Biosimilars: Are We Ready for their Arrival?

Steven Lucio, PharmD, BCPS,
February 17, 2015
Disclosures

Steven Lucio, PharmD, BCPS

- Employee of Novation, a VHA and UHC company
- No financial conflicts
Objectives

• Review the anticipated timeline for approval of biosimilars in the US
• Discuss the clinical, operational, and financial issues that will determine the degree of adoption and use
• Evaluate the European experience with biosimilars and its implications for the US market
Where are we in the biosimilar timeline?

What is next… the Third Star Wars Trilogy… or FDA Biosimilar Approval?
True Timeline for Biosimilars

- **February 9, 2012**: Three initial guidance documents published.
- **March 23, 2010**: Signed into law.
- **August 30, 2012**: Tbo-filgrastim (non-biosimilar) approved and marketed.
- **May 2014**: First biosimilar application filed (filgrastim).
- **August 2014**: Second biosimilar application filed (infliximab).
- **January 7, 2015**: Oncologic Drugs Advisory Committee review of filgrastim application.

March 2010 through January 2015
Biosimilar Status

- Four applications before FDA
  - Filgrastim (Sandoz)
    - Oncologic Drugs Advisory Committee (January 7th) – unanimous recommendation for approval for all originator indications
    - Recommendation supported by European experience
      - 7.5 million patient days of exposure
  - PDUFA Date – March 8th?
  - Court hearing regarding patent litigation process – February 12th
- Other Filings
  - Infliximab (Celltrion)
  - Pegfilgrastim (Apotex)
  - Epoetin (Hospira)

*The Pink Sheet, January 12th and 19th, 2015; IPD Analytics, January 20, 2015*
Basics of Biosimilars
The Principles of Biologic Manufacturing

• As compared to small molecule drugs, all biologics products, whether originator reference or biosimilar, are:
  • More structurally complex
  • More difficult to manufacture and demonstrate variability in their production
  • And are more likely to elicit immunogenic responses

• Clinicians, including pharmacists and physicians, do not dwell on these particular aspects of pharmaceutical manufacturing on a day to day basis

• Education on these elements is ongoing, but more training is required
Biologic Medications Are More Complex Than Generics

Vancomycin
$\text{C}_{66}\text{H}_{75}\text{Cl}_{2}\text{N}_{9}\text{O}_{24}$

Aspirin
$\text{C}_9\text{H}_8\text{O}_4$

Rituximab
$\text{C}_{6416}\text{H}_{9874}\text{N}_{1688}\text{O}_{1987}\text{S}_{44}$

Filgrastim
$\text{C}_{845}\text{H}_{1343}\text{N}_{233}\text{O}_{243}\text{S}_{9}$

Biologic Manufacturing Is More Complex
Biologic Manufacturing is Complex (Remember this Slide When we Talk about Patent Litigation!)

Biologic Manufacturing is Inherently Variable (Remember this slide when we discuss the filgrastim application)

Figure 1 Comparison of the pre- and post-change Aranesp batches measured by capillary zone electrophoresis. (a) Relative content of the individual isoforms of the pre-change ($n = 18$) and the post-change ($n = 4$) batches. (b) Representative electropherograms; peaks are labeled with the isoform number.

*Nature Biotechnology* 2011;29:310-312
## Biologics Can Generate Immune Responses

*Large globular proteins that can induce a range of immune responses*

*Factors contributing to immunogenicity:*
  - Post-translational modifications
  - Higher order structure
  - Aggregation

<table>
<thead>
<tr>
<th>Product</th>
<th>Antibody formation (%)</th>
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<tbody>
<tr>
<td>Erythropoietin</td>
<td>&lt; 1</td>
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<tr>
<td>Factor VIII</td>
<td>15-52</td>
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<tr>
<td>Factor IX</td>
<td>1-2</td>
</tr>
<tr>
<td>Interferon α</td>
<td>44</td>
</tr>
<tr>
<td>Interferon β</td>
<td>&lt; 5</td>
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<tr>
<td>IL1 Ra</td>
<td>2</td>
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<tr>
<td>Growth hormone</td>
<td>1-2</td>
</tr>
<tr>
<td>Infliximab</td>
<td>17-60</td>
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Understanding Biosimilar Legislation
## Approval Pathways (Small Molecules)

