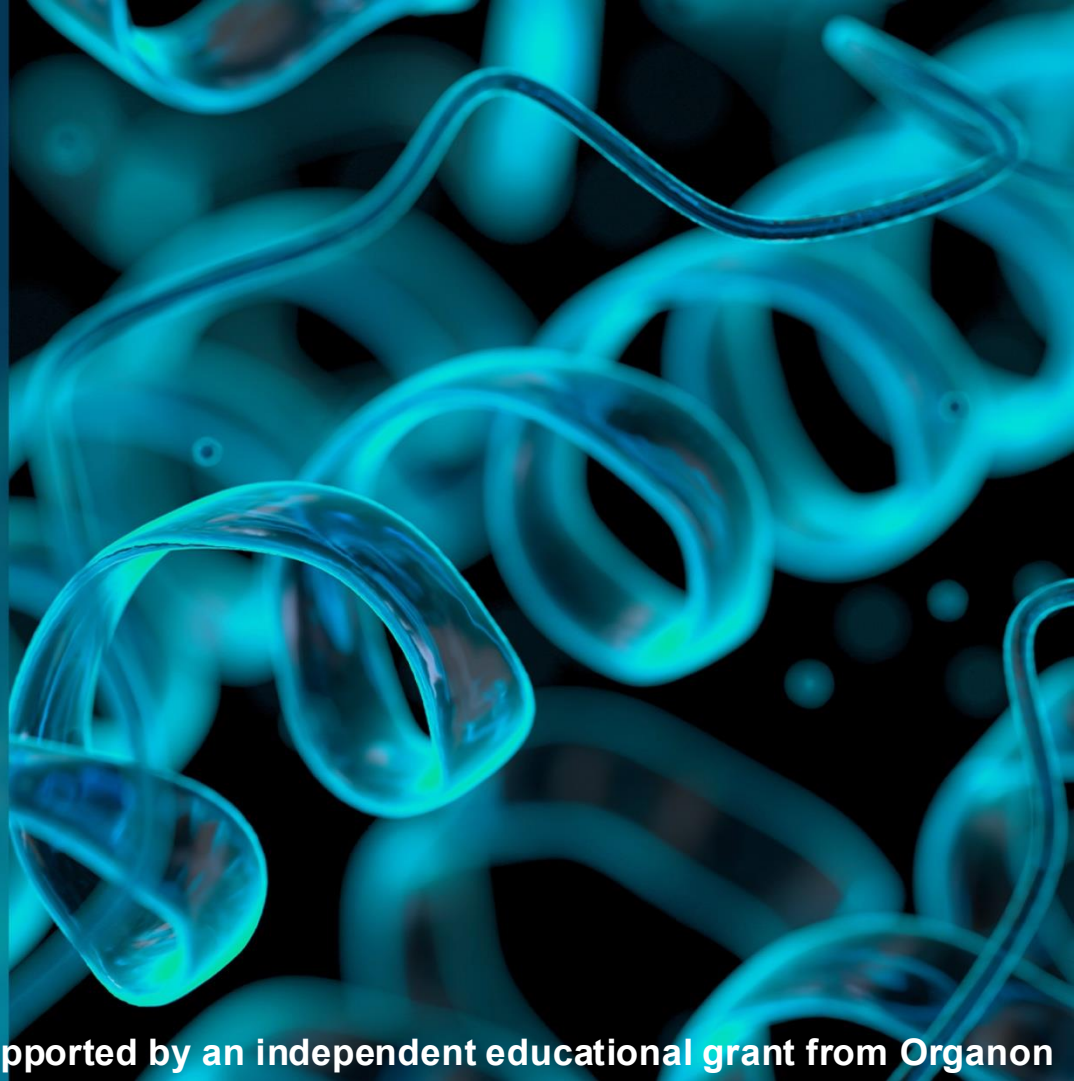
# From Policy to Practice:

## Navigating the Evolving Biosimilar Landscape



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Supported by an independent educational grant from Organon

# Learning Objectives

- Describe the clinical and practical benefits of biosimilars in IBD management, with emphasis on affordability and improved treatment access
- Analyze current evidence on the safety and effectiveness of biosimilars for the treatment of IBD
- Assess the current biosimilar approval and regulatory landscape that impacts market access, adoption, and availability, including recent policy developments
- Evaluate ongoing challenges to biosimilar integration in IBD care and outline strategies to improve biosimilar access

**IBD = inflammatory bowel disease.**

***This CME activity includes brand names for participant clarity purposes only. No product promotion or recommendation should be inferred.***

From Policy to Practice

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# Definition and Development of Biosimilars

**Christina Ha, MD, FACG**
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# Disclosures

- **Christina Ha, MD FACG:** Consultant – AbbVie, Bausch Health, Johnson & Johnson, Eli Lilly, Takeda; advisory board – AbbVie, Bausch Health, Johnson & Johnson, Eli Lilly, Takeda; educational programming support – AbbVie, Celltrion, Johnson & Johnson, Eli Lilly, Takeda; DSMB – Takeda; steering committee – MILESTONE IBD; member – IBD Education Group

# Costs of IBD Care

- Annual cost of IBD in US: $50 billion, direct medical costs $14.6-31.6 billion
- 2021 mean annual direct per person costs in US
  - Crohn's disease $12,000
  - UC $9000

- Challenges
  - Increased incidence/prevalence of IBD worldwide
  - Early implementation of advanced therapies is recommended by guidelines
- Advanced therapies increase direct costs... (initially)
  - Costs to develop biologic ≈ $390 million
  - Social determinants of health: Limit access to more higher cost agents → delayed initiation of recommended therapies, greater healthcare utilization

**UC = ulcerative colitis.**

**Burisch J, et al. *Clin Gastroenterol Hepatol*. 2025;23(3):386-395. Lexchin J. *JAMA Netw Open*. 2020;3(4):e204753.**

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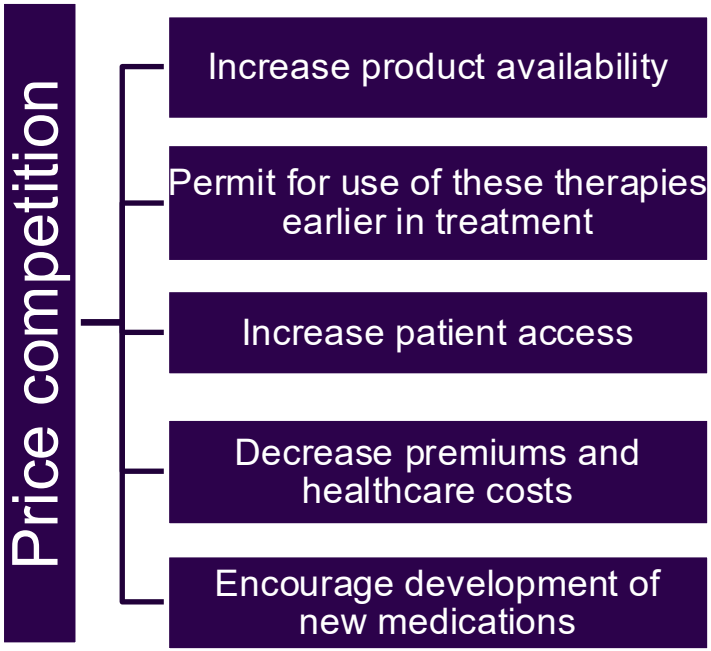
# The Case for Biosimilars: Costs Limit Access to Biologics




- 2021 – US spent $260 billion on biologics across all disease states (46% of pharmaceutical drug spending)
- Biosimilars – $2.2 billion in total savings among patients with IBD
- Infliximab biosimilars → $260-842 million in savings to US health system during first 5 years of market availability
- Infliximab biosimilars – decreased costs of originator infusion by 53%

Paglinco SR, et al. *Am J Managed Care*. 2025;31(1):e295-301. US Dept of Health. Accessed Nov 17, 2025. https://oig.hhs.gov/reports/all/2023/biosimilars-have-lowered-costs-for-medicare-part-b-and-enrollees-but-opportunities-for-substantial-spending-reductions-still-exist/. Association for Accessible Medicines (AAM). Accessed Nov 17, 2025. https://accessiblemeds.org/wp-content/uploads/2025/09/AAM-2025-Generic-Biosimilar-Medicines-Savings-Report-WEB.pdf.

