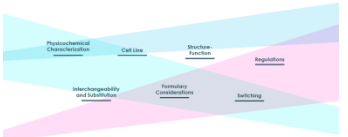

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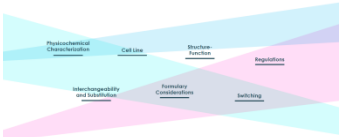
- Chairman, Saudi Scientific Board of Pharmacy

GaBI Scientific Meetings

First GCC Stakeholder Meeting on **Approval Process, Interchangeability/Substitution and Safety of Biosimilars**

20 November 2017, Holiday Inn Izdihar Riyadh, Saudi Arabia



Formulary considerations for biosimilars for health systems

Professor Ahmed H Al-jedai, PharmD, MBA, BCPS, FCCP, FAST

20 November 2017

GaBi
GENERICS AND BIOSIMILARS INITIATIVE
Building trust in cost-effective treatments

SPS Saudi Pharmaceutical Society الجمعية الصيدلية السعودية
PPCI Pro Pharma Communications International

Formulary Considerations for Biosimilars in healthcare systems

Ahmed Aljedai, Pharm.D., M.B.A, BCPS, FCCP, FAST

Director, Pharmaceutical Care Division

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Chairman, Saudi Board of Pharmacy, Riyadh- Saudi Arabia

The Industry

- Spending on medicinal products will reach 1.3 trillion EUR by 2020

- Introduction of biosimilars is expected to have cumulative potential savings of 50–100 billion EUR by 2020

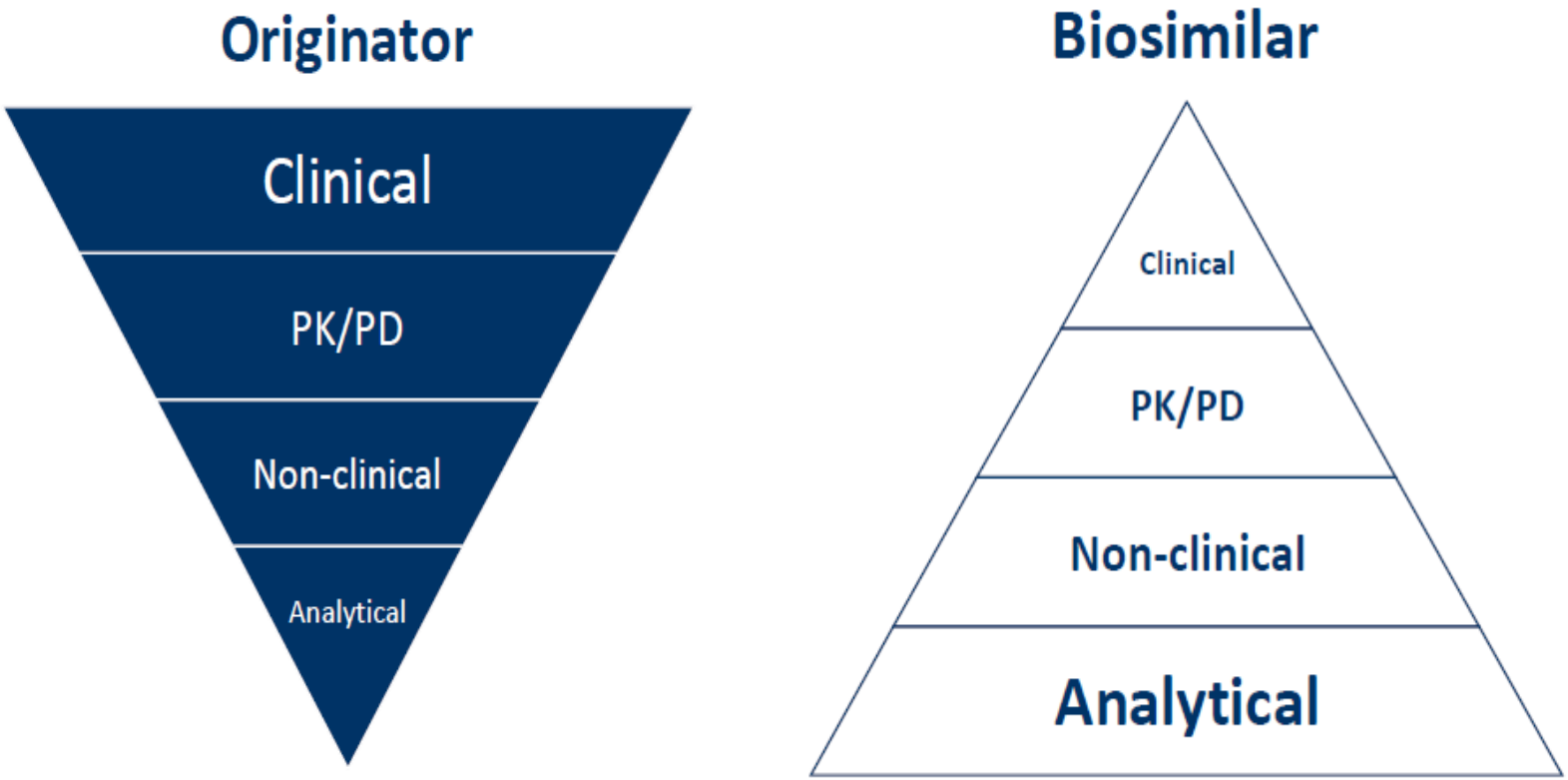
- Price reductions for biosimilars are expected to range from 20% to 40%