<table>
<thead>
<tr>
<th>Product type</th>
<th>Application type</th>
<th>Application pathway</th>
<th>Clinical studies</th>
<th>Application requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug (Food Drug and Cosmetic Act)</td>
<td>New Drug Application (NDA)</td>
<td>505(b)1</td>
<td>Yes</td>
<td>Full evaluation of safety and efficacy</td>
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<tr>
<td></td>
<td></td>
<td>505(b)2</td>
<td>Yes</td>
<td>Studies do not have to be done by the application sponsor</td>
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<tr>
<td></td>
<td>Abbreviated New Drug Application (ANDA)*</td>
<td>505(j)</td>
<td>No</td>
<td>Approval based upon bioequivalence determination</td>
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</table>

*Created by Hatch-Waxman Amendments

## Approval Pathways (Biologics)

<table>
<thead>
<tr>
<th>Product type</th>
<th>Application type</th>
<th>Application pathway</th>
<th>Clinical studies</th>
<th>Application requirements</th>
<th>Application used</th>
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</thead>
<tbody>
<tr>
<td>Biologic (Public Health Service Act)</td>
<td>Biologics License Application (BLA)</td>
<td>351(a)</td>
<td>Yes</td>
<td>Full evaluation of purity, safety and potency</td>
<td>Tbo-filgrastim (Teva)</td>
</tr>
<tr>
<td>Biosimilar Application (established 2010)</td>
<td>Biosimilar Application (established 2010)</td>
<td>351(k)</td>
<td>Yes</td>
<td>Yes, but abbreviated process (one clinical trial)</td>
<td>Filgrastim/EP2006 (Sandoz)</td>
</tr>
</tbody>
</table>

Interpreting the “Pyramid”

- Clinical Immunogenicity
- Animal Studies
- Clinical Knowledge (e.g., Post-Market Experience)
- Human Pharmacokinetics and Pharmacodynamics
- Structural and Functional Characterization

"...the less you should have to do here."
"The more work you do here..."

Adapted from FDA Webinar: Biosimilar Biological Products
Interpreting State Legislation Related to Biologics and Biosimilar Substitution

The Regulatory Unknown

• What will biosimilars be named? (e.g. non-proprietary name)
• What will be the requirements for biosimilar interchangeability?
  • Guidance document planned for 2015
• How will the Food and Drug Administration address extrapolation?
• When will the Food and Drug Administration make these decisions?
• How will the patent litigation process impact the timing of product launches?
Biosimilar Patent Litigation Process

Within 20 days of FDA accepting a biosimilar application for review, access to BLA information and manufacturing processes must be provided to the reference product sponsor and patent owner.

Sensabaugh SM. *Drug Inf J.* 2011;45:155-162
Next Step in Judicial Process

- February 12
- U.S. District Court for the Northern District of California (San Francisco)
  - Amgen vs. Sandoz
- Key issues
  - Is the information exchange and “patent dance” optional or mandatory?
  - Can notification of intent to market be provided prior to FDA approval?

IPD Analytics, January 20, 2015
“A clear understanding of the scientific principles of the biosimilar concept and access to unbiased information on licensed biosimilars are important for physicians to make informed and appropriate treatment choices for their patients.”

### Biosimilars Approved in Europe

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Date First Approved</th>
<th>Suppliers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somatropin</td>
<td>Apr. 2006</td>
<td>Sandoz Gmb, Biopartners GmbH</td>
</tr>
<tr>
<td>Epoetin alfa</td>
<td>Aug. 2007</td>
<td>Hexal AG, MEDICE Pharma GmbH &amp; Co. KG</td>
</tr>
<tr>
<td>Epoetin zeta</td>
<td>Dec. 2007</td>
<td>STADA Arzneimittel AG, Hospira</td>
</tr>
<tr>
<td>Filgrastim</td>
<td>Sept. 2008</td>
<td>Ratiopharm GmbH, CT Arneimittel, Teva, Sandoz, Hexal AG, Hospira</td>
</tr>
</tbody>
</table>