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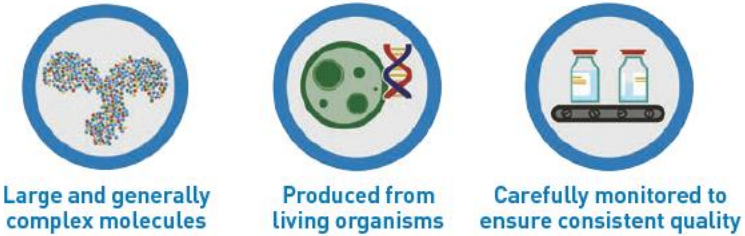
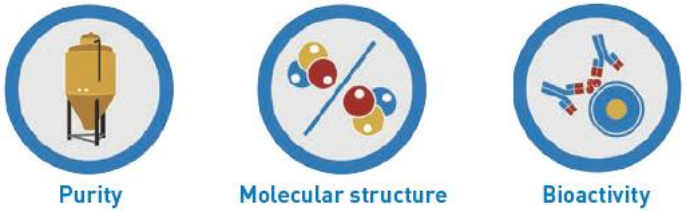
# Biosimilars: FDA Definitions and Requirements

- A biological product that is **HIGHLY similar** to the reference product with only **MINOR** differences in **clinically inactive** components




- No **CLINICALLY MEANINGFUL DIFFERENCE** between the biological product and the reference product in terms of
  - Safety
  - Purity
  - Potency




The data from these comparisons must show that the biosimilar is highly similar to the reference product.

**REFERENCE** product = the “name brand” biologic

Food Drug Administration (FDA). Accessed Nov 17, 2025. https://www.fda.gov/media/108905/download?attachment.

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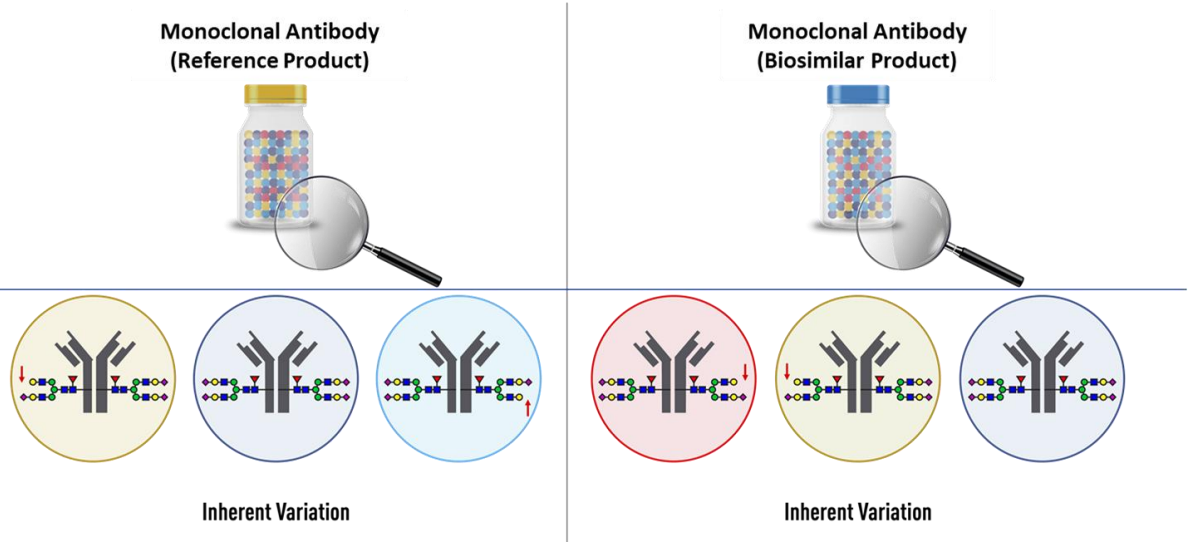
# Biologics Have Inherent Variability

- As part of the manufacturing process, different lots of biological products contain millions of slightly different versions of the same protein or antibody, called ***LOT-TO-LOT VARIATION***

**Expanded view**: Biosimilars are highly similar to the reference product.

**Close-up view**: Inherent variations exist in both reference products and biosimilars, but studies are conducted to confirm that they do not lead to clinically meaningful differences.




**No evidence that these changes lead to differences in clinical practice**

**Adapted from FDA. Updated Oct 16, 2024. Accessed Nov 17, 2025.
https://www.fda.gov/drugs/biosimilars/curriculum-materials-health-care-degree-programs-biosimilars.**

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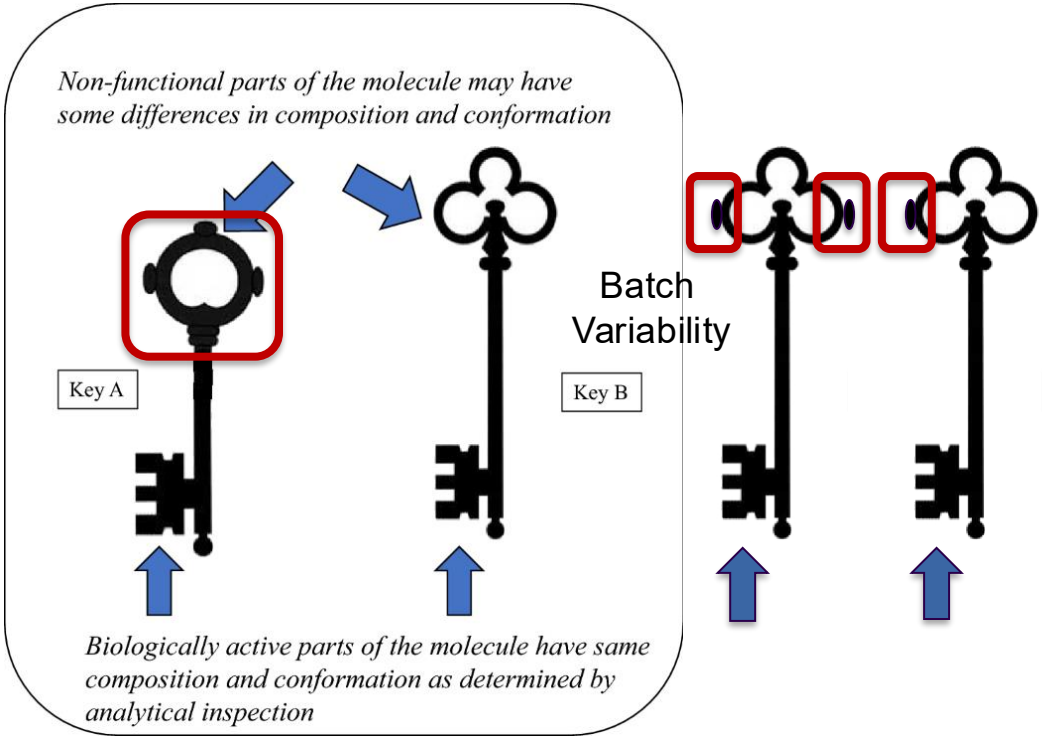
# Basics of Biosimilars: Common Misconceptions




Webster CJ, et al. *BioDrugs*. 2019;33(6):603-611. Slide courtesy David Choi, PharmD.

