BIOSIMILARS: US OVERVIEW
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DISCUSSION TOPICS

- Current Market
- BSUFA Negotiations
- Medicare Part D + CMS Reimbursement
- Legal Questions (Amgen v Sandoz)
- Regulatory Questions (FDA Guidances)
- Industry Representation
CURRENT US MARKET

Biosimilar Applications Submitted To FDA

<table>
<thead>
<tr>
<th>Sponsor</th>
<th>Product</th>
<th>Reference</th>
<th>Reference Sponsor</th>
<th>Submission Date</th>
<th>User Fee Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Samsung Bioepis</td>
<td>Remsima (DAI)</td>
<td>Remsima</td>
<td>Johnson &amp; Johnson</td>
<td>2016-09</td>
<td>2017-01</td>
</tr>
<tr>
<td>Sandoz</td>
<td>Pegfilgrastim</td>
<td>Neulasta</td>
<td>Amgen</td>
<td>2015-09</td>
<td>2015-07</td>
</tr>
<tr>
<td>Celltrion</td>
<td>Inflectra (glypt)</td>
<td>Remsima</td>
<td>Johnson &amp; Johnson</td>
<td>2015-10-05</td>
<td>2015-04-06</td>
</tr>
<tr>
<td>Pﬁzer (Biosim)</td>
<td>Enbrel (to be called Pleural)</td>
<td>Enbrel</td>
<td>Amgen, Pfizer</td>
<td>2014-12-16</td>
<td>2015-05-16</td>
</tr>
<tr>
<td>Apotex</td>
<td>Filgrastim (to be called Granfil)</td>
<td>Neupogen</td>
<td>Amgen</td>
<td>2014-12</td>
<td>2015-10</td>
</tr>
<tr>
<td>Apotex</td>
<td>Pegfilgrastim</td>
<td>Neulasta</td>
<td>Amgen</td>
<td>2014-10 to 2015-11</td>
<td>2015-10 to 2015-06</td>
</tr>
<tr>
<td>Sandoz</td>
<td>Filgrastim (Zarzio)</td>
<td>Neupogen</td>
<td>Amgen</td>
<td>2014-06</td>
<td>2015-08-06</td>
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BSUFA NEGOTIATIONS

- Biosimilar User Fee Act of 2012 (BSUFA) authorizes FDA to collect fees from manufacturers to expedite review of biosimilar biological products
- Fees under PDUFA are 1/3-product, 1/3-establishment, 1/3-application
- FDA and Industry negotiations nearing conclusion
- Issues being discussed:
  - Finances; FDA is concerned about consistent funding; Industry is concerned about balancing funding with budget allocations from Congress
  - Meeting management – discussion on meetings between sponsor and FDA re various response deadlines, written/face-to-face responses, scope of meetings, modifying timelines, etc.
  - Potentially Receiving earlier feedback in advance of Advisory Committee meetings
  - Length of review - currently 10 months could be extended slightly
MEDICARE PART D

- Federal Healthcare Coverage for Medicare patients (generally over 65yo, or younger people with disabilities) includes a “coverage gap”
  - Gap = period of consumer payment for Rx between initial coverage and catastrophic coverage; **brand pharmaceutical manufacturers provide 50% discount**
  - Heavy generic uptake
  - Are biosimilars included? No (not currently)
- Some argue that biosimilar products should be treated as single source products, and inclusion in the gap discount program for formulary/uptake purposes
  - Biosimilars are not generics, so are subject to higher co-payments
- Others argue that re-opening the statute would risk more regulation of prices and could deter investment in the biosimilars industry

CMS REIMBURSEMENT

- CMS has advanced a proposal to combine all biosimilars under 1 **general reimbursement code** (similar to generics)
  - Shortsighted
  - Could subject biosimilars to frequent price fluctuations
  - Will reduce incentive to enter biosimilars market
  - Complications with varying indications and interchangeability
- **Biosimilars Forum** has discussed an alternative proposal with CBO that would allow **unique reimbursement codes** for Biosimilars
  - Due to increased incentive to enter and compete savings over 10 years increase from $25B to $31B
  - Uptake estimated at 15%-35%
  - Estimates 20%-40% discount relative to reference product
CMS POLICY ON BIOSIMILARS IS CONFOUNDING

