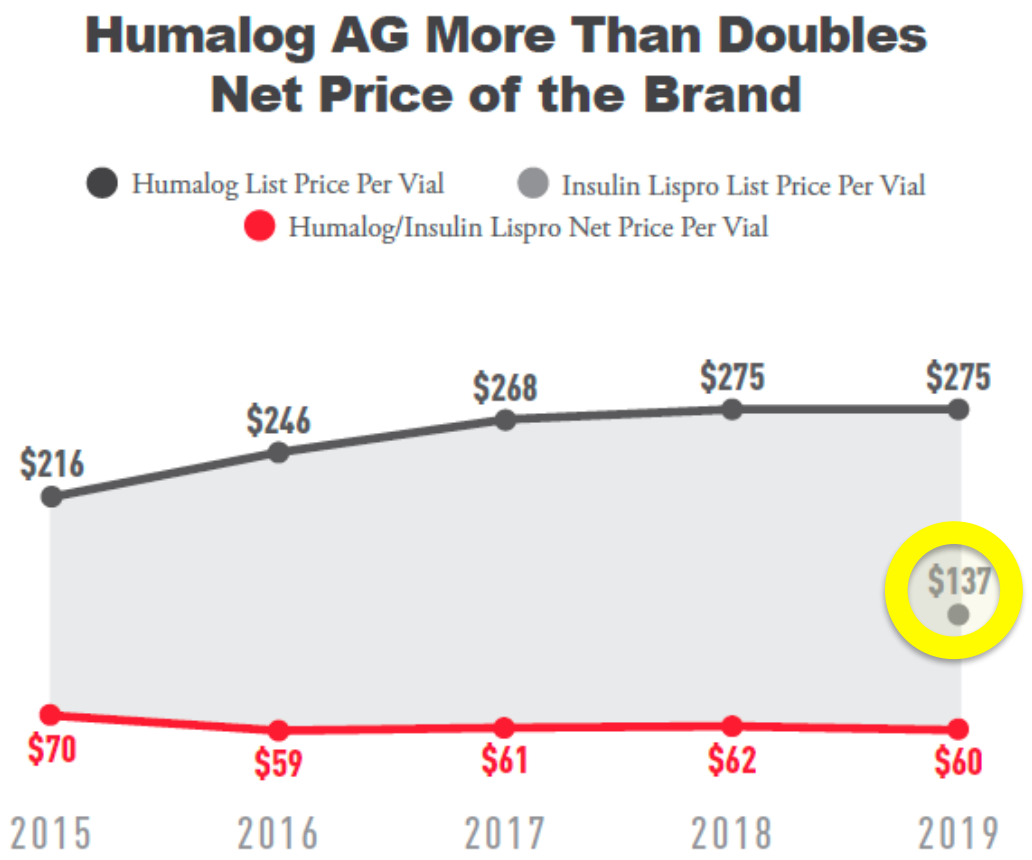
What Doesn't Work: Manufacturer "Authorized Generic" of Humalog

- An authorized generic (AG) creates the illusion of generic competition as it is the **exact** same drug as the brand with a different label name, but with a higher net price.
- In 2019, Lilly released an AG of Humalog (insulin lispro) with a list price of $137, which is more than double the net price of the brand.
- Manufacturers offer AGs to increase profits rather than promote competition.
- Rather than lowering the list price of Humalog, Lilly introduced an AG in a veiled attempt to distract and ease scrutiny on list prices of insulin.



The last list price increase for Humalog vial was May 2017. The net price in the chart represents the revenue Lilly realized per Humalog and Insulin Lispro vial after rebates and discounts. Increases in list prices do not always create increases in net prices.

Sources: "Inaccessible Insulin: The Broken Promise of Eli Lilly's Authorized Generic" Offices of U.S. Senator Elizabeth Warren and U.S. Senator Richard Blumenthal, Dec 2019.
"2019 Integrated Summary Report" Eli Lilly, 2019.
"FDA List of Authorized Generic Drugs." FDA, April 2020.
"Drugmakers Master Rolling Out Their Own Generics To Stifle Competition." KHN, Aug 2019.