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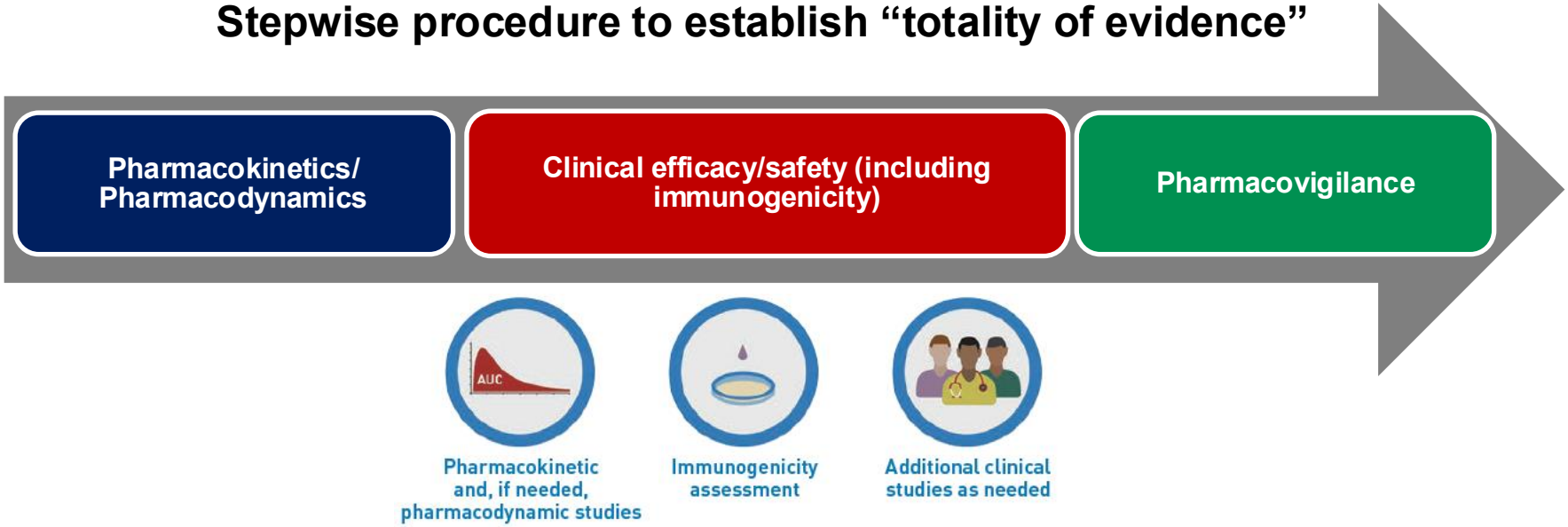
# General Principles to Demonstrate Biosimilarity for Indication Extrapolation: "Totality of Evidence" Is Evaluated

**Stepwise procedure to establish "totality of evidence"**




FDA. Accessed Nov 17, 2025. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/scientific-considerations-demonstrating-biosimilarity-reference-product. European Medicines Agency (EMA). Accessed Nov 17, 2025. https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-similar-biological-medicinal-products-containing-biotechnology-derived-proteins-active-substance-non-clinical-and-clinical-issues-revision-1_en.pdf.

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# Key Learning Points

- All biologic agents have variability from "batch to batch"
- Biosimilars are an inherent part of the IBD treatment landscape
- Biosimilars do not represent a new mechanism of action
- Unlike generics, biosimilars undergo a rigorous process mandated by the FDA to confer highly similar effectiveness, safety, immunogenicity and required longitudinal monitoring

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# Barriers to Market Entry and Patient Access

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# Disclosures

- **David Choi, PharmD, BCACP:** Speaker's bureau – Janssen, Abbvie, Eli Lilly; consultant – Bristol Myers Squibb, Boehringer Ingelheim, Abbvie, Eli Lilly, Janssen, Pfizer

# US Biosimilar Approval Process

- Abbreviated Approval Pathway (The Biologics Price Competition and Innovation Act of 2009) – totality of evidence
  - Analytical studies
    - Provide data to support the structural and functional similarity
  - Nonclinical
    - Animal studies
    - Provide toxicology or pharmacology information
  - Clinic studies
    - Comparative pharmacology studies demonstrates similar pharmacokinetics and effects
    - Comparative clinical studies (does not have to be done for every disease state)


FDA. Accessed Nov 17, 2025. https://www.fda.gov/drugs/biosimilars/review-and-approval.

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# UK Biosimilar Approval Process

- Committee for Medicinal Products for Human Use Guidelines
  - Comprehensive physiochemical and biologic characterization
  - Pivotal comparative pharmacokinetic study
  - Confirmatory efficacy trial (not always necessary)
    - Justification should be provided that comparable efficacy/safety can be derived from comparable binding properties and functional characteristics
  - The dose, frequency, and route of administration must be the same but deviations are possible (strength), pharmaceutical form, formulation, excipients, or presentation with additional data
  - Once approved a biosimilar is considered interchangeable


**Medicines & Healthcare Products Regulatory Agency. Access Nov 17, 2025. https://www.gov.uk/government/publications/guidance-on-the-licensing-of-biosimilar-products/guidance-on-the-licensing-of-biosimilar-products**

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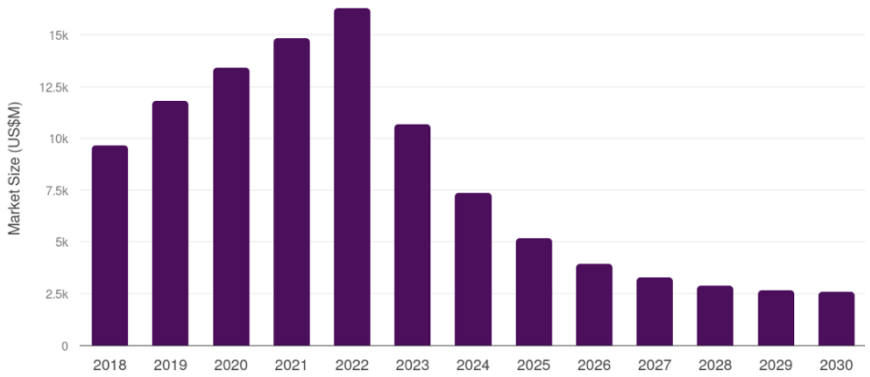
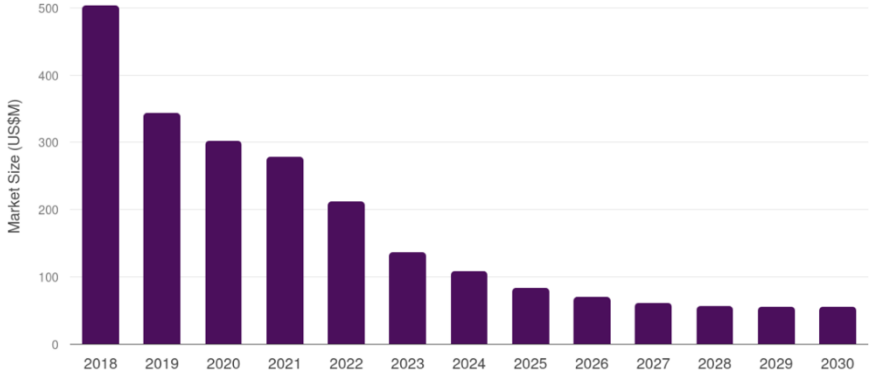
# Market Access to Biosimilars (Patent Litigation)

