HIGH PRICES & NO EXCUSES: 6 ANTICOMPETITIVE GAMES

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Crucial Topic

- Important exercise: patents get attention; post-patent entry often does not
- I have comprehensively studied patents and antitrust in pharmaceutical industry
  - Co-author of leading IP/antitrust treatise
  - Author of more than 100 articles (40 on pharmaceutical antitrust law)
  - Author of amicus curiae briefs on behalf of hundreds of professors
  - Frequently cited in media (1000+ times) and courts (including U.S. Supreme Court)

No (or Weak) Patents Delay Generics

- Brand profits from monopoly (each day = millions)
- Regulatory regime used to delay entry: FDA exclusivity, reformulation time, petition process, distribution restrictions
- This behavior and others also follows from patenting of secondary advances
- “Off-patent” not coming as quickly as it used to as brands obtain weaker patents covering developments after active-ingredient patent expires
- **Small molecule example**: Pfizer’s strongest Lipitor patents expired in March 2010 & June 2011, but settlement with generics delayed entry until after these periods because of minor patents expiring in 2016
- **Biologic example**: AbbVie’s composition-of-matter patent on inflammatory-disease-treating Humira expired in 2016, but patent thicket of 100+ patents (indication/method of treatment (22), formulation (14), manufacturing (24), “other” (15)) extends protection until 2034…53 patents obtained in 2015 and 2016 alone
  - *AbbVie Long-Term Strategy*, Oct. 30, 2015, http://www.biotechduediligence.com/uploads/6/3/6/7/6367956/abbvie_strategy_presentation__1_.pdf;
  - Cynthia Koons, *This Shield of Patents Protects the World’s Best-Selling Drug*, BLOOMBERG BUSINESSWEEK, Sept. 7, 2017, https://www.bloomberg.com/news/articles/2017-09-07/this-shield-of-patents-protects-the-world-s-best-selling-drug.

Game 1: Pay-for-delay Settlements

- *FTC v. Actavis*: Settlements by which brands pay generics to delay entering market can have "significant anticompetitive effects" and violate antitrust law
- Parties can settle without payment: 2015 FTC Report shows number of settlements (170) increasing while "pay for delay" deals fall from 40 (FY2012) to 14 (FY2015), with only 5 above $7m litigation costs
- 89% of patents in settled litigation are secondary patents; brand less likely to win on these (32%) than on active-ingredient (92%) patents
  - C. Scott Hemphill & Bhaven Sampat, *Drug Patents at the Supreme Court*, 339 SCIENCE 1386, 1387 (2013) (drugs first eligible for challenges between 2000 and 2008)
- Most post-*Actavis* cases cover secondary patents: Actos (method of use), AndroGel (formulation), Cephalon (particle size), Effexor (extended release), K-Dur (formulation), Lidoderm (skin application), Loestrin (contraception method), Niaspan (time release), Opana (time release), Solodyn (treatment method), Wellbutrin (extended release)
  - **AndroGel**: Patent for synthetic testosterone expired in 1950s
  - **Loestrin**: FDA approved active ingredients in 1970s
  - **Niaspan**: Active ingredient niacin sold since early 20th century

Game 2: Product Hopping

- Brand firms often switch to new versions of drug products; many switches not connected to generic entry
- But some changes, with patient migration to reformulated product, have one purpose: **delay generics**
  - Prevent operation of state substitution laws and Hatch-Waxman Act
  - Aim to switch market to reformulated version before generic of original version enters market
  - Each switch results in delay from generic reformulation, FDA approval, patent litigation
- **Secondary patents** give extra protection: Prilosec to Nexium = 13 years; Suboxone tablet to film = 14 years; Namenda IR to XR = 14 years
- Even if **no patent**, delay from FDA exclusivity and time it takes to reformulate drug
  - Warner Chilcott engaged in multiple hops on acne-treating Doryx (first available in 1985 as unpatented capsule): (1) capsule to 75- and 100-mg tablets, (2) 150-mg single-scored tablet, (3) 75- and 100-mg single-scored tablets, (4) 150-mg dual-scored tablet
  - Also stopped selling capsules, removed capsules from website, worked with retailers to auto-reference tablet in filling prescriptions, informed purchasers and doctors that capsules replaced by tablets, bought back and destroyed capsules

Game 3: Citizen Petitions

- Citizen petitions are meant to raise legitimate safety concerns with FDA
- But my empirical study of all petitions filed between 2011 and 2015 against pending generics ("505(q)" petitions) found that FDA denies 92%; also 98% of late-filed petitions (within 6 months of expiration of patent or FDA exclusivity), 100% of simultaneous petitions (when FDA resolves petition on same day it approves generic)
  - Michael A. Carrier & Carl J. Minniti III, *Citizen Petitions: Long, Late-Filed, and At-Last Denied,* 66 AMERICAN UNIVERSITY LAW REVIEW 305 (2016)
- **Last-minute petition example**: Bayer's petition on IUD Mirena 1 day before patent expiration
- **Bottleneck example**: Allergan's dry-eye-treating Restasis petitions delay generics
  - Feb. 2014 petition denied Nov. 2014; Dec. 2014 petition denied Feb. 2016; Aug. 2017 petition filed
    - Each petition challenges generics' use of in vitro (as opposed to human) testing protocols
  - In 135-page opinion, Judge Bryson invalidated 6 Restasis patents, but generics Mylan, Teva, Akorn still cannot enter market because of Aug. 2017 petition