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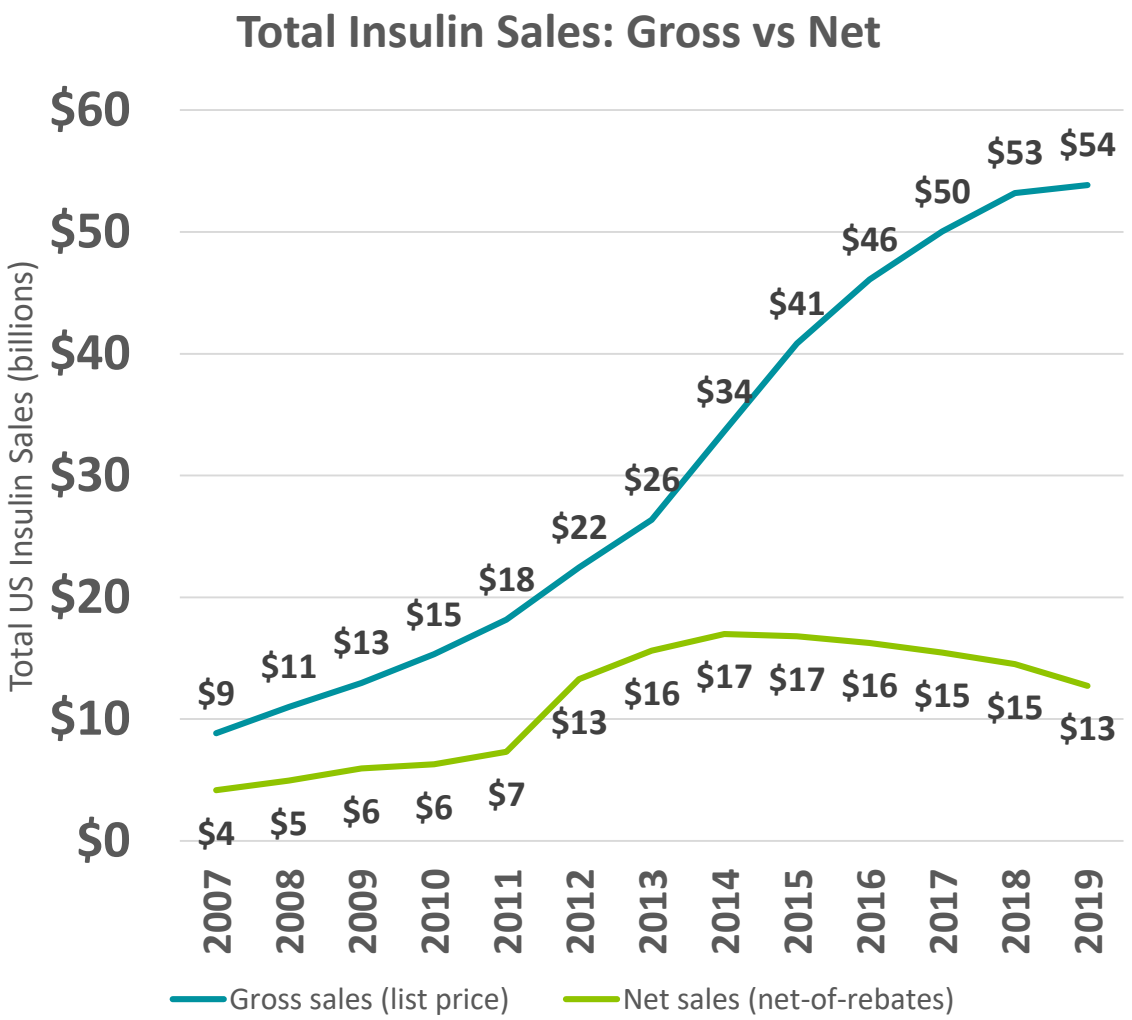
In Face of Continuous Manufacturer List Price Increases, Rebates and Discounts Reduce "Total Net Costs"

- Massive manufacturer list price increases drove total insulin sales from $9 billion in 2007 to $54 billion in 2019.
- PBM-negotiated rebates, statutory rebates, and other manufacturer discounts (e.g., 340b discounts, patient assistance programs, and manufacturer fees) kept net costs to the health system low (i.e., net-of-rebates/discounts), and even reduced total net costs from 2014 to 2019.
- Total savings to the US health system from rebates/discounts exceeded $40 billion in 2019.
- An analysis by the GAO showed PBMs passed 99.6% of rebates collected to Part D plan sponsors in 2016.