**US Type: Adalimumab Market, 2018-2030**




**UK Type: Adalimumab Market, 2018-2030**




**Grand View Research. Accessed Nov 17, 2025. https://shorturl.at/dqN9l; https://shorturl.at/nyH0A.**

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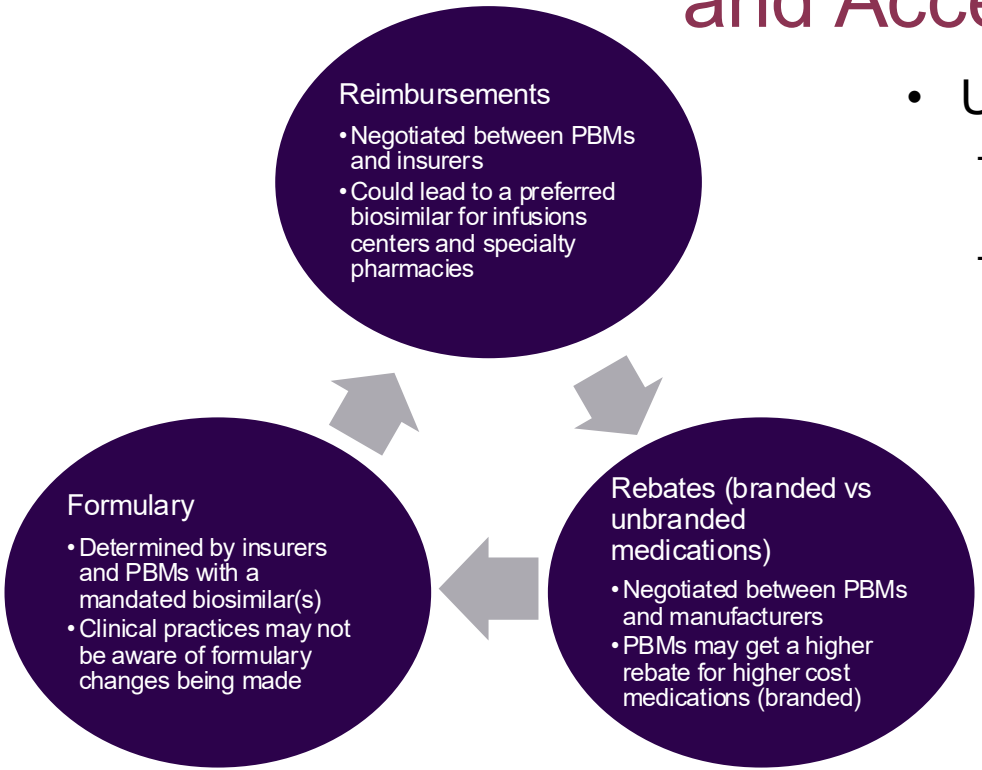
# The PBM Story: How PBM Decisions Impact Cost and Access




- Unknown
  - Safety of multiple biosimilars switches
  - Follow the money: Cost savings to employers and patients vs profit for insurance companies... who is saving money?

**PBM = payer and pharmacy benefit manager.**

**Jeremias S. Accessed Nov 17, 2025. https://www.centerforbiosimilars.com/view/breaking-down-biosimilar-barriers-payer-and-pbm-policies.**

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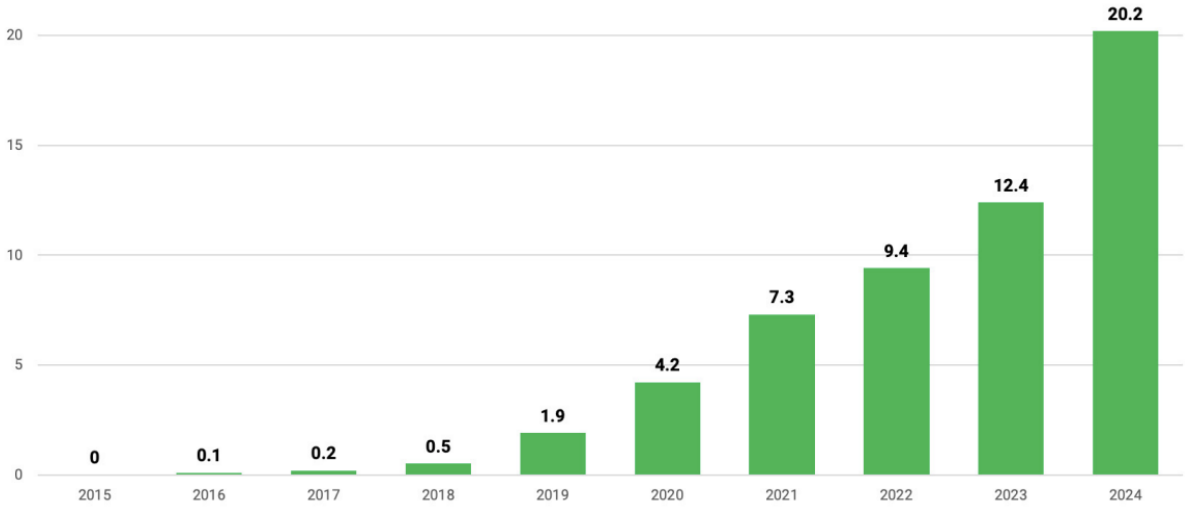
# Biosimilars Have Generated $56.2 Billion in Savings Since 2015

## Savings Reflect Provider Confidence and Robust Price Competition

### Biosimilars Generated $20.2 Billion in Savings in 2024




Source: IQVIA National Prescription Audit, December 2024; IQVIA Institute, June 2025.

US Dept of Health and Human Services. Accessed Nov 17, 2025. https://www.hhs.gov/press-room/fact-sheet-bringing-lower-cost-biosimilar-drugs-to-american-patients.html. AAM. Accessed Nov 17, 2025. https://accessiblemeds.org/wp-content/uploads/2025/09/AAM-2025-Generic-Biosimilar-Medicines-Savings-Report-WEB.pdf.

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# From Policy to Practice:

## Navigating the Evolving Biosimilar Landscape


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# Disclosures

- **Raymond K. Cross, MD, MS:** Advisory board/consulting – AbbVie, Bristol Myers Squibb, Genentech, Magellan Health, Option Care, Pfizer, Samsung Bioepis, Sandoz; speaker's bureau – AbbVie, Celltrion, Bristol Myers Squibb, Janssen, Pfizer; Executive Committee Member – IBD Education Group; scientific co-director – CorEvitas Registry; DSMB – Gilead; Research Grants – Janssen, Takeda

# Case 1

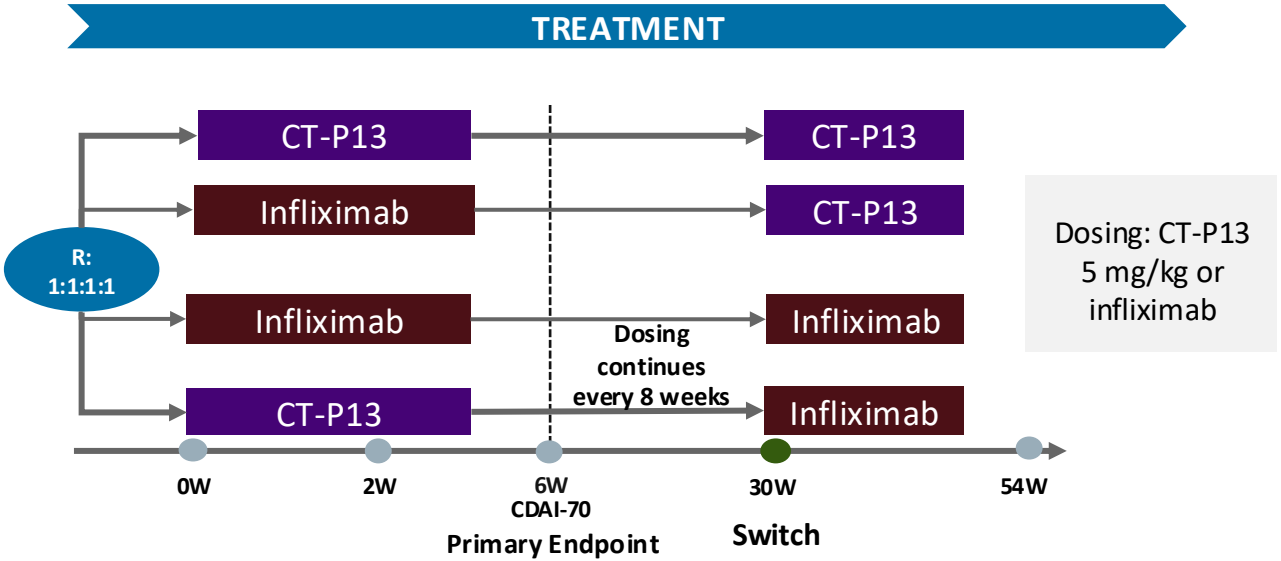
- 28-year-old woman with ulcerative colitis doing well on infliximab (reference product) with no changes needed during routine follow up. However, she recently called your office with concerns because of a letter from her insurance provider informing her that they will no longer cover the infliximab biologic and instead switch to a biosimilar

# Discussion

- How do you and your staff explain the concept of biosimilars to patients?
- What areas do you focus on in the transition from reference product or biosimilar to a biosimilar or different biosimilar?
- Do you obtain any specific diagnostic testing after the change from one product to another?