Definitions

- **Biologicals–** drugs derived from living cells or organisms, consisting of large highly complex molecular entities which may be difficult to characterise
- **Biosimilars–** biological product that is highly similar but not identical, to the licensed originator biological medicine and shows no clinically meaningful difference in terms of quality, safety and efficacy (safety, purity, and potency- FDA)
- **Interchangeability –** the medical practice of changing one medicine for another that is expected to achieve the same clinical effect in a given clinical setting and in any patient on the initiative or with the agreement of the prescriber

1. EMA. Guideline on similar biological medicinal products. CHMP/437/04 Rev 1/2014. Available: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2014/10/WC500176768.pdf
2. US FDA. Guidance for Industry: Scientific Considerations in Demonstrating Biosimilarity to a Reference Product [2015]. Available: www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM291128.pdf

Differences in Development

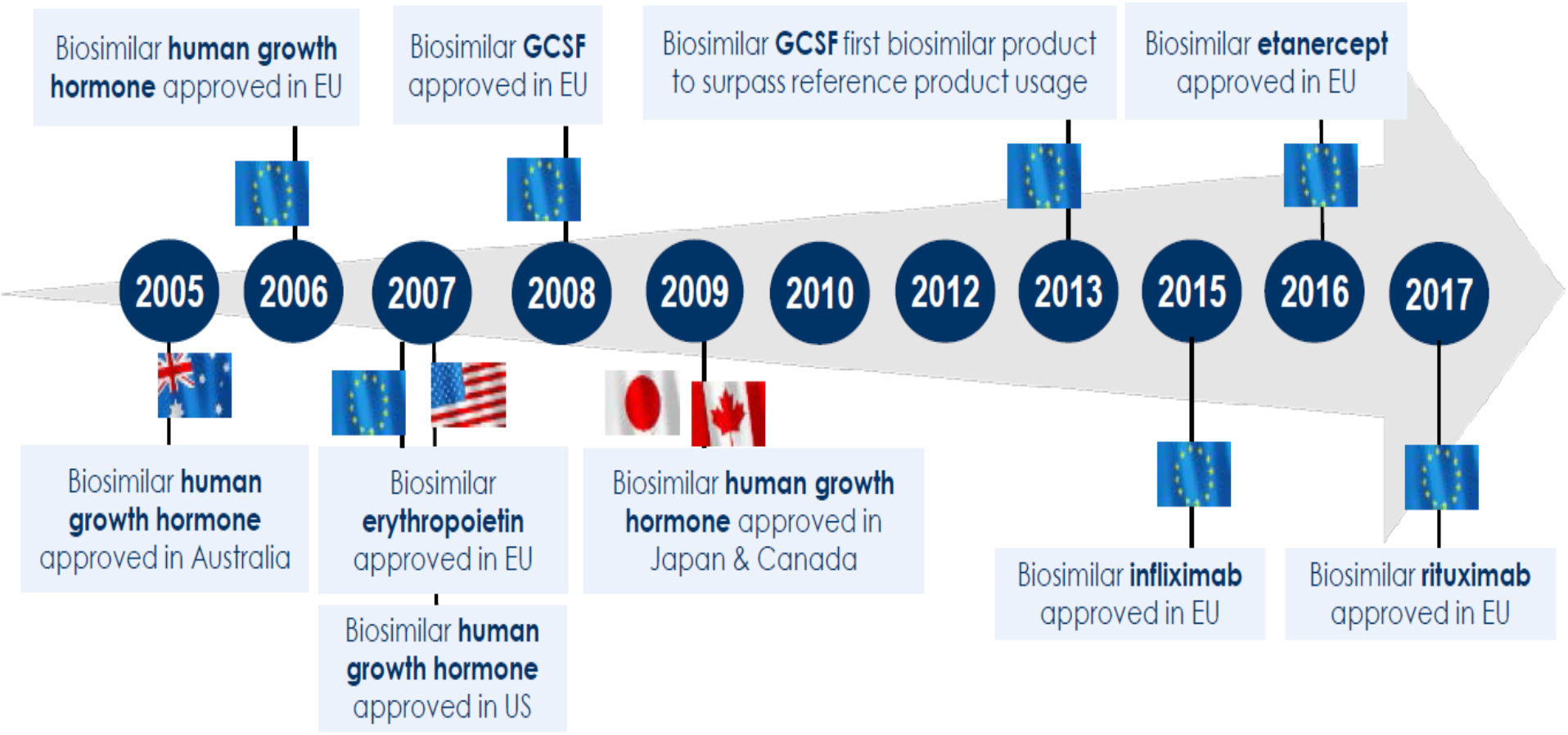


Major goal is to determine *clinical effect*

Major goal is to determine *similarity*

1. McCamish M, et al. *Mabs. 2011;3(2)*:209–17 and
2. McCamish M, Woollett G, Clin Pharmacol Ther. 2012;91(3):405-17

Timeline



1. Gascon P et al Support Care Cancer. 2013; 21(10): 2925–2932.
2. Romer et al Horm Res 2009; 72(6): 359-369.

EMA

- Guidance on regulatory requirements of biosimilars, 2005
- First approved biosimilar from first generation biologics, Somatropin in 2006
- First approved monoclonal antibody biosimilar, 2013
- Updated Biosimilar Guideline, 2013

Questions and answers on biosimilar medicines (similar biological medicinal products). EMA. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Medicine_QA/2009/12/WC500020062.pdf

FDA