<table>
<thead>
<tr>
<th>Medicare Part B</th>
<th>Medicare Part D</th>
<th>Medicaid</th>
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</thead>
<tbody>
<tr>
<td>CMS views biosimilars as multisource generics</td>
<td>Views biosimilars as non-branded products</td>
<td>Views biosimilars as branded products</td>
</tr>
<tr>
<td>Biosimilars will share a J-code and payment rate</td>
<td>Biosimilars are excluded from the coverage gap</td>
<td>Branded products pay 23.1% mandates rebate (13% for generics)</td>
</tr>
<tr>
<td>Biosimilars likely to have differences in approved indications and interchangeability</td>
<td>Coverage unlikely to reflect generic coverage in the gap leaving patients with high cost sharing</td>
<td>Medicaid views biosimilars as branded primarily for rebate purposes</td>
</tr>
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LEGAL QUESTIONS

- Biosimilars Price Competition and Innovation Act of 2009 (BPCIA) establishes an abbreviated pathway for regulatory approval of biosimilars
- Patent dispute resolution in BPCIA is a complicated process
  - Applicants “shall provide” copy of application and information on manufacturing process to sponsor
  - Parties must identify patents to be litigated and applicant must provide detailed statement of “factual and legal basis” for why sponsor’s patents are “invalid, unenforceable or will not be infringed.”
  - Deadlines and negotiations ensue—the “Patent Dance”
  - Allows for preliminary injunction before first commercial marketing of biosimilar—to “be resolved expeditiously” (180-day notice period)
- Amgen Inc. v Sandoz Inc. – Court held that Sandoz’s decision NOT to disclose its aBLA (application) to Amgen was permissible under BPCIA
  - The court interpreted “shall provide” as only applying within the scope of the information-exchange section of the statute, which also sets forth the only remedy for the Sponsor—to sue for patent infringement
REGULATORY QUESTIONS

- **Naming**—FDA has *proposed* a non-proprietary name + unique 4-letter suffix
  - Current pending legislation would exempt biologics from drug law provisions that refer to an “official compendium”—allowing FDA full discretion over biologics naming, rather than USP or USAN (AMA)
  - Lawmakers say it responds to FDA concerns that USP standards could delay licensure of biosimilar and interchangeable products
  - USP states it would “strip biologics of the protections provided by public quality standards”

- **Interchangeability**—BPCIA allows biologics to be interchangeable, i.e., “switchable” if the product: (1) is biosimilar to reference product, (2) produces same clinical result, and (3) creates no greater risk than not switching from reference product
  - FDA has been silent
  - Will affect labeling for indications

POLITICAL QUESTIONS

**BIOSIMILARS FORUM**

> “to advance biosimilars in the US with the intent of expanding access and availability of biological medicines and improving healthcare.”

- **Members**
  - Allergan
  - Amgen
  - Boehringer Ingelheim
  - Coherus BioSciences
  - EMD Serono
  - EPIRUS Biopharmaceuticals
  - Merck and Co.
  - Pfizer
  - Samsung Bioepis
  - Sandoz
  - Teva

**BIOSIMILARS COUNCIL**

> “to ensure a positive regulatory, reimbursement, political and policy environment for biosimilar products and to educate the public and patients about the safety and effectiveness of biosimilars”

- **Members**
  - Accord Healthcare
  - Amneal BioSciences
  - ApoBiologix
  - Biocon
  - Dr. Reddy’s
  - Momenta
  - Mylan
  - Pfenex
  - Sandoz
  - Sun Pharmaceutical
  - Teva
  - Zydus
QUESTIONS?

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