Sources: Visante Analysis of SSR Health Data
"Medicare Part D: Use of Pharmacy Benefit Managers and Efforts to Manage Drug Expenditures and Utilization"
GAO, July 2019

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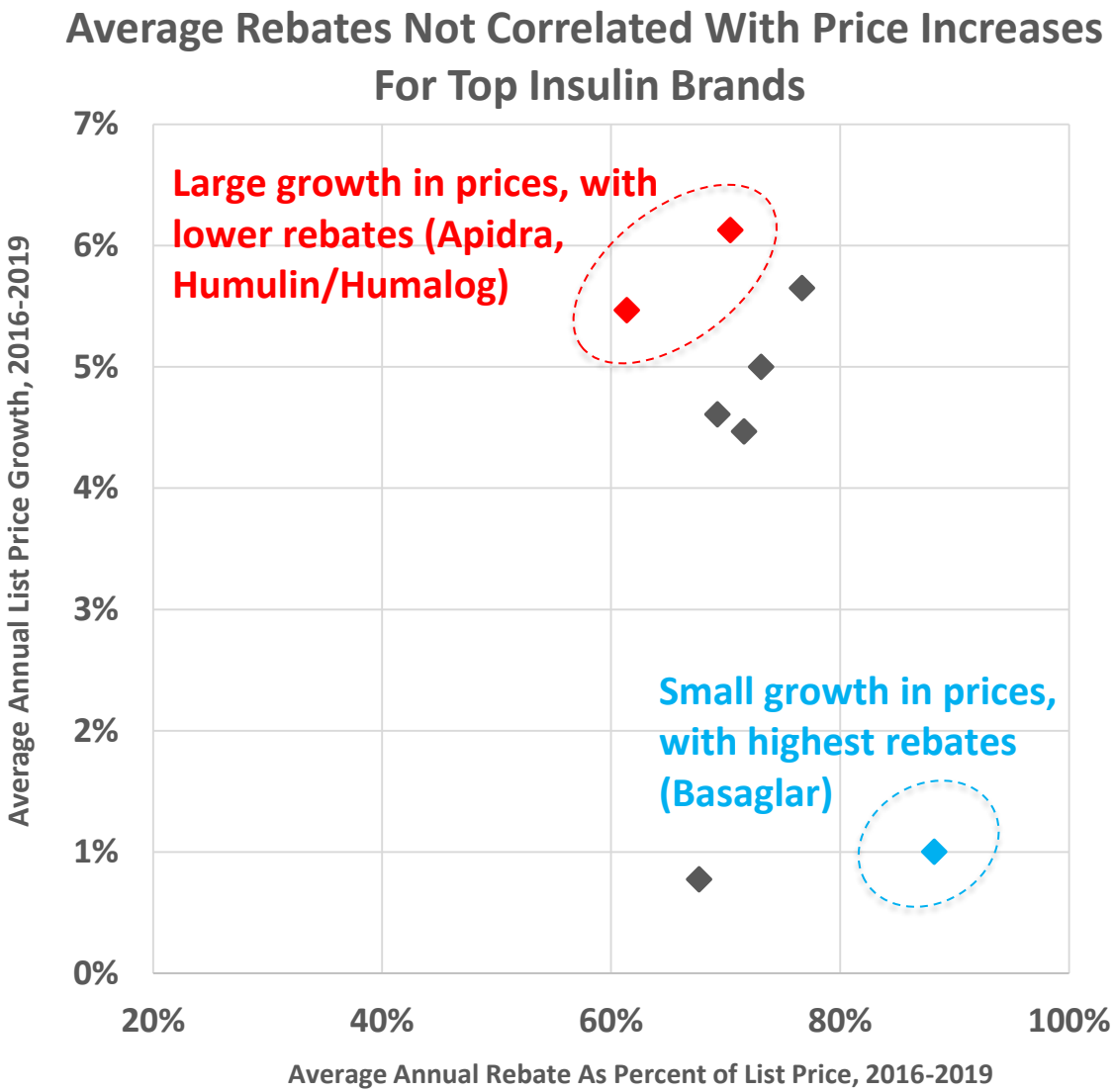
Top Insulin Brands: No Correlation Between Rebates and Price Increases

- **For the eight top insulin products by 2019 sales, there is no correlation between the growing list prices set by drugmakers and the average rebate levels that they negotiate with PBMs.**
- Top insulins with lower average rebates (in red) have actually had *higher* annual price growth during the 2016-2019 period.
- Insulin with highest average rebate (in blue) had small average price increase.
- A similar analysis across all top 200 drugs also shows no correlation between rebate levels and list price growth.