# CT-P13 in Biologic-Naive Patients with Active CD: Randomized, Double-Blind, Phase 3 Non-Inferiority Study

- Double-blind RCT to assess non-inferiority of infliximab biosimilar CT-P13 compared with infliximab (N = 220)
- All patients were bio-naive with symptomatic CD




CD = Crohn's disease; RCT = randomized controlled trial; W = weeks.
Ye BD, et al. *Lancet*. 2019;393(10182):1699-1707.

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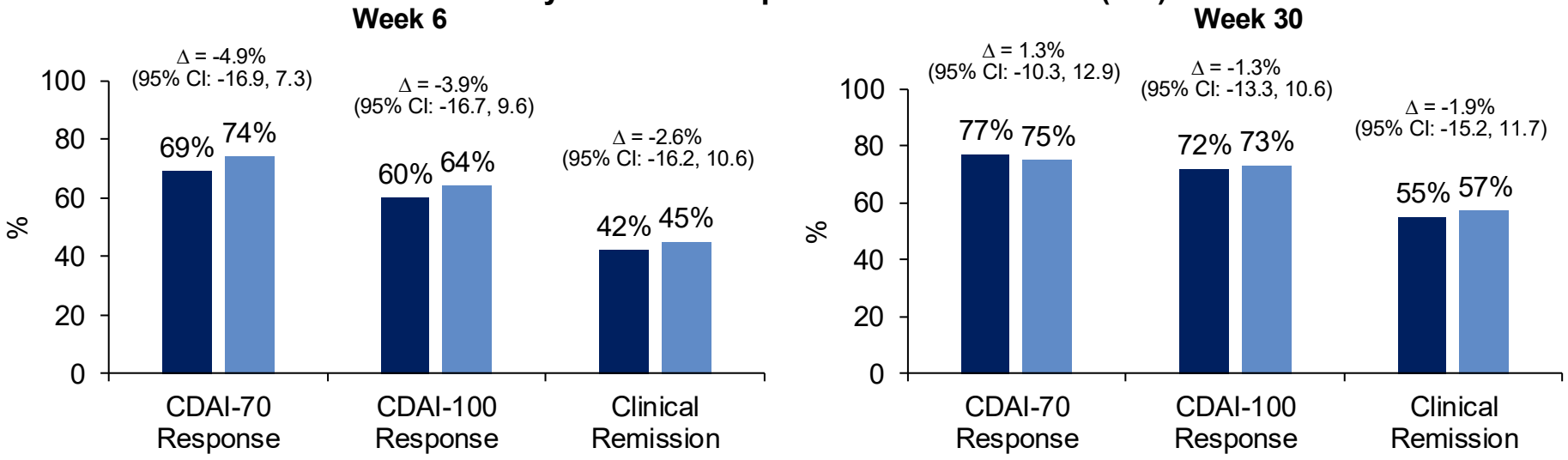
# CT-P13 in Biologic-Naive Patients with Active CD: Randomized, Double-Blind, Phase 3 Non-Inferiority Study

**Efficacy: Clinical Response and Remission (ITT)**




- No difference in CRP at week 6 and later
- No difference in AEs
- No difference in PK/PD findings

**CRP = c-reactive protein; AE = adverse event; PK = pharmacokinetics; PD = pharmacodynamics; ITT = intention to treat; CDAI = Crohn's Disease Activity Index.**

**Ye BD, et al. *Lancet*. 2019;393(10182):1699-1707.**

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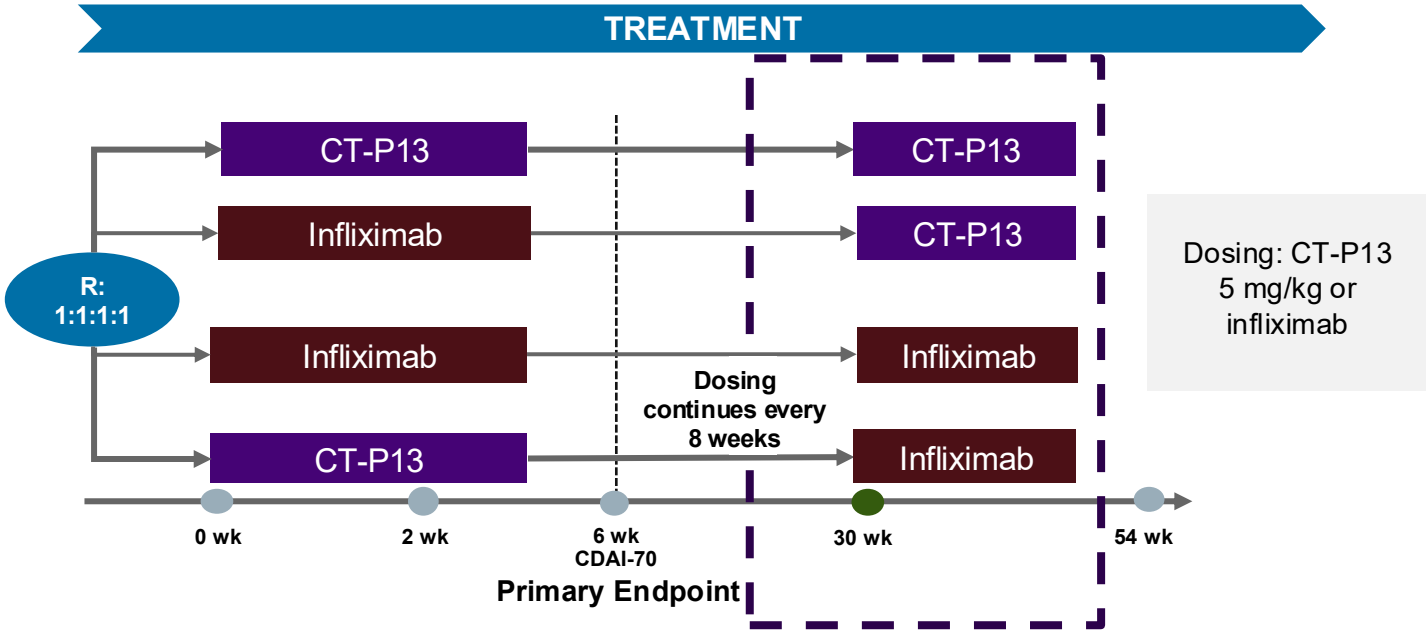
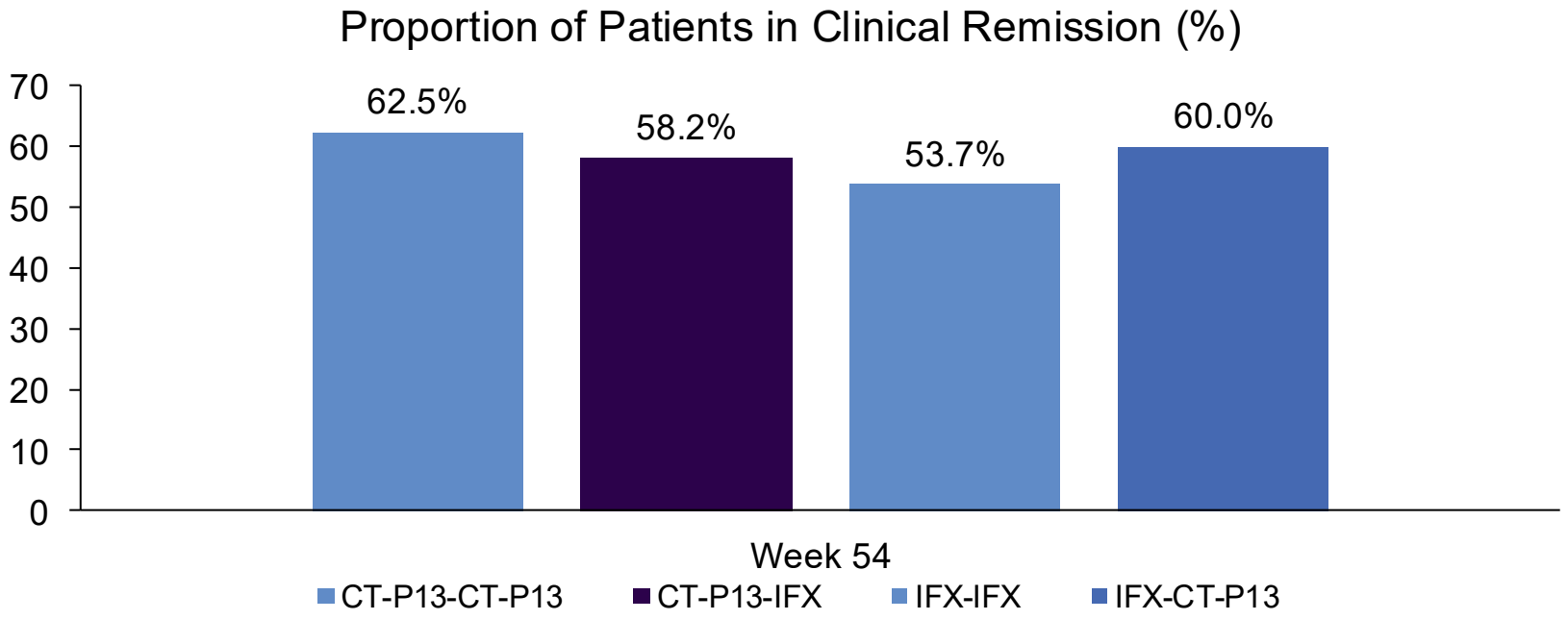
# Infliximab and CT-P13 in Biologic-Naive Patients with Active CD: **Switch at Week 30**