Inflectra (infliximab; Hospira), first biosimilar monoclonal antibody approved September 10, 2013

1st and 2nd Generation Product Shares Epoetin and Filgrastim Markets in Q4 2011

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Germany</th>
<th>UK</th>
<th>France</th>
<th>Sweden</th>
<th>Italy</th>
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<tbody>
<tr>
<td><strong>Epoetin (market share by revenue)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Darbepoetin</td>
<td>60.8%</td>
<td>70.7%</td>
<td>68.6%</td>
<td>67.6%</td>
<td>41.2%</td>
</tr>
<tr>
<td>Epoetin</td>
<td>12.9%</td>
<td>26.0%</td>
<td>26.8%</td>
<td>10.7%</td>
<td>52.0%</td>
</tr>
<tr>
<td>Biosimilars</td>
<td>26.3%</td>
<td>3.2%</td>
<td>4.6%</td>
<td>21.7%</td>
<td>6.8%</td>
</tr>
<tr>
<td><strong>Filgrastim (market share by revenue)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pegfilgrastim</td>
<td>73.5%</td>
<td>57.1%</td>
<td>77.0%</td>
<td>58.6%</td>
<td>59.4%</td>
</tr>
<tr>
<td>Filgrastim</td>
<td>14.6%</td>
<td>5.1%</td>
<td>11.2%</td>
<td>13.7%</td>
<td>24.9%</td>
</tr>
<tr>
<td>Biosimilars</td>
<td>11.9%</td>
<td>37.8%</td>
<td>11.8%</td>
<td>27.7%</td>
<td>15.7%</td>
</tr>
</tbody>
</table>

The Challenge of Biosimilar Extrapolation?

Biosimilar Monoclonal Antibodies: A Canadian Regulatory Perspective on Clinically Relevant Differences and Extrapolation

Bradley J. Scott, PhD, Agnes V. L. Tu, PhD

The challenge of indication extrapolation

Brian G. Feagan,*, Denis Choquette, Bernd Meibohm, Guangyong Zou, Anthony S. Russell

ScienceDirect

VIEWPOINT

Biosimilars: in support of extrapolation of indications

Hans C. Ebbers*

Available online at www.sciencedirect.com

Journal of Crohn’s and Colitis (2014) 8, 431–435

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2014 Novation Confidential.
Does comparability here →

Equal comparability here? →

What “Else” Can We Learn From Europe?

- “Biosimilars have been on the European Market for several years and have performed as expected in all licensed indications, including extrapolated indications.”

- “In our view, generation of redundant or merely ‘comforting’ data should not be requested. Instead extrapolation should be based on sound and objective scientific criteria.”

Use of Biosimilars in Extrapolated Indications

• Consideration of extrapolation across indications must be scientifically sound, requires:
  
  • Similarity with reference product convincingly demonstrated,
  
  • Relevant mechanism of action and/or receptor are the same in extrapolated indications,
  
  • Safety profile of biosimilar properly characterized and acceptable
  
  • May vary by product – filgrastim vs. epoetin vs. infliximab vs. rituxumab

Health-System Pharmacy Formulary Management Strategies
Important Issues for P & T Committees

- Addition of biosimilars to health system formularies will be a much more involved process compared to small molecule generics
  - Involvement of Pharmacy and Therapeutics Committee required
  - Review will include a more detailed evaluation of safety and efficacy
  - Mechanisms for prescribing, administration and documentation will be more complex than generic products
The infrastructure for formulary evaluation and therapeutic interchange already exists within healthcare organizations.

Existing examples:
- Low molecular weight heparins
- Carbapenem antibiotics
- Echinocandin antifungals
- Insulins
- Tacrolimus and other transplant medications
- Topical thrombins
- Tumor necrosis factor – alpha inhibitors
- Erythropoietin stimulating agents
- Somatropin (human growth hormone)
- IVIG
Formulary Management: Key Questions

• Will the biosimilar product be endorsed only for labeled indications or for off-label indications as well?

