Sessions on Economics: Global Pricing of Drugs

Pharm 532

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May 13, 2009

Agenda

- Background/review
- Multi-market pricing theory
- Strategic and operational pricing in practice
- Observed price differentials

Review from Last Session

Economics of Pharmaceuticals (Newhouse, 2004)

Three salient economic facts:

1. High fixed (sunk) costs relative to marginal costs
2. NCEs have temporary legal monopoly
3. Developing drugs is risky

Economics of Pharmaceuticals (cont'd) (Newhouse, 2004)

Five implications:

1. Patent owner can exploit monopoly power
2. R&D costs must generate a sufficient return
3. Supply price must cover development costs
4. Regulators can "hold up" manufacturers for the cost of development
5. Manufacturers have powerful incentives to spend money on marketing

Prescription Drug Prices: Why Do Some Pay More Than Others?—Richard Frank (Health Affairs)

- Some think the "law of one price prevails."
- Studies show that cash payers in US pay more.
- Differential pricing is a feature of the market.
- Opportunities for arbitrage are limited
  - 92% of sales through wholesalers
- Three mechanisms for price concessions:
  - Chargebacks, rebates, and discounts

US Prescription Drug Prices (R. Frank)

- Manufacturers price is 74% of retail price: 23% for retail dispensing; 3% wholesalers.
- Markups higher for generics—incentives to dispense them.
- Price-volume contracts make price variable.
- "One can view the proliferation of price concessions in the pharmaceutical market as an indication that competitive forces have weakened the market power of sellers of prescription drugs."
- Premature to impose price controls

"The Political Economy of Pharmaceutical Industry"—Comanor, 1986

- Cites Kefauver investigations in 1959.
  - Industry admitted profits, but said they are needed for R&D for new drugs.
  - Committee cited me-toos.
- 1962 Amendments—shifted from toxicity to risk-benefit.
- Rate of innovation declined: "Government regulation was the apparent problem…"
- 1984—Hatch-Waxman. Bioequalence/exclusivity tradeoff

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"The Political Economy of Pharmaceutical Industry"—Comanor, 1986

- Issue: Competition or Monopoly
  - Controversy about degree of monopoly power
  - Still see "extensive competition"
  - Brand loyalty a factor
- Issue:R&D
  - Expenditures large—but innovation elsewhere
  - Analysts did empirical studies—determinants; scale economies—with conflicting results
  - Cost and returns—if such high rates, why not much investment? Varying results.

"The Political Economy of Pharmaceutical Industry"—Comanor, 1986

- Issue: Advertising and Promotion
  - Spent more than on R&D
- Issue: Regulation
  - Proposal—3 yr market exclusivity + licensing.

"The Political Economy of Pharmaceutical Industry"—Comanor, 1986

"The conflict between consumer interests in (1) low-priced pharmaceuticals and (2) the development of new drugs that are both safe and effective is as pronounced as ever."

"However, there is greater recognition that a trade-off between static and dynamic efficiency exists…"

What is missing?—"supply response of innovation to the level of their returns…"

Need to find new ways to finance pharmaceutical R&D.

"The Private Uses Of Public Interests: Incentives and Institutions"—Joseph Stiglitz (JEP, 1998)

that. The issue was, what was the theory and evidence concerning the relations between particular actions and "credibility," however that was defined. What credibility meant and how it was established seemed issues beyond rational inquiry. Empirical evidence—at least beyond an anecdote or two—and theoretical analysis should have been able to shed light on the merit of alternative policies. While that is where the conversation should have begun, it almost never got that far. What occurred was often worse than Gresham's Law: it was not only that bad arguments seemed to drive out good, but good economists, responding to implicit incentives, adopted bad arguments to win their battles. In a process of cognitive dissonance reduction, possibly combined with some intellectual atrophy, sometimes good economists even seemed to come to believe their specious arguments.

Politics, Politics, Politics

"If real estate is about location, location, location,

health reform is about politics, politics, politics."

-J.S. Hacker on U.S. health reform
"Putting Politics First", Health Affairs, 2008

"Differential Pricing for Pharmaceuticals: Reconciling Access, R&D, and Patents"

PA Danzon and A Towse
(IJHCFM, Vol. 3, 2003)

Introduction

- "reviews economic case for patents"
- Analyzes "potential for differential pricing to increase affordability of on-patent drugs in developing countries while preserving incentives for innovation."
- Focus is on drugs that serve both high income and developing country (DC) markets.