Sources: Visante estimates and analysis of SSR Health data, 2020.
"Reconsidering Drug Prices, Rebates, and PBMs," *Visante, 2018.*

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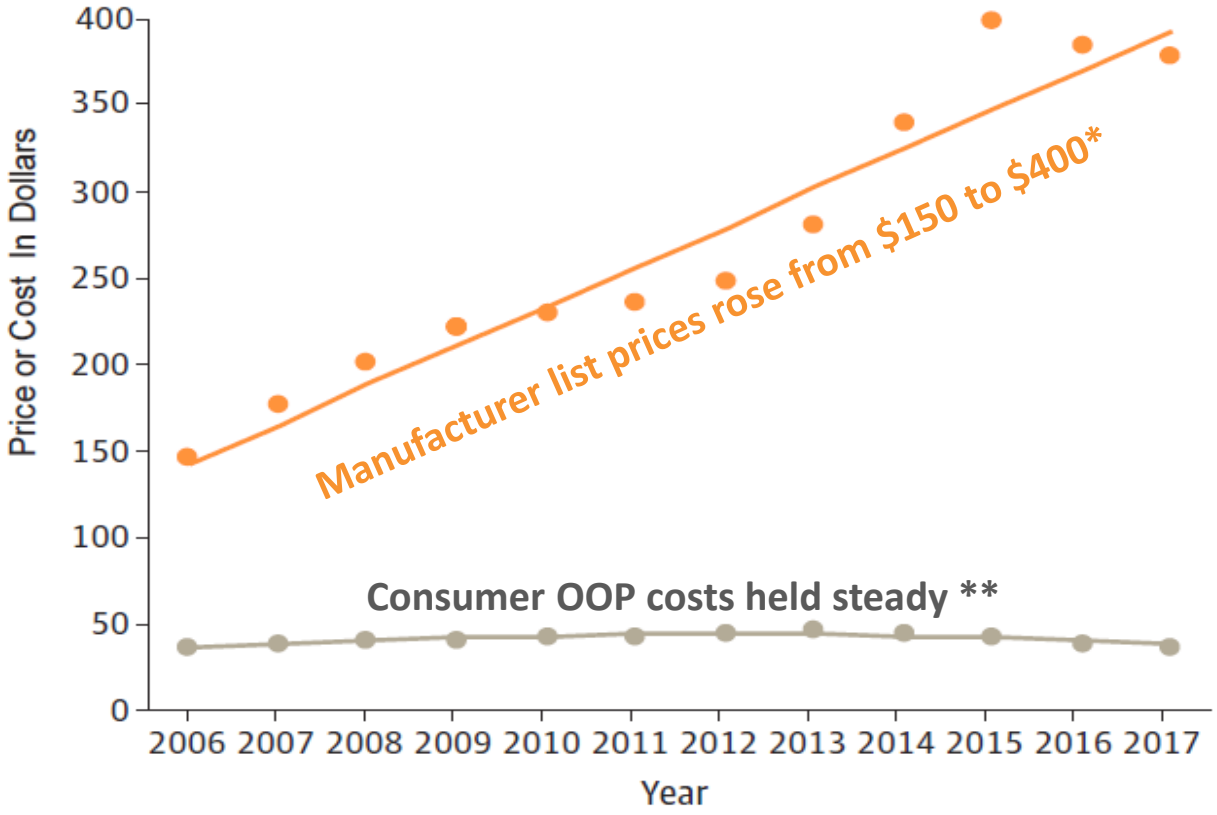
Despite Manufacturer Price Increases, Out-of-Pocket Costs Remained Flat

- A recent study examined more than 10 million claims from consumers with commercial health insurance.
- Results showed median monthly consumer out-of-pocket (OOP) costs on insulin remained relatively flat, despite insulin list prices rising more than 2.5 times, from $150 to $400 per month.

Prices Increased While Consumer OOP Costs Steady



Source: "Trends in Insulin Out-of-Pocket Costs and Reimbursement Price Among US Patients With Private Health Insurance, 2006-2017". JAMA , Jun 2020

* Estimated by calculating the median non-$0 OOP payment toward the annual deductible per 30-day equivalent insulin fill among HDHP-HSA claims.

