Effective Patent Life of Antiretroviral Drugs in the U.S 1987-2006: A Public Health Perspective

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Outline

- Background
- Study Objectives
- Data Sources
- Methods
- Results
- Conclusions
- Limitations
- Implications

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Background: Access, Prices and Patents

- Society is faced with balancing the reward from innovation for finding new drugs with adequate access to affordable drugs.
- Difficult balance for antiretrovirals (ARVs) and drugs targeting life-threatening diseases.
- High prices of patented ARVs reduce access.
- Generic drug entry reduces prices.
- Patents are the main barrier to generic entry.
Study Objectives

- To examine the effective patent life periods of new molecular entities (NMEs) approved for marketing in the United States between 1987 and 2006
- To compare the effective patent life of ARVs and other therapeutic classes
Conceptual Model: Drug Patent Life

Pre-NDA (New Drug Application) patent time

First U.S. Patent and Trademark Office right of priority date

FDA review time

NDA received date

NDA approval date

Patent statutory term expiration date

Effective patent life (Post-NDA patent time)

Pharmaceutical patent extension expiration date

Pediatric extension expiration date
Data Sources

- FDA and U.S. Patent and Trademark Office
- NMEs approved during the period 1987-2006
- NMEs with at least one patent listed in the FDA Orange Book (OB)
  - OB lists drugs approved by the FDA and patents affecting new drugs
  - Excludes manufacturing process patents
- Drugs discontinued from the market were excluded from the analysis
- Data was updated to December 31, 2006
Methods

- First and last patents used to estimate minimum and maximum effective patent life
- A comparison between the effective patent life of ARVs and all other NMEs was performed
- Sub-analysis ARVs and all other NMEs
  - Priority review (FDA considered drug to be an improvement)
    - Orphan drugs
- Group comparison t-tests
- SPSS vs. 15 used for the analysis
Results
Drug Sample

532 NMEs approved in 1987-2006
- 105 without a patent listed in the OB
- 43 discontinued

384 included in the study
  21 (5.5%) ARVs
  363 (94.5%) NMEs from other classes
FDA Review Time. Antiretrovirals and Other Therapeutic Classes. 1987-2006

Years

<table>
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<tr>
<th>Category</th>
<th>Review Time (Years)</th>
<th>Sample Size</th>
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<tr>
<td>ARVs</td>
<td>0.47*</td>
<td>(n=21)</td>
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<td>Other Classes</td>
<td>1.88</td>
<td>(n=363)</td>
</tr>
<tr>
<td>Priority review</td>
<td>0.45*</td>
<td>(n=20)</td>
</tr>
<tr>
<td>All drugs</td>
<td>1.45</td>
<td>(n=130)</td>
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</table>

*p<.001

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FDA NDA Approval to First Patent Expiration Time. Antiretrovirals and Other Therapeutic Classes. 1987-2006

Years

<table>
<thead>
<tr>
<th></th>
<th>All drugs (n=21)</th>
<th>Priority review (n=20)</th>
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</thead>
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<td>ARVs</td>
<td>13.8*</td>
<td>14.1*</td>
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<tr>
<td>Other Classes</td>
<td>10.9</td>
<td>10.5</td>
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*p<.01

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FDA NDA Approval to Last Patent Expiration Time. Antiretrovirals and Other Therapeutic Classes. 1987-2006

Years

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<th></th>
<th>Average</th>
<th>p-value</th>
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<td>ARVs</td>
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<td>&lt;.01</td>
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<tr>
<td>Other Classes</td>
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<td>.06</td>
</tr>
<tr>
<td>All drugs</td>
<td>17.6‡</td>
<td>.06</td>
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<tr>
<td>Priority review</td>
<td>14.8</td>
<td></td>
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(n=21) (n=363) (n=20) (n=130)