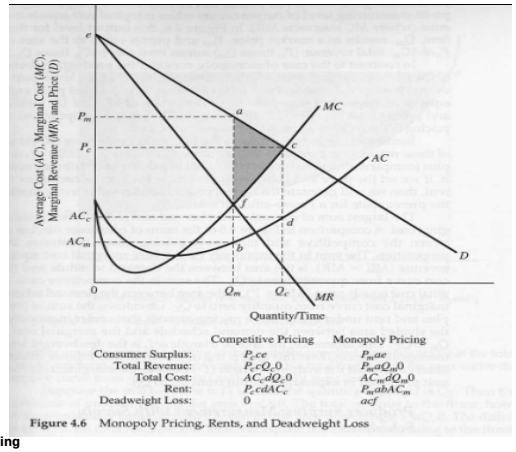
Cost Structure of Research-Based Pharmaceuticals and Economic Role of Patents

- US Pharma Industry spends 15.6% of sales on R&D. (Scherer: in 2002, 18% of Big Pharma sales went to R&D.)
  - This omits opportunity or capital cost of funds (therefore, about 30%)
- Two key aspects:
  1. "R&D is a fixed, globally joint cost." (Invariant to # of countries that will use the drug.)
  2. This global joint cost is largely sunk at product launch/pricing.
- As a result: "Marginal cost includes only the variable cost of producing and selling additional units, which is usually very low."
- ". . .free entry and the resulting marginal cost pricing are incompatible with sustained incentives for R&D."

Cost Structure of Research-Based Pharmaceuticals and Economic Role of Patents

- First best efficiency: all consume for whom marginal benefit exceeds marginal cost.
- Patents are second best solution to the problem of large fixed costs of R&D:
  - Some don't consume for whom MB>MC.
  - Could publicly subsidize but would require taxes—which create distortions/equity issues as well as administrative issues.
  - Alternatives: government purchase of patent or licensing rights
- Still, patent holders should be willing to charge lower prices in lower income markets.

Monopoly vs. Competitive Pricing & Rents



	Competitive Pricing	Monopoly Pricing
Consumer Surplus:	$P_c ce$	$P_m ae$
Total Revenue:	$P_c cQ_c 0$	$P_m aQ_m 0$
Total Cost:	$AC_c dQ_c 0$	$AC_m dQ_m 0$
Rent:	$P_c cdAC_c$	$P_m abAC_m$
Deadweight Loss:	0	acf

Figure 4.6 Monopoly Pricing, Rents, and Deadweight Loss

Source: Weimer and Vining

Ramsey Pricing: Efficient Payment R&D, New Products, and Patenting

Necessary conditions for 2nd Best Efficiency:

1. P >= MC
2. Sum over all markets of P-MC must be greater than F (normal, risk-adjusted rate of return on capital.)

<u>Ramsey Optimal Pricing (ROP):</u>

- Mark-up over P over MC across markets will depend only on price elasticity of demand (if MC is same in all markets).
  - More price-sensitive (and presumably lower income) users are changed a lower mark-up. Welfare loss is minimized.

ROP, PDM, and Entry

- ROP is similar to PDM result: relative mark-ups above MC are the same.
- Under PDM, could generate more than F.
- In the long run, "dynamic competition", unrestricted entry and exit of firms is needed to create expectation of normal returns at the margin, i.e., "monopolistic competition."
- Entry should keep profits at normal level, and mark-ups similar to ROP levels.

Regulation versus Competition

- Utilities are natural monopolies and have been regulated.
- Same rationale does not apply to pharmaceutical monopolies. (Pure monopoly in drugs is rare.)
- Global nature of joint costs creates incentive for countries to free ride—"paying only marginal cost leaving others to pay the joint costs." (And current politicians don't suffer the consequences of low innovation.)
- Would be difficult to regulate pharmaceutical companies based on costs: they are joint and difficult to attribute measure (incl. "dry holes").

Welfare Conclusions on Price Discrimination

- Issue of static (given set of products) versus dynamic efficiency.
  - PD increases consumption (static world) compared to single price.
- In two countries with same GDP per capita, but different wealth concentration, prices will be higher in concentrated wealth market.

  →Market segmentation within a market could be a good thing.

