aga IBD and Biosimilars

BIOSIMILARS: What health care providers need to know

Section 1: The Biosimilar Development Process

The Biosimilar Development Process

Data to Support Biosimilarity

The goal of a biosimilar development program is to use a **"totality of the evidence"** approach to demonstrate biosimilarity to the reference product, not to independently establish safety and effectiveness of the proposed biosimilar.

Highly Similar

Analytical Studies

Toxicity Tests

Animal Studies

No clinically meaningful difference

Human PK & PD Studies

Immunogenicity Assessment

Additional Clinical Studies

https://www.fda.gov/files/drugs/published/Biosimilar-Development-Process.pdf

Biosimilars Price Competition and Innovation Act (BPCIA)

Legislation to drive cost savings is the biggest factor driving biosimilar development

The BPCIA was established in 2009 to create an **abbreviated licensure pathway** for biological products that are demonstrated to be "**biosimilar**" to or "**interchangeable**" with an FDA-licensed biological product.

fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/ucm216146.pdf

Distinctions between Generics and Biosimilars

	Generics	Biosimilars
QA	~50 QA tests done before possible approval	~250 QA tests done before possible approval
Development	about 3 years	about 7-8 years
Manufacturing	Bioequivalent/identical to reference product and replicable in different laboratories	Same complex amino acid sequence as reference biologic. Unique, living cell line with possible post-translational modification.
Interchangeability	Interchangeable/Automatic substitution	No interchangeability or automatic substitution. Best with new starts or sustained remission+stable dosing.
Immunogenicity	Reactions not easily attributable to product	Reactions may be attributable to both product- and host-related factors
Cost Savings	80-90% discount over reference product	20-30% discount over reference product

Regulatory Requisites Associated with Biosimilars

Pharmacokinetics

what the body does to a drug (Absorption, distribution, metabolism, and excretion (ADME))

Pharmacodynamics

what the drug does to the body (biochemical and physiologic effects)

For biosimilars, highly similar PK or PD alone is generally insufficient to establish "bioequivalence," as they are large & complex proteins with unique manufacturing processes

Extrapolation

Clinical trials in one indication used as rationale for clinical use in other indications for which the originator biological product is approved. Requires appropriate scientific justification.

Interchangeability

Additional requirements to show that the biosimilar produces the same clinical result as the reference product in any given patient. The safety and efficacy of switching will also have been evaluated.

Pharmacovigilance

Post-marketing monitoring, detecting and prevention of adverse events or drug-related problems. Clinical trials are usually too small to detect rarer AEs, especially if duration is limited.

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Section 3: Biosimilars in Clinical Practice

Scenarios for/against Biosimilar use

Positioning biosimilars in clinical practice within IBD treatment paradigms

Adalimumab/infliximab naïve patients (new start)	Same indications and dosing as RP agents
Sustained remission plus stable dosing of adalimumab/infliximab	Could use biosimilar if more cost-effective*
Drug holiday with history of response	Could use biosimilar in re-challenge
Loss of response to adalumumab/infliximab	If attributed to high titer, do not switch
Clinically significant antibodies present to adalimumab/infliximab	Do not use biosimilar
Primary non-response to adalumumab/infliximab	Do not use biosimilar
Patient at high-risk for disease flare/stable dose not identified	Do not switch to biosimilar
Patient has a high-risk condition (e.g. pregnancy)	Do not switch to biosimilar

*Consider checking IFX levels/antibodies before biosimilar switch to identify patients at greater risk of flaring or non-response