- **Small molecules** approved under Food, Drug and Cosmetic Act (FDCA) either as new drug or generic drug (Hatch-Waxman Act 1984)
- **Biologics** under Pubic Health Service Act (PHSA) either as new biologics or as biosimilar biologics established by the Biologics Price Competition and Innovation (BPCI) Act of 2009 (Affordable Care Act aka ObamaCare)
- Biosimilar approval pathway guidance, 2012
- Naming biosimilars guideline, 2017
- Draft guideline for interchangeability, 2017

US FDA. Guidance for Industry: Scientific Considerations in Demonstrating Biosimilarity to a Reference Product [2015]. Available: www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM291128.pdf

Regulatory Approval Requirements

Guidance	FDA	EMA
Stepwise approach	Recommended	Recommended
Preclinical evaluation of PK and PD	Recommended	Recommended
Comparative PK studies	Human studies required	Single-dose comparative human studies required
Comparative PD studies	Human studies recommended	Combine with PK studies where a clinically relevant PD marker is available
Comparative clinical trials	At least 1 adequately powered equivalence trial	At least 1 adequately powered equivalence trial
Safety	At least 1 adequately powered equivalence trial	At least 1 adequately powered equivalence trial
Immunogenicity	Required	Required (12 month head-to-head comparative clinical study)
Equivalence design with strict, predefined margins for clinical study	Recommended	Recommended

SFDA

- Follows EMA approach
- Guidelines on Biosimilars version 1.1, last update 2010
- 4 approved and registered biosimilars: Somatropin, Filgrastim, infliximab and Insulin Glargine

Saudi FDA, Guidelines on Biosimilars, version 1.1, 2010 [online]. Available through URL: http://www.sfda.gov.sa/en/drug/drug_reg/Pages/default.aspx?catid=11&news=Main. Last accessed March 2017

GCC

- Gulf Health Council
- Centralized approach
- Guideline on Biosimilars, 2016
- Follows EMA approach