Differential Pricing Does Not Imply Cost-Shifting

- Objection: DP is cost-shifting from low to high price market
- Mistakenly assumes joint costs should be allocated equally.
- If DCs contribute some money to cover R&D, then prices can be lower in high income countries.
- If prices differences are unsustainable: single price will be higher.

Actual vs. Optimal Price Differences

- World doesn't seem to follow ROP.
- Breakdown of market separation is the problem.
  - Parallel trade
  - Reference pricing
- Traditional patent rules bar unauthorized resale.
  - NAFTA follows this.
  - EU does not.
- PT—standard free trade principles don't apply: no efficiency gain; instead increases social costs. Savings go to intermediaries.

Actual vs. Optimal Price Differences

- External referencing is importing a foreign price.
- This threat will inhibit willingness to grant low prices in low income countries.
- Rational response: single price or narrow band.
- Low income consumers lose; and in long run, high income lose due to lower revenues, less R&D, and less innovation.

Cross-National & US Price Differences

- There is a weak correlation between national income and prices.
  - Monopsony power
  - Only target high income segment in some low-income countries.
- Within US, there is some correlation
  - Tiered copays create some demand elasticity
  - Some value to having intermediary to bargain with drug manufacturers.
  - Medicaid constrains competitive discounting.

Policies to Maintain Separate Markets and Price Differentials

- DP structure only possible if higher income countries "accept the responsibility to pay higher prices"
- How to sustain price differentials?
  - Bar unauthorized imports of patented products="no doctrine of international exhaustion"
  - TRIPS permits countries to choose own policies on international exhaustion.
  - Middle or high income countries should commit to not referencing to low income countries
    - "making these prices unobservable may be the best approach."

Wikipedia on International Exhaustion (May 8, 2007)

- **Exhaustion of rights**, or the **doctrine of exhaustion**, is a concept in intellectual property law whereby an intellectual property owner will lose or "exhaust" certain rights after the first use of the subject matter which is the subject of intellectual property rights. For example, the ability of a trademark owner to control further sales of a product bearing its mark are generally "exhausted" following the sale of that product.
- The concept typically arises in the context of parallel imports, and may therefore be relevant nationally, regionally or internationally, such that if a right becomes "exhausted" in one area or jurisdiction, an intellectual property owner may not be able to enforce its rights in another area or jurisdiction.
- Different countries regulate the applicability of the doctrine of exhaustion in relation to different products in different ways.

Implementing DP through Confidential Rebates

- Used in US managed care.
- Confidentiality makes collusion more difficult.
- Counterargument: value of transparency. (But could have independent third party auditor)
- DCs should be able to negotiate favorable deals (i.e., close to MC). Can use government bargaining power.
- Transparency (ala Global Fund) seems good, BUT: "once prices granted to DC are observable, similar prices may be demanded by middle income countries or advocates for lower drug prices in high income countries."
  - This is an empirical question.

Two Recent Proposals

- EU Commission
  - Voluntary global tiered pricing structure.
  - Lower prices for AIDS, TB, and malaria
  - Production cost + 15% (confidential audit)
- UK Working Group
  - Also voluntary differential pricing

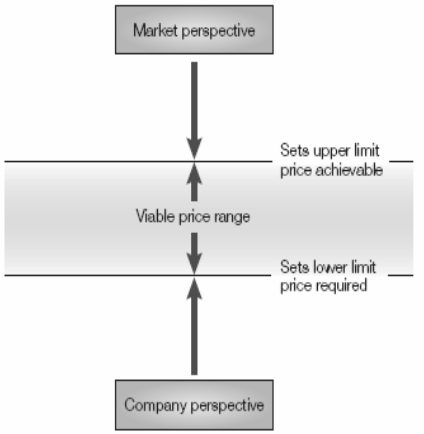
Compulsory Licensing: Doha and Beyond

- TRIPS (1994)—20 year patent protection for new products; LDCs by 2006
- Doha (2001)—extended LDC to 2016.
- Compulsory licenses (negotiated) okay for domestic markets.
- "National Emergencies"—HIV, TB, malaria, epidemics—could dispense with negotiation
- Follow-up discussion broke down in 2002.
- US wanted limits on DCs and diseases.
- There is a case for compulsory licensing, but risk is that the prices may spread to middle income countries.

Pricing Medicines: Theory and Practice, Challenges and Opportunities—Gregson et al.