Game 4: REMS Restrictions

- REMS serve important purpose in making sure risky drugs reach market
- But brands have used REMS to deny samples generics need for bioequivalence testing
  - 2017 study: REMS restricts 41 drugs with sales exceeding $11 billion
    - Alex Brill, *REMS and Restricted Distribution Programs*, June 2017, https://www.gphaonline.org/media/cms/Alex_Brill_REMS_Study_June_2017.pdf
  - More than 150 generics have informed FDA they cannot obtain samples
- In litigated cases, brands have **denied samples** to generics willing to pay market prices and enter into indemnification agreements
  - And brands have ignored FDA letters showing REMS compliance and protections
    - E.g.: 1) Actelion "would sell" sample upon receiving FDA letter but 2) after Apotex provides FDA letter, Actelion responds: "This changes nothing" and "you don't get [the sample]"
- Brands also have not negotiated in good faith for **shared REMS** programs
  - E.g.: Suboxone allegedly turned down invitations to participate in meetings, insisted on unfavorable conditions, refused to share nonpublic information, demanded veto authority and supermajority vote, engaged in delay tactics
    - *See* Michael A. Carrier, *Sharing, Samples, and Generics: An Antitrust Framework*, CORNELL LAW REVIEW, at 37-42 (forthcoming 2017), https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2979565)

Game 5: Non-REMS Distribution Restrictions

- Some companies have imposed distribution restrictions not required by FDA
- 2017 study: Non-REMS programs restrict 33 drugs with sales exceeding $11 billion
  - Alex Brill, *REMS and Restricted Distribution Programs*, June 2017, https://www.gphaonline.org/media/cms/Alex_Brill_REMS_Study_June_2017.pdf
- Martin Shkreli (aka “Pharma Bro”) switched Turing’s distribution system for infection-treating **Daraprim** from nationwide to single source: Walgreen’s Specialty Pharmacy
  - Active ingredient introduced in 1953; distribution limited 62 years later for no safety-related reason
  - Turing official: “would like to do our best to avoid generic competition”; “certainly not going to make it easier” for generics
  - 5000% price increase ($13.50 to $750)
- Retrophin (Shkreli’s prior company) also switched to closed distribution, blocking generic access on cholesterol-deficiency-treating **Chenodal** (400% increase) and kidney-stone-treating **Thiola** (1900% increase)
  - Shkreli: “We do not sell Retrophin products to generic companies. . . . The whole model that generics rely upon is turned upside down with specialty pharmacy distribution”

Game 6: Bundling/Rebates

- **Restasis**: Shire sued Allergan for blocking access to dry-eye-disease-treating Xiidra
  - Xiidra can be prescribed to "much larger population" and lacks Restasis's side effects but limited to 10% Medicare Part D market (vs 35% commercial market)
  - Challenge bundling and exclusive dealing (if include Xiidra on formularies, lose substantial discounts/rebates on other Allergan drugs)
    - Even if plan received Xiidra for free, "the numbers still wouldn't work"
- **Remicade**: J&J had only product on market 1998-2016; Pfizer sued, claiming J&J blocked access to arthritis- and Crohn's-treating rival Inflectra
  - Insurers cannot cover Inflectra; otherwise J&J deny rebates (which apply to multiple products)
  - Inflectra has less than 4% of market; J&J raise Remicade list price 9%
- **EpiPen**: Sanofi sued Mylan for offering high ("practically impossible to refuse") rebates to insurers, PBMs, and state Medicaid programs; had effect of blocking coverage of rival Auvi-Q
  - Auvi-Q market share fell roughly 50% after rebates took effect
- **Exclusive dealing law**: Percentage of market foreclosed important. Also: contract duration, industry prevalence, entry barriers, distribution alternatives
- **Rebate law**: Exclusionary effect on competitors (3rd Cir.) vs. attribution test (attribute discount to product on which plaintiff claims exclusion and see if price below cost) (9th Cir.)

Proposals

- **Antitrust enforcement**: Careful scrutiny of thickets and conduct accompanying secondary patents
- **Settlements**: Continued judicial scrutiny and FTC enforcement; consideration of legislation applying presumptive illegality or expanded 180-day exclusivity period
- **Product hopping**: Scrutiny of reformulations that cannibalize profitable drugs, making no economic sense other than by stifling generic entry (can apply to hard **and soft** switches)
  - *See* Michael A. Carrier & Steve Shadowen, *Product Hopping: A New Framework*, 92 NOTRE DAME LAW REVIEW 167 (2016)
- **REMS**: Antitrust scrutiny for sample denials and delayed negotiations on shared REMS
  - *See* Michael A. Carrier, *Sharing, Samples, and Generics: An Antitrust Framework*, CORNELL LAW REVIEW (forthcoming 2017), https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2979565)
  - CREATES Act would provide bipartisan statutory fix for sample denials and blocked negotiations
- **Non-REMS distribution restrictions**: Rigorous antitrust scrutiny (apply no-economic-sense test)
- **Citizen petitions**: Antitrust scrutiny and enforcement (like FTC case against Shire ViroPharma)
  - Also consider: (1) list of 505(q) petitions and delay in annual reports to Congress; (2) determine if simultaneous generic approvals and petition resolutions caused delay; (3) make easier for FDA to summarily dispose of petitions; (4) determine money and time incurred resolving petitions; (5) certify objections filed within one year
    - *See* Michael A. Carrier, *Five Actions to Stop Citizen Petition Abuse*, 118 COLUMBIA LAW REVIEW ONLINE __ (forthcoming 2018), https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3043541
- **Bundling/rebates**: Robust antitrust scrutiny of exclusive dealing and bundling