



Balancing revenues and costs for orphan drugs: a case study

Aidan Hollis

University of Calgary: Department of Economics and O'Brien
Institute of Public Health

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No conflicts

Why are prices for orphan drugs so high?

1. Benefit to patients
 2. Small number of patients
 - a. Small impact on insurer's budget
 - b. High average cost of drug development per patient
 3. Support for continuing investment
 4. Incentives
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Presentation plan

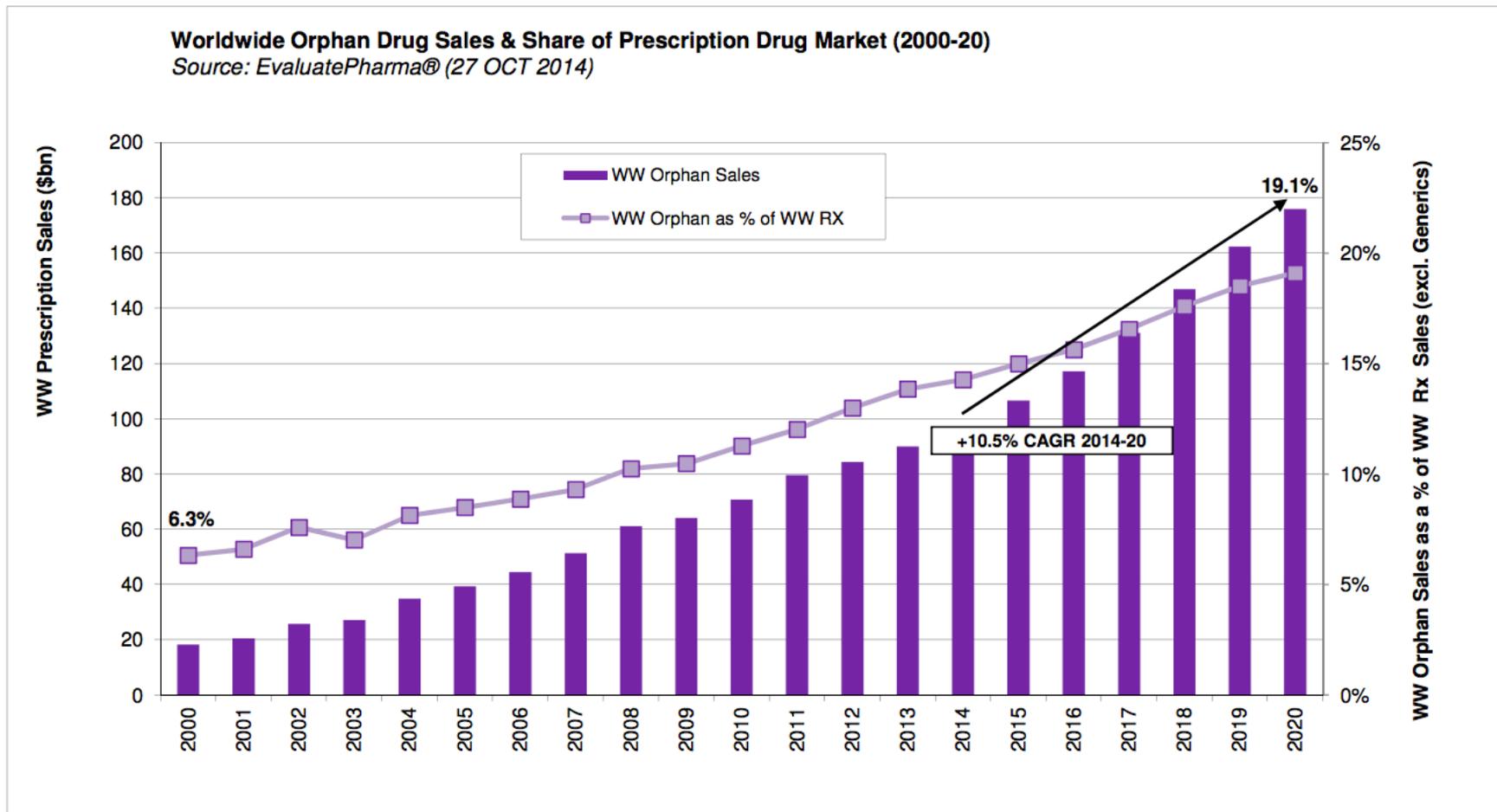
- Why pay attention to orphan drug pricing?
 - Ivacaftor/lumacaftor – an important clinical step and a financial challenge to payers
 - Anticipated Revenues
 - Other costs
 - Costs of R&D
 - Discussion: Implications for why the prices of these products are so high
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Why pay attention to orphan drug pricing?