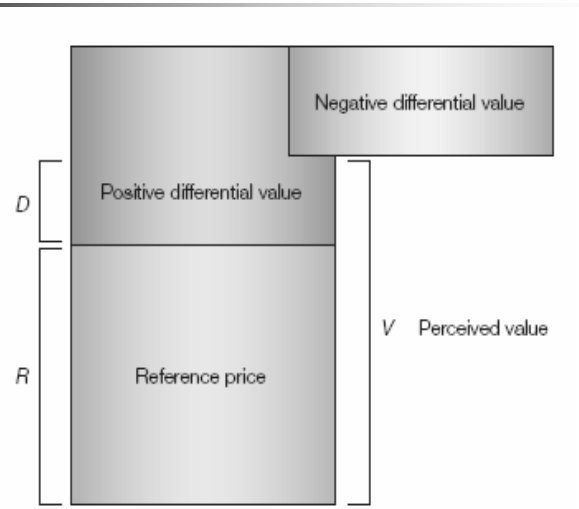
- Background
  - Drug development is risky
  - Fierce competition in branded class (nonprice?)
  - For breakthrough (monopoly) products, price needs to be supported by value.
  - Slowdown in NMEs has increased pressures.
  - Launch price is critical given price controls.
  - Must make pricing strategy and ROI calculation far in advance of launch
- Provide methodological framework used by "many manufacturers."

Viable Price Range: Value to Customer vs. Company Needs



V=R±D

Perceived value (V) =Reference price R ± Perceived Differentiation D



Implications

- Need to demonstrate Differential Value
- Pricing strategy involves demonstrating value over life-cycle.
- Development strategy affects product profile.
- Choice and sequencing of indications is important.
- Choice of comparator is critical.
- Reference price based on standard of care: varies across countries and indication, and is a moving target.

Other points

- PE provides methodological framework for quantifying economic value.
- Communicating value→ "value dossier"
- Need to look globally
  - Free price markets: US, Germany, UK
- Bad news: increasing pressures
- Good news: silo mentality breaking down a bit.

"Prices and Availability of Pharmaceuticals: Evidence from Nine Countries" (Danzon & Furukama)

- Not straightforward to do: each country's "market basket" is different.
  - Generics are 50% of unit volume in US and are increasingly important.
- "...there is no unique, correct measure of price differences"
- Compare 8 countries to the US
- IMS Health Midas data
- Ex-manufacturer price levels.
  - Have to estimate discounts in the US (8%)
- 249 molecules—branded and generic
  - 30-60% of sales in the 9 countries
  - Unit of analysis: molecule-indication
  - Measure price per dose.
- US volume weights
- 1999 exchange rates

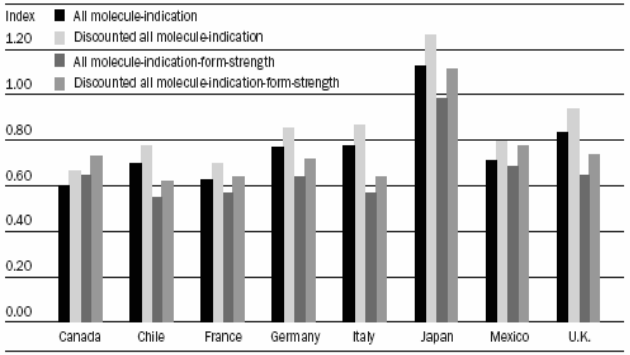
Findings

- Price regulated markets have smaller generic share of in unit volume (except Canada)
- Differences for branded generics (Germany) and unbranded (US).
- Generics drive out branded multi-source
- Japan has highest prices, followed by US.
- Exchange rate changes matter.
- Other countries prices for other medical service even lower than for drugs, relative to US.
- Per capita use of drugs launched recently is much lower than U.S. (esp. Chile and Mexico)
- "Income differentials contribute to price differentials both directly and indirectly." Direct—labor costs; Indirect—WTP for quality
- "Price differentials . . . roughly reflect income differences.."

Price Indices Relative to U.S.