Gulf Health Council. Guideline on Biosimilars, v1.1, 2016 [online]. Available through URL: http://sgh.org.sa/Portals/0/PDF/Cen_registration/GCCGuidelinesonbiosimilars_v11.pdf. Last accessed March 2017


Canada: Guideline released in Q1-2009
USA: Healthcare reform in Q1-2010, which includes biosimilars. Guidelines issued in 2015
Mexico: Have biosimilar guideline
EU: Have established framework. EMA, CHMP released final mAb biosimilars guidance in Q2-2012
Russia: No Guideline yet (Draft issued in 2014)
China: Guideline issued in 2015
Japan: Guideline released in Q1-2009
S. Korea: Biosimilar guideline issued in Q2-2009
India: Guideline issued in Q2-2012
Malaysia: Guideline issued in Q2-2003
Venezuela: Guidelines issued in Q3-2000.
Colombia: Decree signed into law in Sept 2014
Peru: Guidelines under development
Brazil: Guideline issued in Q4-2005, amended in March 2009
Bolivia: No biosimilar guideline yet
Uruguay: New decree Jan 2015.
Chile: Guidelines issued in 2014
Argentina: Guidelines issued.
Australia & New Zealand: Adopted EMA guideline in 2008
WHO Guidelines
Last updated: April 2015
Biosimilars regulation enacted
Biosimilars regulation drafted or in development
No biosimilars regulation
Biosimilars regulation status unknown

Approved Biosimilars

Biosimilar	Approved Indication	Approval/Agency
Somatropin	Präder-Willi syndrome, Turner syndrome, pituitary dwarfism	2006: EMA
Epoetin	Anaemia, kidney failure, cancer follow-up treatment	2007: EMA
Filgrastim	Neutropenia, hematopoietic stem cell transplantation, cancer follow-up	2008: EMA 2015: FDA
Infliximab	Rheumatoid arthritis, Crohn disease, ulcerative colitis, psoriasis, psoriatic arthritis, ankylosing spondylitis	2013: EMA 2016: FDA
Insulin glargine	Diabetes mellitus in adults and paediatrics	2014: EMA
Follitropin	Anovulation	2013: EMA
Etanercept	Rheumatoid arthritis, psoriatic arthritis, plaque psoriasis, ankylosing spondylitis	2016: EMA 2016: FDA
Adalimumab	Crohn disease, ulcerative colitis, rheumatoid arthritis, psoriatic arthritis, plaque psoriasis, ankylosing spondylitis	2016: FDA

What's in the Pipeline today?

- **Bevacizumab (Avastin®), Rituximab (MabThera®) and Trastuzumab (Herceptin®)** biosimilars in registered Phase III Clinical Trials

- EMA: In 2017 biosimilars for use in therapeutic treatment of oncology will be launched

- Patents expiring: FDA 12 years and EMA 10 years by 2020

- Regulations governing healthcare and provision of drugs

1. Schleicher SM, Seidman AD. An Important Step Forward for Biosimilars in Cancer Treatment. *JAMA Oncol.* Published online February 09, 2017. doi:10.1001/jamaoncol.2016.6789
2. James GS, Robert P., Ira J., Susan H., Lesley GS. Biosimilars: Practical Considerations for Pharmacists. Annals of Pharmacotherapy. 1-13;2017. doi:10.1177/1060028017690743

Biosimilars

Opportunities

- Increase access to biologic therapy
- More treatment
- Earlier initiations
- Greater continuity of therapy
- Cost effectiveness

Challenges

- Regulatory requirements
- Time and Cost
- Efficacy and Safety
- Immunogenicity
- Healthcare providers and patients acceptance

Formulary Considerations

- Is P&T committee involvement needed?
- Naming
- Indication extrapolation
- Product labelling
- Therapeutic drug monitoring
- Manufacture attributes
- Logistics of product use

James GS, Robert P., Ira J., Susan H., Lesley GS. Biosimilars: Practical Considerations for Pharmacists. Annals of Pharmacotherapy. 1-13;2017. doi:10.1177/1060028017690743

Biosimilars and Drug Formulary

- No formulary biosimilars
- Cost analysis of formulary biologics and biosimilars
- Review of biologics and biosimilars for particular disease states

Table 1 Considerations for P&T Committee Members Evaluating Biosimilars for Formulary Inclusion[1–4,6–9,12–14,17,24]