• What is the existing level of adverse events with the originator product?
  • How will you ensure appropriate pharmacovigilance with the biosimilar?

• What was the approval history of the biosimilar?

• What information is available concerning the clinical efficacy and safety of the biosimilar?
  • e.g., FDA review document, published trials, European data, AMCP dossier, expert organization guidelines

Formulary Management: Key Questions (Continued)

- What modifications need to be made to existing order sets and protocols to include biosimilar products?
- What education will need to be provided to clinicians to prepare for biosimilar adoption?
- What patient education materials will be needed to support biosimilar use?
- What is the financial value associated with use of a biosimilar?
  - Comparative cost and reimbursement

Tbo-filgrastim, “The non-biosimilar biosimilar”
The Tbo-filgrastim Example

Granix® (Teva)

• Approved August 2012 in the US via a biologics license application (BLA) or 351(a), not the 351(k) biosimilars pathway

• Could not be marketed until November 2013

• However, approved as a biosimilar in EU (TevaGrastim)
  • Authorized September 15, 2008

• Approved for only one of the indications for which Neupogen (filgrastim; Amgen) is licensed
**Tbo-filgrastim Clinical Trial Data**

**Original Article**

**XM02, the First Biosimilar G-CSF, is Safe and Effective in Reducing the Duration of Severe Neutropenia and the Incidence of Febrile Neutropenia in Patients with Non-Hodgkin Lymphoma Receiving Chemotherapy**

**AUTHOR:**

A. ENGERT, L. GRISKEVICIUS, Y. ZUZUGIN, H. LUBNIAU, A. A. DIL GIGLO

**BACKGROUND:**

Recombinant granulocyte colony-stimulating factors (G-CSFs) such as filgrastim or lenograstim are being used to treat chemotherapy-induced neutropenia. The aim of the present study was to investigate a new G-CSF, XM02, compared to filgrastim in terms of safety and efficacy in the prevention of chemotherapy-induced neutropenia in non-Hodgkin lymphoma (NHL). A total of 124 patients receiving chemotherapy were randomized in 3:2 to treatment with daily injections (subcutaneously) of XM02 (n = 83) or filgrastim (n = 41) for at least 5 days and a maximum of 14 days. In subsequent cycles, all patients received XM02. The mean duration of severe neutropenia (DSN) was 0.5 and 6 days in cyclophosphamide (CYP) and high-dose cyclophosphamide (HD-CYP), respectively (p = 0.0195). The incidence of febrile neutropenia (FN) was 11.7% for XM02 and 20.5% for filgrastim (p = 0.0223). The adverse event profile was similar between XM02 and filgrastim. XM02 demonstrated a more effective and similar safety profile as the reference molecule filgrastim. Treatment with XM02 was well tolerated and no patients with NHL receiving chemotherapy XM02 are safe and well tolerated in the doses applied in this study.

**Keywords:** Non-Hodgkin-Lymphoma, chemotherapy, G-CSF, neutropenia, XM02

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**Research Article**

**XM02 is superior to placebo and equivalent to Neupogen™ in reducing the duration of severe neutropenia and the incidence of febrile neutropenia in cycle 1 in breast cancer patients receiving docetaxel/doxorubicin chemotherapy**

A. Del Giglio, A. Enriquez, D. Caneva-Moton, J. Topley

**RESULTS:**

The mean DSN in cycle 1 was 1.1, 1.3, and 3.9 days for placebo, Neupogen™, and XM02, respectively. The incidence of febrile neutropenia (FN) was 11.3% for placebo, 8.9% for Neupogen™, and 8.7% for XM02. There were no significant differences in the incidence of FN in cycle 1 between placebo and XM02 groups. The incidence of FN was significantly lower in the XM02 group compared to the Neupogen™ group. The adverse event profile was similar between placebo and XM02 groups. However, the incidence of FN was significantly lower in the XM02 group compared to the Neupogen™ group.