EXHIBIT 3

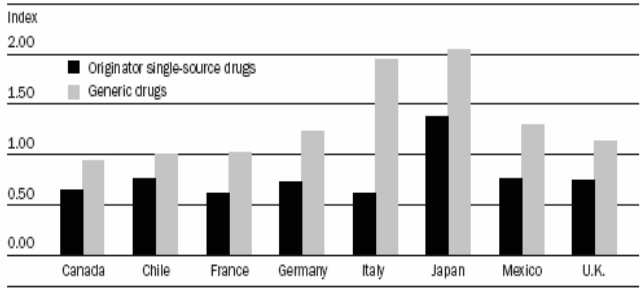
Price Indexes: Matching On Molecule-Indication Versus Molecule-Indication-Form-Strength, Without And With Adjustment For U.S. Manufacturer Discounts, Manufacturer Prices In Eight Countries Relative To U.S. Prices, 1999



SOURCE: Authors' calculations based on data from the IMS Health Midas data set, 1999.
NOTE: United States equals 1.00.

Branded Single-Source vs. Generics

EXHIBIT 4
Price Indexes: On-Patent Brand-Name Drugs (Originator, Single-Source) Versus Generic Drugs, Manufacturer Prices In Eight Countries Relative To U.S. Prices, Adjusted For U.S. Discounts, 1999



SOURCE: Authors' calculations based on data from the IMS Health Midas data set, 1999.
NOTE: United States equals 1.00.

Prices—9 Countries

EXHIBIT 8
Price And Volume Indexes, Relative To Per Capita Income, In Nine Countries, Sample Of 249 Leading U.S. Molecules, 1999

	Canada	Chile	France	Germany	Italy	Japan	Mexico	U.K.	U.S.
GDP per capita	$21,306	$4,864	$24,628	$25,624	$20,487	$35,479	$4,976	$24,874	$33,038
GDP normalized to U.S.	64	15	75	78	62	107	15	75	100
Price index (molecule-indication)	0.67	0.78	0.70	0.86	0.87	127	0.80	0.94	100
Price index normalized by income	104	528	93	110	141	118	529	125	100
Volume (total doses) per capita normalized to U.S.	93	23	100	79	63	54	12	118	100
Volume normalized by income	144	154	134	102	101	50	82	157	100

SOURCE: Authors' calculations based on data from the IMS Health Midas data set, 1999.
NOTE: GDP is gross domestic product.

Multilateral price comparisons (ex-manufacturer) at market exchange rates—From A. Towse

Index UK=100	1999	2001	2003	2003 at 5-yr av ex rates
France	86	81	91	83
Germany	103	90	102	93
Italy	82	85	99	91
Spain	72	72	85	78
UK	100	100	100	100
USA	213	205	189	206

Source: Department of Health (2005) PPRS 8th Report to Parliament

"An Exploratory Analysis of Pharmaceutical Price Disparities and Their Implications Among Six Developed Nations"

By Calfee, Villarreal, DuPre (AEI-Brookings)

Study Design

- 43 prescription drugs high sales volume drugs under patent in 2004.
- IMS MidasHealth
- Did NOT discount U.S. prices.
- 6 wealthy countries

Price Indices & GDP

Table 2
Relative per capita GDP and Pharmaceutical Price Indices for 43 Drugs in Five Developed Nations

	U.S.	Australia	Canada	France	Germany	U.K.
per capita GDP ratio to U.S. (2004)	1.00	0.79	0.79	0.75	0.72	0.79
Laspeyres	1.00	0.52	0.61	0.58	0.53	0.59
ratio of Laspeyres to relative per capita GDP	1.00	0.66	0.77	0.77	0.74	0.75
Paasche	1.00	0.41	0.50	0.43	0.46	0.50
ratio of Paasche to relative per capita GDP	1.00	0.52	0.63	0.57	0.64	0.63

Table 4. Price Indices by Uniqueness

	Australia	Canada	France	Germany	U.K.
Least unique					
Laspeyres	0.40	0.52	0.40	0.41	0.45
Paasche	0.41	0.53	0.38	0.41	0.42
Moderately unique					
Laspeyres	0.44	0.44	0.46	0.51	0.59
Paasche	0.39	0.41	0.38	0.46	0.56
Most unique					
Laspeyres	0.75	0.88	0.96	0.65	0.74
Paasche	0.45	0.62	0.81	0.57	0.60
relative per capita GDP (2004)	0.79	0.79	0.75	0.72	0.79

Findings

- Since 1999, international prices have been declining relative to US
- For “less unique” drugs, prices are much lower relative to US
  - “monopsony power”
- For “highly unique” drugs, proportional to GDP per capita
- For biotech drugs, prices are sometimes higher outside U.S.
- They contrast monopsony power vs. bilateral monopoly.
- “Retards” development of follow-on drugs.
- Prices of foreign biotech drugs are too high.