** Includes the following plan types: HDHP-HSA, HRA, and commercial insurance without a savings account

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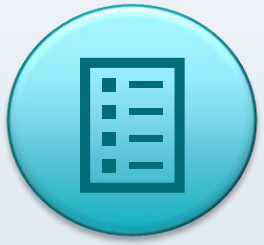
Innovative PBM Programs Reduce Consumer OOP Costs

While some patients still experience unacceptably high out-of-pocket (OOP) costs, PBMs are developing innovative approaches aimed at ensuring affordable access.

Reducing or Eliminating OOP Costs

PBMs are eliminating or reducing OOP costs for all diabetic medications, including insulin, without raising plan costs, premiums, or deductibles.



Adding Insulin to Preventive Drug List

Partnering with health plans to offer insulin before meeting the deductible of high-deductible health plans and health savings accounts.

Providing Diabetic Testing Supplies at No Cost

Helping people better manage their diabetes by eliminating the OOP costs associated with glucose meters and test strips.

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Innovative PBM Programs Aim To Improve Outcomes

In addition to lowering costs, PBMs add value by offering diabetes care management programs

- Provide diabetes education and counseling
  - Lifestyle, exercise, and wellness tips
  - Patient specific action plans and goals
  - Hemoglobin A1C scores and testing regimens
  - Insulin administration training
- Perform medication adherence monitoring
- Provide recommendations to optimize diabetes treatment
- Utilize advanced analytics to improve health outcomes
- Offer associated health services through integrated health centers
  - Monitoring for potential complications and/or adverse reactions
  - Monthly and annual health check-ups for people with diabetes, including screening for diabetic retinopathy, nephropathy and peripheral neuropathy
  - Targeted support and interventions
  - Access clinical decision support systems to assist in diabetes management
  - Enhance provider engagement including integrating and coordinating care

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Public-Private Partnership Innovates to Lower Part D Insulin OOP Costs

- Part D Senior Savings Model is a voluntary five-year model through CMS Innovation Center starting January 1, 2021.
- Allows plans the flexibility to offer non-LIS beneficiaries a max cost-share of $35 per prescription (30-days' supply) on a broad set of insulins in the deductible, initial coverage, and coverage gap phases in Medicare.
- Over 1,750 Part D plans applied to offer the Part D Senior Savings Model for the 2021 plan year.
- All three insulin manufacturers are participating for 2021.
- Currently, there are 60 unique NDCs available under the program and include rapid-acting, short-acting, intermediate-acting, long-acting, mixed, and combination insulins.
- Part D plans must include at least one vial and one pen dosage form of each type of model insulin, where available.
- As this is a new model, outcomes are unknown. However, the model is designed to help those Part D beneficiaries experiencing difficulties paying for insulin.

Sources: "Part D Senior Savings Model CY 2021 Request for Applications for Part D Sponsors" CMS, 2020.
"Calendar Year (CY) 2021 Part D Senior Savings Model Drug National Drug Code (NDC) List CMS, Mar 2020.

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Appendix

Appendix: Types of Insulin

Types of Insulin	Brand Names
Rapid-acting: Usually taken before a meal to cover the blood glucose elevation from eating. This type of insulin is used with longer-acting insulin.	**Humalog – Eli Lilly** **Novolog – Novo Nordisk** **Apidra – Sanofi** **Admelog – Sanofi** (Humalog follow-on) **Fiasp – Novo Nordisk** **Lyumjev – Eli Lilly** **Insulin lispro – Eli Lilly** (Humalog authorized generic) **Insulin aspart – Novo Nordisk** (Novolog authorized generic)
Short-acting: Usually taken about 30 minutes before a meal to cover the blood glucose elevation from eating. This type of insulin is used with longer-acting insulin.	**Humulin R** (regular) – **Eli Lilly** **Novolin R** (regular) – **Novo Nordisk**
Intermediate-acting: Covers the blood glucose elevations when rapid-acting insulins stop working. This type of insulin is often combined with rapid- or short-acting insulin and is usually taken twice a day.	**Humulin N** (NPH) – **Eli Lilly** **Novolin N** (NPH) – **Novo Nordisk**
Long-acting: This type of insulin is often combined, when needed, with rapid- or short-acting insulin. It lowers blood glucose levels when rapid-acting insulins stop working. It is taken once or twice a day.	**Lantus – Sanofi** **Levemir – Novo Nordisk** **Toujeo – Sanofi** **Tresiba – Novo Nordisk** **Basaglar – Eli Lilly** (Lantus follow-on) **Semglee – Mylan/Biocon Ltd.** (FDA approved 6/7/2020)

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