Ye BD, et al. *Lancet*. 2019;393(10182):1699-1707.

# Infliximab and CT-P13 in Biologic-Naive Patients with Active CD: **Clinical Remission at 54 Weeks**




**After switching, no new or unexpected treatment-emergent serious AEs were identified**

**IFX = infliximab.**

**Ye BD, et al. *Lancet*. 2019;393(10182):1699-1707.**

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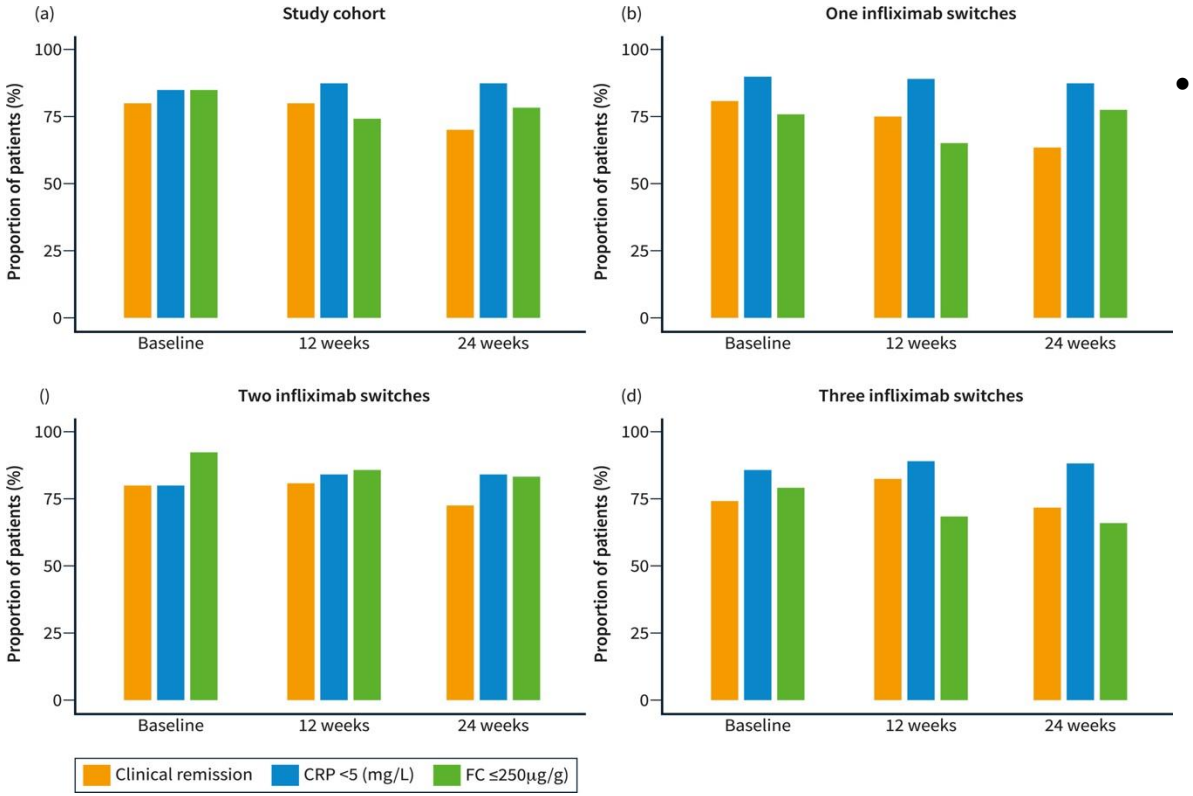
# What's the Evidence for Multiple Switches?




- 297 pts (196 CD, 101 UC) switched to CT-P13
  - 3rd switch – 22.5%
  - 2nd switch – 46.5%
  - 1st switch – 31.0%

**Gros B, et al. *United European Gastroenterol J.* 2023;11(2):179-188.**

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# Key Learning Points

- High quality evidence exists that switching from a reference product to a biosimilar is **safe without loss of efficacy**
  - Also appears that multiple switches are well tolerated

- Important to develop a dialogue or script for discussions with patients
  - Biosimilars are not generics
  - Reference products are biosimilars of themselves
  - Educate colleagues, infusion nurses, and office staff
  - **Emphasize delays in transition can result in relapses of disease**
  - Remind patients to sign up for co-pay programs

- Appropriate and timely counseling can **prevent the nocebo effect**

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**Christina Ha, MD, FACG**

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# Case 2

- 45-year-old male with Crohn's disease is recommended to start advanced therapy. Following guideline-based treatment selection and shared decision-making, adalimumab is recommended.  However, his insurance would prefer to start the patient on an adalimumab biosimilar

# Discussion

- Is a biosimilar appropriate in this case scenario?
- What strategies can we utilize to educate the patient and care team about biosimilars?
- What is the current FDA guidance regarding interchangeability for biosimilars?

# Positioning Biosimilars within IBD Treatment Paradigms

- Same positioning as reference products for treatment-naive patients
- If clinically significant antibodies present to reference product do not use the biosimilar
- If primary non-response to reference product, then would not use the biosimilar
- If drug holiday (+ history of response), could use biosimilar in re-challenge
- Combination therapy with thiopurine or MTX still recommended in the right clinical context

**MTX = methotrexate.**

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# 2025 FDA Guidance on Biosimilars Development → Comparative Analytical vs Comparative Effectiveness Studies

**If comparative analytical data ***PLUS*** demonstration of similar pharmacokinetics and immunogenicity in human clinical studies → comparative effectiveness studies in humans may not be necessary**

- "Eliminating unnecessary clinical trials – using improved analytical testing methods instead of requiring expensive human studies when the science shows they're not needed."
- "Facilitating pharmacy-level substitution – removing barriers by advancing interchangeability so pharmacists can substitute lower-cost biosimilars, just like they do with generic drugs."
- "Reducing red tape to lower the barriers to market entry – providing clearer guidance and more efficient processes to speed up approvals and reduce development uncertainty."

**FDA. Accessed Nov 17, 2025. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-demonstrating-interchangeability-reference-product-update. FDA Accessed Nov 17, 2025. https://www.fda.gov/news-events/press-announcements/fda-moves-accelerate-biosimilar-development-and-lower-drug-costs**

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# Key Terms Associated with Prescribing Biosimilars

- **Medical switching** → Medication exchanged for another at a prescriber's discretion to optimize a patient's benefit
  - eg. → changing from citrate containing adalimumab to citrate free adalimumab
  - eg. → changing from certolizumab pegol self-injectable syringe to certolizumab lyophilized injection due to latex allergy

- **Non-medical switching** → clinically stable patient, on effective and well tolerated biologic agent is switched to another therapeutic alternative
  - Typically, under directive of healthcare plans or system
  - Biosimilar switches are typically non-medical switches

Mysler E, et al. *Drugs*. 2021;81(16):1859-1879.

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# Key Terms Associated with Prescribing Biosimilars

| | |
|---|---|
|  **Transition (Switching)** | • **Physician prescribes a biosimilar** in place of the US FDA-approved reference biological product |
|  **Interchangeability** | • **Same clinical result can be expected**<br>• Risks of use of the biosimilar are not greater<br>• Interchangeability is determined by **regulatory/legal authorities** based on totality of evidence presented |
|  **Automatic Substitution** | • **Pharmacist dispenses interchangeable biosimilar** in place of reference biological product, unless prohibited by the prescriber |

FDA. Accessed Nov 17, 2025. https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/biosimilars. American Pharmacists Association.Accessed Nov 17, 2025. https://www.pharmacist.com/Advocacy/Issues/Biosimilars.

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# FDA-Approved Biosimilars

| Anti-TNF | | Anti-IL 12/23 |
|---|---|---|
| **Infliximab** | **Adalimumab** | **Ustekinumab** |
| *Infliximab (unbranded)*<br>Infliximab-dyyb (Inflectra®)<br>Infliximab-abda (Renflexis®)<br>Infliximab-axxq (Avsola®)<br>Infliximab-qbtx (Ixifi®)<br>Infliximab-dyyb (Zymfentra®) (SQ) | Adalimumab-atto (Amjevita®)<br>Adalimumab-bwwd (Hadlima®)*<br>Adalimumab-adbm (Cyltezo®)*<br>Adalimumab-aqvh (Yusimry®)<br>Adalimumab-fkjp (Hulio®)*<br>Adalimumab-adaz (Hyrimoz®)*<br>Adalimumab-afzb (Abrilada®)*<br>Adalimumab-aacf (Idacio®)<br>Adalimumab-aaty (Yuflyma®)*<br>Adalimumab-ryvk (Simlandi®)* | Ustekinumab-auub (Wezlana®)*<br>Ustekinumab-aekn (Selarsdi®)*<br>Ustekinumab-ttwe (Pyzchiva®)*<br>Ustekinumab-aauz (Otulfi®)*<br>Ustekinumab-srlf (Imuldosa®)<br>Ustekinumab-hmny (Starjemza®)*<br>Ustekinumab-kfce (Yesintek®)*<br>Ustekinumab-stba (Steqeyma®)* |

***Indicates interchangeable status. Vedolizumab biosimilar anticipated timeline 2028-32 (Phase 3 studies underway); golimumab biosimilar anticipated 2025-27.**

**TNF = tumor necrosis factor; IL = interleukin; SQ = subcutaneous.**

**FDA. Accessed Nov 17, 2025. https://www.fda.gov/drugs/biosimilars/biosimilar-product-information.**

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# 2024 FDA Draft Guidance on Biosimilar Interchangeability

If **comparative analytical data plus clinical data** demonstrate the standards per the FDA → **"Interchangeability is *NOT* greater risk than continuation of the reference product", then an additional switch study is *not* required**

- Switch studies between reference and biosimilars consistently show no meaningful differences in key outcomes of effectiveness, safety and pharmacokinetics
- Current analytical technologies can characterize the biologic proteins and model functional effects with high degrees of sensitivity and specificity using ***in vitro assays***

**FDA. Accessed Nov 17, 2025. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-demonstrating-interchangeability-reference-product-update.**

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# 2025 Centers for Medicare Services Update for Biosimilars

- All biosimilars may be substituted as formulary maintenance changes without prior approval
- New interchangeable biological products may be immediately substituted

- Goal: To provide access to more affordable advanced therapy options earlier
- Note: Part D automatic substitutions may occur immediately → patients may be notified after the change is made

**Centers for Medicare Services. Accessed Nov 17, 2025. https://www.cms.gov/newsroom/fact-sheets/contract-year-2025-medicare-advantage-and-part-d-final-rule-cms-4205-f**

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# Addressing Clinician Knowledge Gaps about Biosimilars

- Addressing these knowledge gaps requires
  - Continuing medical education programs
  - Providing clinicians with updated information on biosimilar development, regulatory frameworks, and clinical evidence
  - Collaboration with pharmacists
  - Utilizing the expertise of pharmacists who are often deeply knowledgeable about biosimilars and can provide guidance on appropriate selection and switching strategies
  - Access to reliable data sources
  - Encouraging clinicians to consult credible scientific literature and databases to stay informed about the latest research on biosimilars

**Gibofsky A, et al. *Am J Manag Care*. 2022;28(12 Suppl):S227-S233.**

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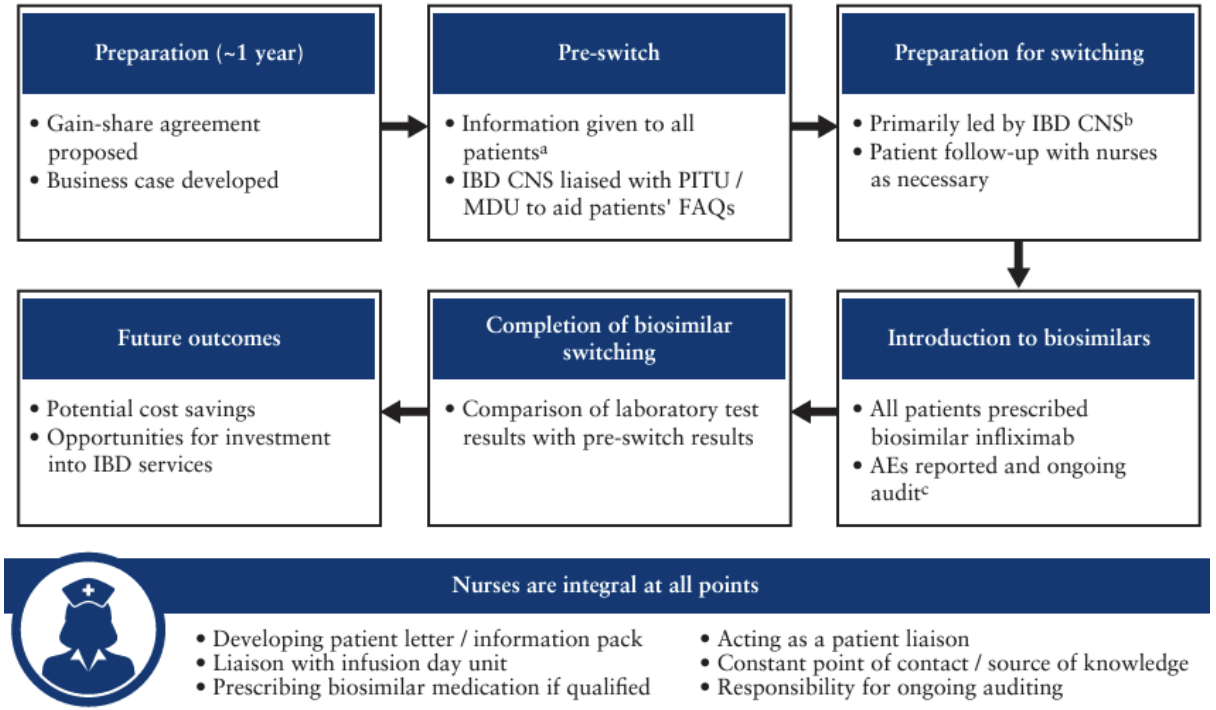
# Allied Health Teams Are Key When Starting or Transitioning Patients with IBD to Biosimilars