**Key Words:** Breast cancer, Neupogen™, XM02, Neutropenia.

---

**Abstract**

**Background:**

Recruitment granulocyte colony-stimulating factors (G-CSFs) such as filgrastim or lenograstim are being used to treat chemotherapy-induced neutropenia. The aim of the present study was to investigate a new G-CSF, XM02, compared to filgrastim in terms of safety and efficacy in the prevention of chemotherapy-induced neutropenia in non-Hodgkin lymphoma (NHL). A total of 124 patients receiving chemotherapy were randomized in 3:2 to treatment with daily injections (subcutaneously) of XM02 (n = 83) or filgrastim (n = 41) for at least 5 days and a maximum of 14 days. In subsequent cycles, all patients received XM02. The mean duration of severe neutropenia (DSN) was 0.5 and 6 days in cyclophosphamide (CYP) and high-dose cyclophosphamide (HD-CYP), respectively (p = 0.0195). The incidence of febrile neutropenia (FN) was 11.7% for XM02 and 20.5% for filgrastim (p = 0.0223). The adverse event profile was similar between XM02 and filgrastim. XM02 demonstrated a more effective and similar safety profile as the reference molecule filgrastim. Treatment with XM02 was well tolerated and no patients with NHL receiving chemotherapy XM02 are safe and well tolerated in the doses applied in this study.

**Keywords:** Non-Hodgkin-Lymphoma, chemotherapy, G-CSF, neutropenia, XM02

---

**Introduction**

Myelotoxic chemotherapy frequently leads to neutropenia. Recombinant granulocyte colony-stimulating factors (G-CSFs) are effective pharmacological substances and are successfully applied in the prevention of chemotherapy-induced neutropenia and the associated risk of infection. [1-3]

**Abstract**

**Background:**

Recruitment granulocyte colony-stimulating factors (G-CSFs) are effective pharmacological substances and are successfully applied in the prevention of chemotherapy-induced neutropenia and the associated risk of infection. [1-3]

**Conclusion:**

XM02 is superior to placebo and equivalent to Neupogen™ in reducing the duration of severe neutropenia and the incidence of febrile neutropenia in cycle 1 in breast cancer patients receiving docetaxel/doxorubicin chemotherapy.
Mean Absolute Neutrophil Counts (XM02-02)

Figure 1
Mean (± SD) of Absolute Neutrophil Counts in Cycle 1 – FA Set.
Oncologic Drugs Advisory Committee – Sandoz Filgrastim

Table 7. Summary of relevant EP2006 clinical studies

<table>
<thead>
<tr>
<th>Study (Dates)</th>
<th>Design Features</th>
<th>Objectives</th>
<th>Dose/Route/Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Studies using US-licensed Neupogen (the reference product)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EP06-109 (25-Feb-2011 to 22-Apr-2011)</td>
<td>Randomized, double-blind 2-way crossover in HS (N=28)</td>
<td>1. ANC, PK 2. CD34⁺, safety</td>
<td>10 mcg/kg, SC single dose</td>
</tr>
<tr>
<td>EP06-302 (26-Dec-2011 to 17-Jun-2013)</td>
<td>Randomized double-blinded, active controlled study (N=204)</td>
<td>1. Safety, efficacy Included a Cycle 1 PK sub-study (n=54)</td>
<td>5 mcg/kg, SC multiple dose</td>
</tr>
<tr>
<td><strong>Studies using EU-approved Neupogen</strong></td>
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<td></td>
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<tr>
<td>EP06-103 (29-Aug-2006 to 05-Dec-2006)</td>
<td>Randomized, double-blind 2-way crossover in HS, with two dose groups (N=28/dose)</td>
<td>1. ANC 2. PK, CD34⁺, safety</td>
<td>2.5 &amp; 5 mcg/kg, SC single and multiple (7d) dose</td>
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<tr>
<td>EP06-105 (21-Apr-2008 to 26-May-2008)</td>
<td>Randomized, double-blind 2-way crossover in HS (N=24)</td>
<td>1. ANC 2. PK, safety</td>
<td>1 mcg/kg, SC single dose</td>
</tr>
</tbody>
</table>

HS, healthy subjects; ANC, absolute neutrophil count; PK, pharmacokinetics; SC, subcutaneous.
Sandoz (Filgrastim) Clinical Response

Figure 21. Daily mean ANC in Cycle 1 (Study EP06-302).

