Biologics: A regulatory update and implications for practice
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Background
As of November 3, 2017, seven biosimilars have been approved by the United States Food and Drug Administration (FDA), including one for cancer, but only three products are currently on the market and none have received interchangeability status. The FDA released guidance in January 2017 regarding interchangeability. Once this status is granted pharmacists will potentially be dispensing a biosimilar when they receive a prescription for a biologic.

Objective
To provide pharmacists with an understanding of biosimilars, what the market looks like today and the regulations surrounding them, as well as where to find important resources pertaining to biosimilars.

Method
We have gathered the necessary information from the FDA, reliable news sources, and pharmaceutical companies, to be able to present a clear picture of what pharmacists need to know about biosimilars in the United States.

Results
Biologic drugs, also known as originator or reference products, are large, complex molecules that are made from living cells or organisms. They are associated with immunogenic properties and are unstable. This complexity contributes to their hefty price tag. The Biologics Price Competition and Innovation Act of 2009 (BPCIA), a subset of the Public Health Service Act, was passed to try to encourage competitive pricing by allowing for an abbreviated pathway called 351(k), for “copies” of biologic drugs. This attempt was to be for biologics what the Hatch-Waxman Act was for small molecules, but unlike small molecules where complete copies can be made, it is impossible to ensure identical copies of biologics. Instead, a “highly similar” product can be made called a biosimilar.

The FDA states that the biosimilar must be highly similar with the same safety, purity, and potency as the reference product except for minor differences in clinically inactive components. The biosimilar must have the same mechanisms of action, routes of administration, dosage forms, and dosage strengths as the reference product and only the indications and conditions of use that have been approved for the reference product can be approved for the biosimilar. Biosimilar developers do not need to provide full clinical efficacy and safety data to the FDA, instead they must show that they are structurally and functionally similar to the reference product in analytical assessments. The FDA released additional guidance on how to evaluate analytical similarity in September 2017. In addition to analytical studies, animal toxicity studies are also required. Clinical trials are then run to assess the pharmacokinetics, pharmacodynamics, safety, efficacy, and immunogenicity of the biosimilar.

In order to be considered “interchangeable” the biosimilar must produce the same clinical result as the originator product in any patient and if given more than once to a patient it must show the same safety and efficacy whether the biosimilar or originator product is used with or without alternating them. If this is proven, the FDA states that the interchangeable biosimilar may be used interchangeably with the originator product without the intervention of the healthcare provider who prescribed the reference product. It is important to remember that individual states regulate the substitution laws. At least 35 states have passed legislation regarding the rules for biosimilar substitution. Pharmacists should know their state substitution laws in regards to biosimilars. The FDA provides the Purple Book which lists licensed biological products including those determined to be biosimilars. It will also list if the biosimilar has been granted interchangeability status with the originator product, but at this time none have been granted this status. The Purple Book is an important resource for pharmacists to be aware of as a reference. The FDA released guidance in January 2017 regarding nonproprietary naming of biological products. In this state they state that biosimilars should have a non-proprietary name as their core name followed by a distinguishing suffix that is devoid of meaning and composed of four lower case letters.

Biosimilar Approvals in the US

<table>
<thead>
<tr>
<th>Reference Drug</th>
<th>Biosimilar</th>
<th>Biosimilar Company</th>
<th>Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neupogen</td>
<td>Zarzis</td>
<td>Sandoz</td>
<td>3/6/2015</td>
</tr>
<tr>
<td>Remicade</td>
<td>Inflectra</td>
<td>Celgene/Momenta</td>
<td>5/1/2016</td>
</tr>
<tr>
<td>Enbrel</td>
<td>Solara</td>
<td>Sandoz</td>
<td>3/6/2016</td>
</tr>
<tr>
<td>Humira</td>
<td>Amjevita</td>
<td>Amgen</td>
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<tr>
<td>Humira</td>
<td>Erelzi</td>
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<td>3/6/2016</td>
</tr>
<tr>
<td>Asacit</td>
<td>Cyltezo</td>
<td>Amgen/Allergan</td>
<td>1/3/2017</td>
</tr>
</tbody>
</table>

Pros and Cons of Biosimilars

- The average daily cost of a biologic in the US is $69 compared with only $22 for chemical (small-molecule) drugs
- $50+ billion in annualized biologic sales will lose patent protection over the next five years
- Increased access to biotherapeutics

Conclusions
Pharmacists play a vital role in regards to biosimilars. They must be the experts on biosimilars so they can provide education to other healthcare providers and patients. Once interchangeability status is granted the role of a pharmacist will grow, so it is important that pharmacists in all settings know what biosimilars are, know the current FDA approved biosimilars, as well as which ones are on the market, and the regulations surrounding them. In addition, pharmacists will need to know where to go to find information about biosimilars as more continue to enter the market.

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References included in QR (QuickResponse) code link.
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Author Notes on Presentation
Katelyn Heim: Nothing to disclose
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References:


