Biosimilars - Experiences from Europe

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Agenda

• The Global trend for Biologicals
• An European overview of present status of biosimilars
• What can be learnt form Infliximab in the Nordics?
• Discussion
Spending on Specialty medicines has risen rapidly, growing faster than the total market.

Specialty medicines now account for 35% of European medicine spend,

Europe market trends
Sales and Growth

<table>
<thead>
<tr>
<th></th>
<th>Specialty Sales/Growth MAT Dec 2015</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Sales € Bn</td>
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<tr>
<td>Europe Total</td>
<td>70.6</td>
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<tr>
<td>Germany</td>
<td>15.3</td>
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<tr>
<td>France</td>
<td>10.8</td>
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<td>Italy</td>
<td>9.5</td>
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<tr>
<td>Spain</td>
<td>7.9</td>
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<td>UK</td>
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<td>Netherlands</td>
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<td>Belgium</td>
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Specialty Sales
Traditional Sales
Specialty growth
Total European Pharma growth
Biologics growth continues to put pressure on payers

Such a trend is putting additional financial pressure on healthcare budgets

Source: IMS Health, MIDAS 2015
Historically, only ~12% of biologicals have been exposed to biosimilar competition.
Loss of exclusivity drives biosimilar interest

Key products: protection expired or losing protection by 2022

Europe top molecules sales (MAT 12/2015), €

<table>
<thead>
<tr>
<th>Product</th>
<th>EU expiry date</th>
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<tbody>
<tr>
<td>ADALIMUMAB (Humira)</td>
<td>2018</td>
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<tr>
<td>ETANERCEPT (Enbrel)</td>
<td>Expired</td>
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<tr>
<td>INFLIXIMAB (Remicade)</td>
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<tr>
<td>TRASTUZUMAB (Herceptin)</td>
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<td>BEVACIZUMAB (Avastin)</td>
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<tr>
<td>RITUXIMAB (Mabthera)</td>
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<td>INSULIN GLARGINE (Lantus)</td>
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<tr>
<td>AFLIBERCEPT (Eylea)</td>
<td>2020</td>
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</table>
The biosimilars pipeline is extensive

- Adalimumab (Humira)
- Etanercept (Enbrel)
- Infliximab (Remicade)
- Rituximab (Mabthera)
- Tocilizumab (Actemra)
- Golimumab (Simponi)
- Abatacept (Orencia)
- Golimumab (Simponi)
New biosimilars are not dominated by generic companies

Number of products in registration, pre-registration, and phase III
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The Impact of Biosimilar Competition

• IMS has prepared as a set of indicators to monitor the impact of biosimilars in the European markets at the request of the European Commission services with initial contributions from EFPIA, EGA, and EuropaBio.

• The report sets out to describe the effects on price, volume and market share following the arrival and presence of biosimilar competition in the EEA.

• This first report is based on full year 2014 data; the objective thereafter is to annually publish the previous year’s updated indicators.

Five Observations by IMS Health

• In this document IMS Health suggests five key observations based on the data from the report

Reading guide

• IMS Health has developed a simplified guide to read the report that has a broad set of KPIs for multiple countries

• EPO and Austria are used as the example
Observation one:
Competition drives down the price

- The increased competition affects not just the price for the directly comparable product but also the price of the whole product class
- It can have an almost as large or even a larger impact on the total market price as it has on the biosimilar/reference product price
- The countries with the highest reduction show reduction of 50-70%
- *In order to achieve long-term savings, there should be a competition with multiple players; however, too high short term savings might preclude this*
Observation two: The correlation between biosimilars MS and price reduction is weak

- For the 3 classes we can see the same pattern; high savings can be achieved even if the share is low.

- Price reduction can be achieved through price regulation interventions and/or commercial decisions of manufacturers.