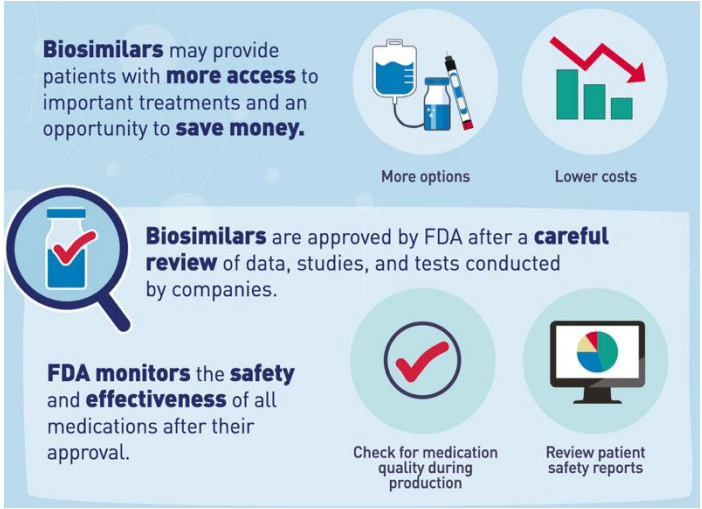



**CNS = clinical nurse specialists; MDU = medical day unit; PITU = planned investigation treatment unit.**
**Armuzzi A, et al. *J Crohns Colitis*. 2019;13(2):259-266.**

# How to Approach Biosimilars with Patients

- **Education**
  - Use the active ingredient name, not the brand name
  - Define a biosimilar, clarify the reason for biosimilar use, review practical implications
  - Resources
    - www.FDA.gov/biosimilars
    - www.crohnscolitisfoundation.org

- **Reassurance**
  - Safe, effective
  - No change in treatment targets
  - Same drug assays




FDA. Accessed Nov 17, 2025. https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/biosimilars.

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# From Policy to Practice:

## Navigating the Evolving Biosimilar Landscape

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*University of Chicago Medicine Inflammatory Bowel Disease Center*

# Case 3

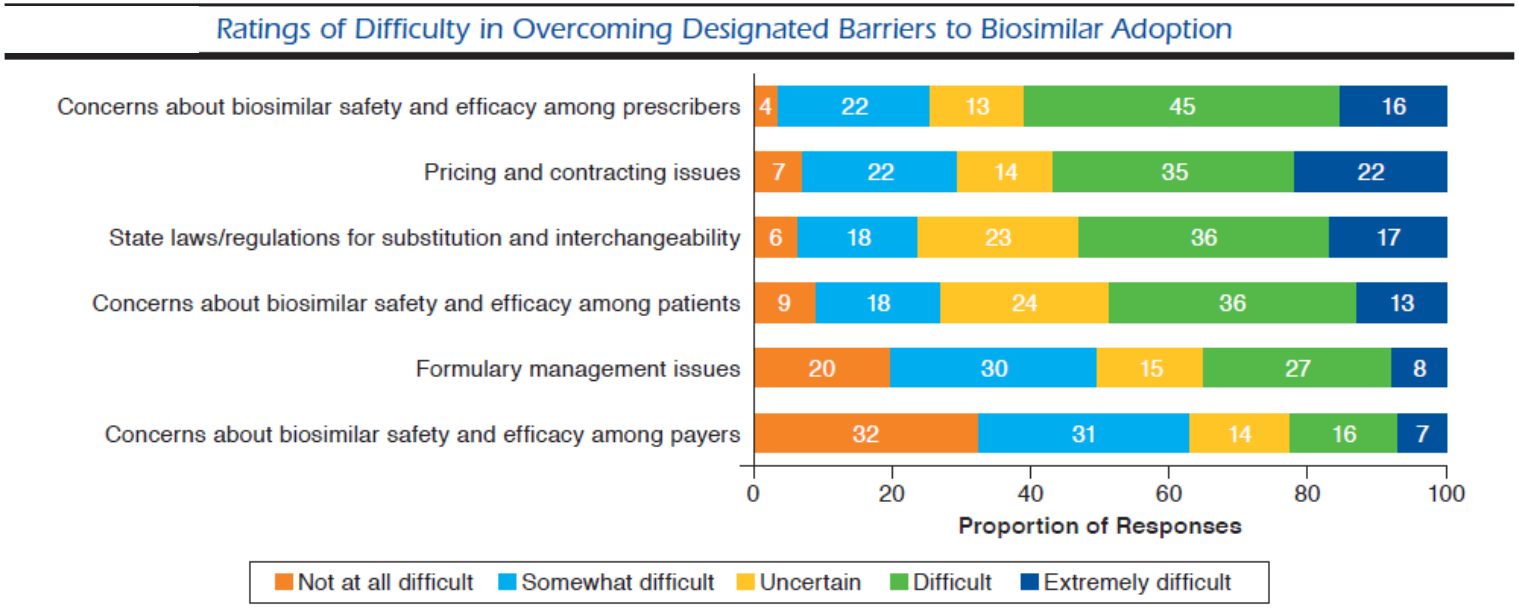
- A 68-year-old Medicare beneficiary with well-controlled CD on originator adalimumab recently received notice of an upcoming switch to a biosimilar product mandated by her plan

- Current therapy: Adalimumab 40 mg every 7 days
- Labs: CRP <5 mg/dL, FCP 76 mcg/g
- Last colonoscopy 3 months ago: Endoscopic remission

- The pharmacy must navigate this transition carefully, addressing any patient concerns, coordinating with the prescriber, and ensuring timely access to the new therapy

AIBD

# Barriers to Adopting Biosimilars: Survey of Managed Care and Specialty Pharmacy Professionals




Greene L, et al. *J Manag Care Spec Pharm*. 2019;25(8):904-912.

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# Communication

# Medicare: Maintenance Changes

- Medicare Part D plans can switch patients from a reference biologic to a biosimilar
- Beneficiaries should be notified 30 day prior to switch
- Can affect all patients (new, continuation of therapy)

**Centers for Medicare and Medicaid Services. Accessed Nov 17, 2025. https://www.cms.gov/newsroom/fact-sheets/contract-year-2025-medicare-advantage-and-part-d-final-rule-cms-4205-f.**

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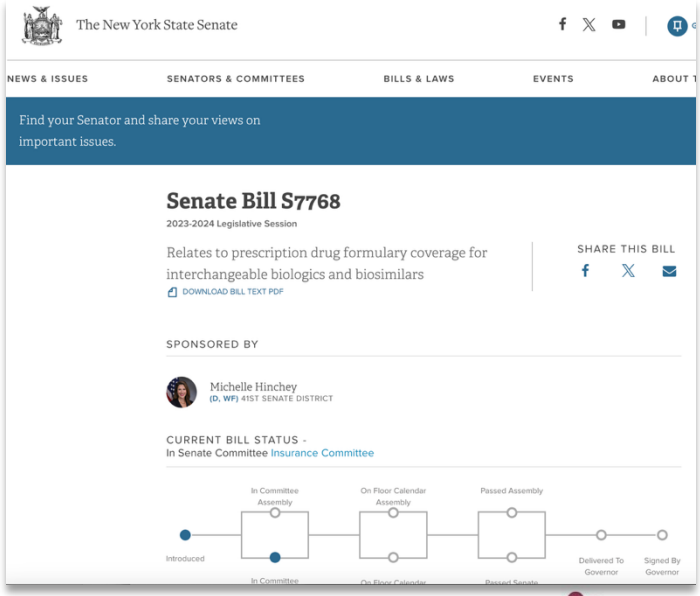
# Resources to Stay Apprised of Healthcare Coverage Changes that Impact Patient Access

- Manufacturers' websites, sales reps, and medical science liaisons
- Patient organization websites (crohnscolitisfoundation.org, for example)
- State government websites
- FDA.gov




New York State Senate. Accessed Nov 17, 2025. https://www.nysenate.gov/legislation/bills/2023/S7768.

# Key Learning Points

- Increasing number of biosimilars are part of the IBD treatment landscape
- Biosimilars have yielded substantial costs savings to the healthcare system (about $2.2 billion for patients with IBD)
- Updated process for biosimilar approval may allow for earlier market entry
- Data consistently demonstrates similar effectiveness, pharmacokinetics, immunogenicity, and safety
- Without patient education by knowledgeable clinicians, biosimilar switching may lead to an undesirable nocebo effect, and poor patient acceptance
- Best practices in switching require clinicians to be knowledgeable about the science behind, and clinical evidence for, the safety and efficacy of biosimilars, as well as biosimilar regulations and policies

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