Clinical Considerations
• Indications • Evaluation of efficacy and safety using available data • Immunogenicity
Product Considerations
• Nomenclature • Manufacturing and supply chain considerations • Packaging, labeling, and storage
Institutional Considerations
• Substitutions and interchangeability • Therapeutic interchange • Transition of care • Pharmacovigilance • Cost • Reimbursement • Provider and patient education • Information technology

Table 2 American Society of Health-System Pharmacists (ASHP) Policy Guidelines on Approval of Biosimilar Medications[30]

- Encourage the development of safe and effective biosimilars to make such medications more affordable and accessible.
- Encourage research on the effectiveness, safety, and interchangeability of biosimilar medications.
- Support legislation and regulations to allow FDA approvals of biosimilars.
- Support legislation and regulation to allow FDA approval of biosimilar medications that are determined to be interchangeable and may be substituted for the reference product without intervention of the prescriber.
- Oppose implementation of any state laws regarding biosimilar interchangeability prior to finalization of FDA guidance.
- Oppose any state legislation that would require a pharmacist to notify a prescriber when a biosimilar designated as interchangeable is dispensed.
- Require post-marketing surveillance for all biosimilar medications to ensure their continued safety, efficacy, purity, quality, identity, and strength.
- Advocate for adequate reimbursement for biosimilar medications that are designated as interchangeable.
- Develop and promote ASHP-directed education of pharmacists about biosimilar medications and their appropriate use within hospitals and health systems.
- Advocate and encourage pharmacist evaluation and the application of the formulary system before biosimilar medications are used in hospitals and health systems.

Cost Analysis: Infliximab

Drug name	Cost per unit (SAR)*	Cost reduction
Remicade® 100 mg vial for injection	2127.95	↓22.5%
Remsima® 100 mg powder for solution for infusion	1650	

* Market prices as per SFDA

Saudi FDA, Registered Drugs and Herbal Products List. Available through URL: http://www.sfda.gov.sa/en/drug/drug_reg/Pages/default.aspx?catid=11&news=Main. Last accessed March 2017

Cost Analysis: Insulin Glargine

Drug name	Cost per unit (SAR)*	Cost reduction
Lantus Solostar® 100 units/mL prefilled pen	**296.45**	**↓10%**
Vivaro® 100 units/mL prefilled pen	**266.8**	

* Market prices as per SFDA

Saudi FDA, Registered Drugs and Herbal Products List. Available through URL: http://www.sfda.gov.sa/en/drug/drug_reg/Pages/default.aspx?catid=11&news=Main. Last accessed March 2017

Cost Analysis: Filgrastim

Drug name	Cost per unit (SAR)*	Cost reduction
Neupogen® 30 MU/0.5 mL PFS	459.75	↓76.7%
Zarzio® 30 MU/0.5 mL PFS	107.1	

* Market prices as per SFDA

Saudi FDA, Registered Drugs and Herbal Products List. Available through URL: http://www.sfda.gov.sa/en/drug/drug_reg/Pages/default.aspx?catid=11&news=Main. Last accessed March 2017