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<table>
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<tr>
<th>Year</th>
<th>Drug Name</th>
<th>Time</th>
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<tbody>
<tr>
<td>1987</td>
<td>zidovudine (Retrovir)</td>
<td>18.5</td>
</tr>
<tr>
<td>1991</td>
<td>didanosine (Videx)</td>
<td>20.3</td>
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<tr>
<td>1992</td>
<td>zalcitabine (Hivid)</td>
<td>16.0</td>
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<tr>
<td>1994</td>
<td>stavudine (Zerit)</td>
<td>14.5</td>
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<tr>
<td>1995</td>
<td>lamivudine (Epivir)</td>
<td>21.0</td>
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<tr>
<td>1996</td>
<td>saquinavir mesylate (Invirase)</td>
<td>15.0</td>
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<tr>
<td>1996</td>
<td>nevirapine (Viramune)</td>
<td>15.9</td>
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<tr>
<td>1996</td>
<td>ritonavir (Norvir)</td>
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<tr>
<td>1997</td>
<td>saquinavir mesylate (Invirase)</td>
<td>24.9</td>
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<tr>
<td>1997</td>
<td>indinavir sulfate (Crixivan)</td>
<td>21.2</td>
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<tr>
<td>1998</td>
<td>delavirdine mesylate (Rescriptor)</td>
<td>21.2</td>
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<tr>
<td>1998</td>
<td>nefinavir mesylate (Viracept)</td>
<td>17.1</td>
</tr>
<tr>
<td>1999</td>
<td>efavirenz (Sustiva)</td>
<td>20.6</td>
</tr>
<tr>
<td>1999</td>
<td>abacavir sulfate (Ziagen)</td>
<td>19.9</td>
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<tr>
<td>2000</td>
<td>amprenavir (Agenerase)</td>
<td>18.6</td>
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<tr>
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<td>lopinavir; ritonavir (Kaletra)</td>
<td>20.2</td>
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<tr>
<td>2001</td>
<td>tenofovir disoproxil fumarate (Viread)</td>
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</tr>
<tr>
<td>2003</td>
<td>enfuvirtide (Fuzeon)</td>
<td>12.2</td>
</tr>
<tr>
<td>2003</td>
<td>emtricitabine (Emtriva)</td>
<td>18.2</td>
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<tr>
<td>2003</td>
<td>atazanavir sulfate (Reyataz)</td>
<td>15.5</td>
</tr>
<tr>
<td>2005</td>
<td>tipranavir (Aptivus)</td>
<td>14.4</td>
</tr>
<tr>
<td>2006</td>
<td>darunavir ethanolate (Prezista)</td>
<td>9.4</td>
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Conclusions, Limitations and Implications
Conclusions

- Statistically significant difference in effective patent life of ARVs vs. other classes
- ARVs had an average of 2.9 years more effective first patent life than other classes
- ARVs had an average of 2.8 years more effective last patent life than other classes
Conclusions

- Shorter ARV FDA review time explains 50% of the difference in effective patent life
- Effective patent life for the last patent of 7 ARVs (33.3%) exceeded 20 years
Limitations of the Study

- **Subject Selection**
  - Includes first product number of the first NDA and excludes successive NDAs (line extensions)

- **Patent Selection**
  - Includes first and last patent listed in the OB
  - Excludes other patents listed in the OB and patents not listed

- **Intellectual property**
  - Excludes intellectual property rights other than patents (i.e. exclusivity)
A Public Health Perspective

- Shortening ARV development and the FDA drug review process increased ARV effective patent life
  - Faster entry to new drugs
  - Potential for improved access for HIV patients
- Implications for other therapeutic categories
  - ARVs higher risk benefit ratio than other therapeutic classes
  - Pandemic disease
  - Perspectives: Patients, FDA, Health plans, Industry
A Public Health Perspective (&2)

- ARV may generate higher rewards for pharmaceutical companies
  - Less development opportunity costs
  - Longer effective patent life without generic competition
- Need for balancing intellectual drug property rights and access to ARVs
  - Balance at the therapeutic category level

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An International Public Health Perspective

- The U.S. pharmaceutical patent and FDA exclusivity system exceeds TRIPS
  - Patent extensions and pediatric exclusivity
- Bilateral agreements may extend pharmaceutical intellectual property protection in developing countries
  - Effects on prices and access

TRIPS: Trade-Related Aspects of Intellectual Property Rights (World Trade Organization)
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Results of this study were presented at the iHEA 6th World Congress. Copenhagen, July 11, 2007

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