- Orphan drugs represent a growing share of drug expenditures
- 21 of 45 drugs approved by the FDA in 2015 had orphan indications



Increasing share of total drug spend



Orphan drugs are challenging

- The typical cost-effectiveness approach can be applied to some orphan drugs.
 - But in many cases, pricing is such that the estimated cost per QALY is many times the standard threshold.
 - Aggravating this, for some drugs it is difficult to assess effectiveness because of lack of clarity about the natural history of the disease.
 - To help make things concrete, I examine the particular case of Vertex's drugs ivacaftor and ivacaftor:lumacaftor.
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ivacaftor and lumacaftor

- Ivacaftor (Kalydeco) and ivacaftor:lumacaftor (Orkambi) are the first new drugs to act on the underlying causes of cystic fibrosis (CF)
 - They address the needs of about 2,500 patients (ivacaftor) and 23,000 patients (ivacaftor:lumacaftor) globally.
 - Both drugs improve patient outcomes and are to be used for the rest of the patient's life.
 - Kalydeco is priced at around \$300,000 per person
 - Orkambi is priced at around \$260,000 per person
 - I assume that most insurers have negotiated confidential discounts.
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Expected revenues

- Cystic Fibrosis Foundation Therapeutics financed much of the research on these drugs and had a royalty of approximately 10% on the sales of these products.
 - It sold the royalty rights to Royalty Pharma in 2013 for \$3.3bn cash.
 - Implication: the net present value of the expected future sales of Kalydeco and Orkambi was approximately \$33bn in 2013.
 - This estimate is highly credible, since Royalty Pharma would have thoroughly evaluated the royalty stream for which it paid \$3.3bn.
 - We get about the same estimate by taking the NPV of sales, assuming an average price of \$200,000 per year, and 25% of the global CF population.
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Production and SGA Costs

- I used Vertex's 2015 8-K report to calculate that Vertex had production, royalty, sales, general and administrative, and interest costs related to Kalydeco and Orkambi of roughly 51.5% of revenues from those products.
 - This is relatively high, compared to other mature big pharma firms.
 - The remaining 48.5% of revenues are profits or “economics rents” attributable to its rights to the exclusive sales of Kalydeco and Orkambi.
 - Assuming a similar proportion of costs over time, this implies roughly \$16bn in net present value of profits.
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R&D Costs (1)

- The best measure of expected R&D costs is the estimates from other studies.
 - A 2011 systematic review suggests estimated average R&D costs ranging from \$160m to \$1800m per NCE.
 - DiMasi 2016 suggests \$2.8bn per drug
 - These estimates include cost of capital, risk-adjustment etc.
 - I adjust for:
 - CFFT paid for most of the pre-clinical expenses and part of Stage 1 clinical trials for ivacaftor
 - Vertex was eligible for a US tax credit on certain clinical trial expenses
 - Vertex's net cost of R&D, adjusting for risk and cost of capital, was in the range of \$2.5bn.
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R&D Costs (2)

- I also examined Vertex's 10-K reports for its claimed R&D expenses, which were substantial
 - I multiplied Vertex's claimed development costs in each calendar year by the share of patients listed as being in a clinical trial for ivacaftor or lumacaftor.
 - I adjusted for risk (using DiMasi's transition probabilities) and the orphan drug tax credit, to obtain a similar total "expected" R&D cost.
 - At least, I do not find that there is any reason to expect that DiMasi's estimates of R&D cost are unrealistic.
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Revenues vs. Costs

	NPV
Projected revenues	\$33bn
Projected production, SGA, interest	\$17bn
Estimated R&D cost	\$2.5bn
Net profit to Vertex	\$13bn

- Vertex will generate substantial profits, even after fully accounting for all costs, including risk-adjustment
 - The R&D cost is not actual cost, but is adjusted for the risk of failure
 - Vertex would be *fully compensated* if net profits were zero.
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Benefit to patients

- Certainly there is a real benefit to patients.
- But expenditure on this product has an opportunity cost in the rest of the system, and since the cost per QALY for ivacaftor is over \$350,000* (before confidential discounts), we couldn't even get close to supporting the use of ivacaftor or lumacaftor.
- So there has to be another reason...

* Note that CDEC estimated over \$800,000 cost per QALY

Small number of patients

- Given the small number of patients, even a very high price represents a small impact on the insurer's budget
 - But then, if Vertex can increase its revenues by \$10m, why wouldn't every firm want the same?
 - Given the small number of patients, the average cost per patient has to be high.
 - This is true, but then why are Vertex's revenues so much greater than its risk-adjusted costs?
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Support for continuing investment

- Vertex needs the revenues to support its on-going program of research into drugs for CF and other diseases.
 - This puts the normal way of funding research on its head. Firms don't have a right to get a boatload of cash just because they are going to do research. They get paid money because they deliver a drug that is valued by the market.
 - Vertex will have the right to earn money from its investment into new drugs.
 - Vertex has the right to do whatever it wants with the money it earns, including paying dividends to shareholders.
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- Another perspective is that if we want to encourage firms to invest in research in therapies for rare diseases, we need to allow them to earn massive excess profits far above those that would more than compensate them for the risks of their investment and the relevant cost of capital.
 - Excessive profits for one firm simply mean that other useful therapies are not funded.
 - We don't even get more incentives for investment, which depend on aggregate spending!
 - If insurers are going to ignore cost-effectiveness, they should at least ensure that returns are reasonable.
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