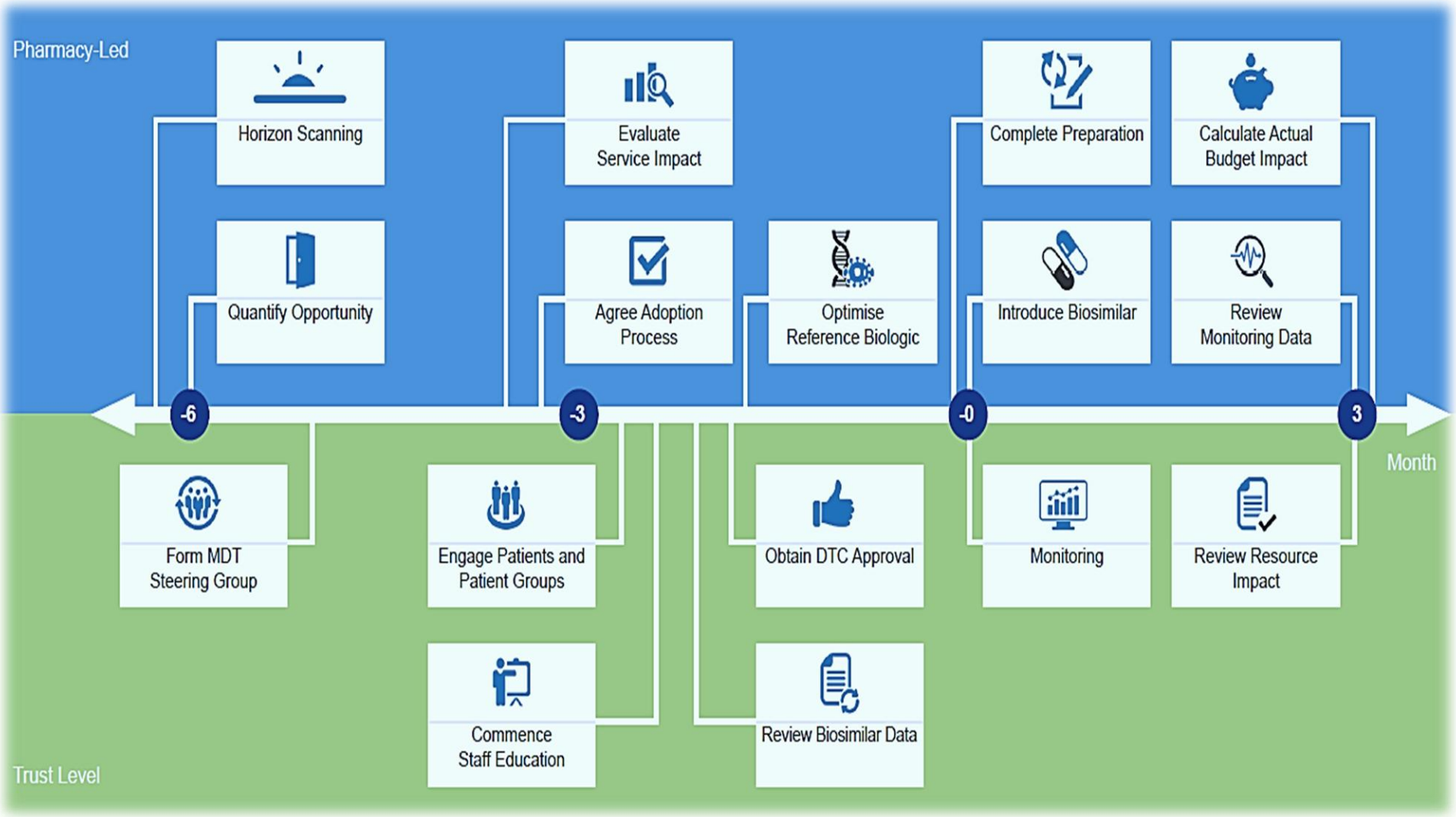
Cost Analysis: Somatoropin (Growth Hormone)

Drug name	Cost per unit (SAR)*	Cost reduction
Norditropin® 5 mg/1.5 mL prefilled pen	479.35	↓62-69%
Norditropin® 10 mg/1.5 mL prefilled pen	955.45	
Omnitrope® 5 mg/1.5 mL solution for injection cartridge	1568	
Omnitrope® 10 mg/1.5 mL solution for injection cartridge	2513.25	

* Market prices as per SFDA

Saudi FDA, Registered Drugs and Herbal Products List. Available through URL: http://www.sfda.gov.sa/en/drug/drug_reg/Pages/default.aspx?catid=11&news=Main. Last accessed March 2017

Adoption Process: P&T



Purple Book

- Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchange-ability Evaluations
- Access via FDA website
- Includes date biologic licensed, biosimilar to or interchangeable with a reference biological product (an already-licensed FDA biological product)
- Last list published September 2017

- **Others:**
- FDA, EMA, SFDA websites

FDA: Purple Book access:
https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/therapeuticbiologicapplications/biosimilars/ucm411418.htm

Pharmacists Role

- Manage introduction of biosimilars
- Informed decisions
- Educate healthcare providers
- Educate patients

Summary

- Biosimilars can be thoroughly analysed and characterised
- Systematically developed to be highly similar to their reference biologic
- Clinical studies aim to confirm the characterisation work
- Extrapolation builds on the entire similarity exercise
- Post authorisation studies continue safety monitoring
- Biosimilars must meet the same quality standards as originator products
- Biosimilars may increase patient access to biologic medicines and contribute to savings
- Influence of evolving regulatory guidelines

Eleryan MG et al. Biosimilars: potential implications for clinicians, Clin Cosmet Investig Dermatol, 2016;17:135-42