- Even if the biosimilar product does not end to be the product sold it is likely an essential step to generate a competitive environment, which leads to price reduction.
Observation three: Competition can also influence the originator’s behaviour

- *In the Biosimilar classes we have seen a multitude of different originators’ behaviours:*
  - Originators launching innovative long-acting/pegylated products without a price premium versus the short-acting, changing the treatment paradigm and therefore usage pattern
  - Originators effectively reducing the price levels
  - There is also a trend when originator companies are looking to launch biosimilar products
Observation four: Lower prices has the most impact on usage in countries with low initial usage

- For Epoetins, we can see
  - significant increases in consumption for countries with low starting volumes
  - volume reductions in countries with a high use based on safety warnings
- Lowered prices impact usage but we also need to be aware of other factors:
  - New indications or restriction of indications (as the EPO safety warnings)
  - General economic conditions
  - Changes in diagnosing and prevalence of diseases

- **In countries which used to have low usage/availability in the classes the price reductions seem to have a significant impact on the increased access.**
Observation five: The product profile differences can explain differences in impact on the KPIs

- The differences in approved indications are relatively small for HGH and G-CSF, somewhat larger for EPO and the largest for Anti-TNF.

- As a result, different products are used for different indications which impact the patients for which they compete in the class. This is most obvious in Anti-TNF.

- Frequency of administration and mode of administration also impact the competition within a class:
  - We can see the differences in frequency impacting both for EPO and G-CSF but mainly for selected patients (for example patients recovering at home after a chemotherapy cycle).
  - The main differences are seen in Anti-TNF between a more frequent subcutaneous injection in home treatment and or a less frequent intravenous infusion in a hospital setting.
  - User friendliness of device, simpler preparation or no need for refrigeration has mainly been a differentiator for Growth Hormones.

- There are relevant product differentiations in all four classes which impact the product mix.
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Recent additions to EMA list of approved Biosimilars

<table>
<thead>
<tr>
<th>Medicine Name</th>
<th>Active Substan</th>
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Therapy classes exposed to biosimilar competition

Size of classes in 2015 sales versus total European Biologics market

Market Share based on MAT 09 2015 sales values

- Oncology
- Fertility
- Anti –TNF
- G-CSF
- EPO
- HGH

IMS Health BIOSIMILAR BRIEF
Infliximab uptake – EU5 countries

Remsima/Inflectra uptake, %

DOT

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

France Germany Italy Spain UK


Infliximab as % of total

DOT

0% 10% 20% 30% 40% 50% 60%
Infliximab uptake - Nordic countries versus UK and NL
Norway

Norway had an earlier start due to earlier LOE

- Establish process for purchasing process for Anti TNF built on key specialists medical assessment through LIS (cooperation between counties) → one decision for the country
- Very strong supporter from Steinar Madsen, Medical Director at Drug Agency
- Calmed switch worries with NORswitch study
- Patients used to generic switching. Well managed patient interaction
- Very attractive pricing of Rensima by Orion
- The hospital keeps the saving under a DRG system
Denmark

Denmark had a later patent expiration than Norway

- Tradition of high generic usage/discipline at very low prices which has lead to a very “balanced” cost development despite early adoption of innovation
- Fast recent cost growth
- RADS process is efficient and was used to achieve a consensus of that switching is safe
- Amgross pro-active in negotiations
- Benefits with the regions
Sweden

- TLV agrees price for products in the reimbursement system
- 21 county councils/regions owns the budget
- Lack of critical mass/ championship/ insight / peer influence in many regions to push “new” approaches fast

→ 3 counties with very high uptake (Skane, Blekinge, Halland), the rest only some test usage
Finland

- Remicade won with a 42% decrease in price 2012 the three year hospital tender that covers 90% of the market

- Orion have 72% price decrease of Remsima to the rest of the hospitals

- Once the three year contract expired, the market saw a very quick switch
20% usage of infliximab usage is biosimilar

Infliximab use

Trusts use of biosimilar

Source: IMS Health. HPA, Oct-Dec 15
The top users

Among trusts using >50% biosimilar infliximab, speed & penetration of uptake is varied

Infliximab biosimilar usage
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Why so large variations between classes?

- **Length of treatment** - short treatment cycles makes issues of switching less urgent

- **Patient administration** - administration by health care professionals simplifies switching

- **Potential for innovation in class** - clinically meaningful improvements can cause significant differences in impact

- **Clinical evidence/ champions** - combination of the strength of clinical data and the existence of well informed champions promoting the use
Why is the difference so large between countries?

- Culture of brands versus and generics
- Strength of clinical evidence/ champions
- Organization of healthcare – fragmentation
- Organization of purchasing – integration with KOL
- “Incentives” to the prescriber – positive and negative
Considerations for hospital pharmacists

• What is needed to get the best price?
• How to build a strong clinical support / KOL championship?
• What should be the base-line and the follow-up of switched patients

• What are the payers strategy?
Thank you!

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