The number of subjects in each arm and at each time point is shown at the bottom of the graph.

# Comparative Properties

<table>
<thead>
<tr>
<th></th>
<th>Amgen G-CSF</th>
<th>Teva G-CSF</th>
<th>Sandoz G-CSF</th>
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</thead>
<tbody>
<tr>
<td>Brand name</td>
<td>Neupogen®</td>
<td>Granix®</td>
<td>Zarxio® (proposed)</td>
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<tr>
<td>Generic name</td>
<td>Filgrastim</td>
<td>Tbo-filgrastim</td>
<td>Filgrastim?</td>
</tr>
<tr>
<td>Application type</td>
<td>BLA – 351(a)</td>
<td>BLA – 351(a)</td>
<td>BLA – 351(k)</td>
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<tr>
<td>Ingredient</td>
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<td>r-metHuG-CSF</td>
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<td>Molecular Weight</td>
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<td>18,800 daltons</td>
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<tr>
<td>Protein length</td>
<td>175 amino acids</td>
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<td>Expression system</td>
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<td>Dosages</td>
<td>300 mcg, 480 mcg</td>
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<td>Storage conditions</td>
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## Comparative Properties

<table>
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<th>Indications</th>
<th>Neupogen®</th>
<th>Granix®</th>
<th>Zarxio</th>
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<tbody>
<tr>
<td>Cancer patients receiving myelosuppressive chemotherapy</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes?</td>
</tr>
<tr>
<td>Patients with acute myeloid leukemia receiving induction or consolidation chemotherapy</td>
<td>Yes</td>
<td>No</td>
<td>Yes?</td>
</tr>
<tr>
<td>Cancer patients receiving bone marrow transplant</td>
<td>Yes</td>
<td>No</td>
<td>Yes?</td>
</tr>
<tr>
<td>Patients undergoing peripheral blood progenitor cell collection and therapy</td>
<td>Yes</td>
<td>No</td>
<td>Yes?</td>
</tr>
<tr>
<td>Patients with severe chronic neutropenia</td>
<td>Yes</td>
<td>No</td>
<td>Yes?</td>
</tr>
<tr>
<td>Pregnancy category</td>
<td>C</td>
<td>C</td>
<td>?</td>
</tr>
<tr>
<td>Data for use in pediatrics</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
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</tbody>
</table>
Content of EP2006, US-licensed Neupogen, and EU-approved Neupogen

Reimbursement and Other Considerations
Aetna Approval Criteria

Aetna considers tbo-fl格拉尼特 (Granix, Neutoval) for the prevention of febrile neutropenia (FN) medically necessary in adult and pediatric members with cancer for any of the following indications:

I. Primary prophylaxis

A. Individuals with non-myeloid malignancies receiving myelosuppressive chemotherapy that is expected to result in a 20% or higher incidence of FN (see appendix); or

B. Individuals receiving non-myelosuppressive chemotherapy who are considered to be at high risk for chemotherapy-induced FN infectious complications because of bone marrow compromise or co-morbidity, including any of the following (not an all-inclusive list):
   1. Active infections or open wounds;
   2. Age greater than 65 years;
   3. Bone marrow involvement by tumor producing cytopenias;
   4. Extensive prior treatment including large radiation ports;
   5. Poor nutritional status;
   6. Poor performance status
   7. Previous episodes of FN;
   8. Other serious co-morbidities.

II. Secondary prophylaxis for members who experienced a febrile neutropenic complication from a prior cycle of chemotherapy (for which primary prophylaxis was not received).

III. Therapeutic use in high-risk, febrile, neutropenic members who have any of the following prognostic factors that are predictive of clinical deterioration:

   A. Age greater than 65 years;
   B. Being hospitalized at the time of the development of fever;
   C. Hypotension;
   D. Invasive fungal infection;
   E. Multi-organ dysfunction;
   F. Pneumonia;
   G. Prolonged (greater than 10 days) and profound (absolute neutrophil count less than 1 x 10^9/L) neutropenia;
   H. Uncontrolled primary disease.
Anthem Approval Criteria

**APPROVAL CRITERIA**

I. **Requests for filgrastim (Neupogen), pegfilgrastim (Neulasta), sargramostim**

C. **Adjunctive Treatment**

1. Adjunctive treatment of individuals with FN and high risk for infection-associated complications as demonstrated by any of the following:
   a. Expected prolonged (greater than 10 day) and profound (less than 0.1 \times 10^9/L) neutropenia; or
   b. Age greater than 65 years; or
   c. Uncontrolled primary disease; or
   d. Pneumonia; or
   e. Hypotension and multi organ dysfunction (sepsis syndrome); or
   f. Invasive fungal infection; or
   g. Hospitalized at the time of the development of fever
   j. Liver dysfunction (i.e. elevated bilirubin); or
   k. The presence of open wounds or active infections; or
   l. Recent surgery (generally within the past 12 weeks); or
   m. Advanced cancer; or
   n. Other serious comorbidities

https://www.anthem.com/provider/noapplication/f0/s0/t0/pw_b157349.pdf?na=pharinfo, accessed June 6, 2014
Caremark Tbo-filgrastim Coverage

- Cancer patients receiving myelosuppressive chemotherapy
- Patients with acute myeloid leukemia receiving induction or consolidation chemotherapy
- Cancer patients receiving bone marrow transplant
- Patients undergoing peripheral blood progenitor cell collection and therapy
- Patients with severe chronic neutropenia

BCBS – Coverage Across Various States

- Illinois
  - GRANIX – Tier 4
  - Neupogen – Tier 5 (prior authorization)

- Michigan
  - GRANIX (preferred brand)

- Montana
  - Neupogen (preferred brand)
Summary

• Health system pharmacists eagerly await the introduction of biosimilars

• However, many hurdles to adoption exist including:
  • Lack of familiarity with the nuances of biologic manufacturing
  • Limited understanding of regulatory requirements and the remaining need for clarification of outstanding issues
  • Competition for attention and resources with other critical concerns
  • Degree of cost savings not defined
  • Desire for confirmatory data (i.e. comfort data) persists
Competition Continues!


The Washington Post (1/17, Millman) “Wonkblog” reported on the FDA panel vote from earlier this month that recommended approval for “the first in a new class of drugs called ‘biosimilars,’” the “copycat version of the blockbuster drug Neupogen [filgrastim].” Neupogen is “primarily used to help chemotherapy patients fight off infection.” The agency’s “almost-certain approval of the Neupogen copycat will open the door to a new range of biosimilar drugs that will offer lower-cost competition,” and comes at a time when the US “faces the dual challenge of expanding patient access to treatments while constraining how much the country spends on health care.” The chief concern in approving a biosimilar is that “the FDA has to make a determination that it will behave the same way, it will have the same clinical profile,” as the brand name version of the drug, according to Leah Christi, FDA associate director for therapeutic biologics.
Biosimilar Opportunities

• Several factors should support a willingness to consider biosimilars and help facilitate their adoption
  • Need for financial relief for high cost drugs will not abate
  • Desire for alternatives to limited distribution, originator products given recent decisions of branded suppliers
  • Opportunity to expand influence of specialty pharmaceuticals
  • Existence of formulary management infrastructure already in place to support and sustain therapeutic interchange where clinically appropriate
Conclusions

• The biosimilar approval mechanism will offer a process for the introduction of clinically similar, less-expensive biologics.

• However, biosimilar adoption will be more complex and will require substantial education of pharmacists, physicians, patients, and many other stakeholders and greater resource investment by health care organizations.

• The biosimilar market will continue to be influenced by numerous regulatory decisions, legal rulings and marketing approaches.

• Limited uptake of initial biosimilar opportunities could greatly minimize the potential for success of subsequent more complex products.