IBD *and Biosimilars*

What Health Care Providers Need to Know

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aga American Gastroenterological Association

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Learning Objectives

Section 3: Biosimilars in Clinical Practice

- Review cases involving all the scenarios for/against biosimilar use including the “unknowns”
- Discuss reimbursement considerations

Biosimilars in Clinical Practice

Section 3

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Key terms associated with prescribing biosimilars

Transition (Switching)

- **Physician prescribes a biosimilar** in place of the US FDA-approved originator biological product[1]

Interchangeability

- The **same clinical result can be expected**, and the risks of use of the biosimilar are not greater[2]
- Interchangeability is determined by **regulatory/legal authorities** based on the totality of the evidence presented[2]

Automatic Substitution

- **Pharmacist dispenses interchangeable biosimilar** in place of originator biological product, unless prohibited by the prescriber[3]

1. US FDA. Information for consumers (biosimilars). Accessed April 2015. Accessed April 2015. **2.** US FDA. Information for industry (biosimilars). Accessed April 2015. **3.** NCSL. State laws and legislation related to biologic medications and substitution of biosimilars. Accessed April 2015.

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Status of biosimilars for IBD in the United States

Adalimumab biosimilars

- Abrilada (adalimumab-afzb)
- Cyltezo (BI 695501) (adalimumab-adbm)
- Hadlima (SB5) (adalimumab-bwwd)
- Amgevita (adalimumab-atto)
- Hyrimoz (adalimumab-adaz)

Infliximab biosimilars

- Ixifi (infliximab-qbtx)
- Renflexis (infliximab-abda)
- Inflectra (CT-P13) (infliximab-dyyb)

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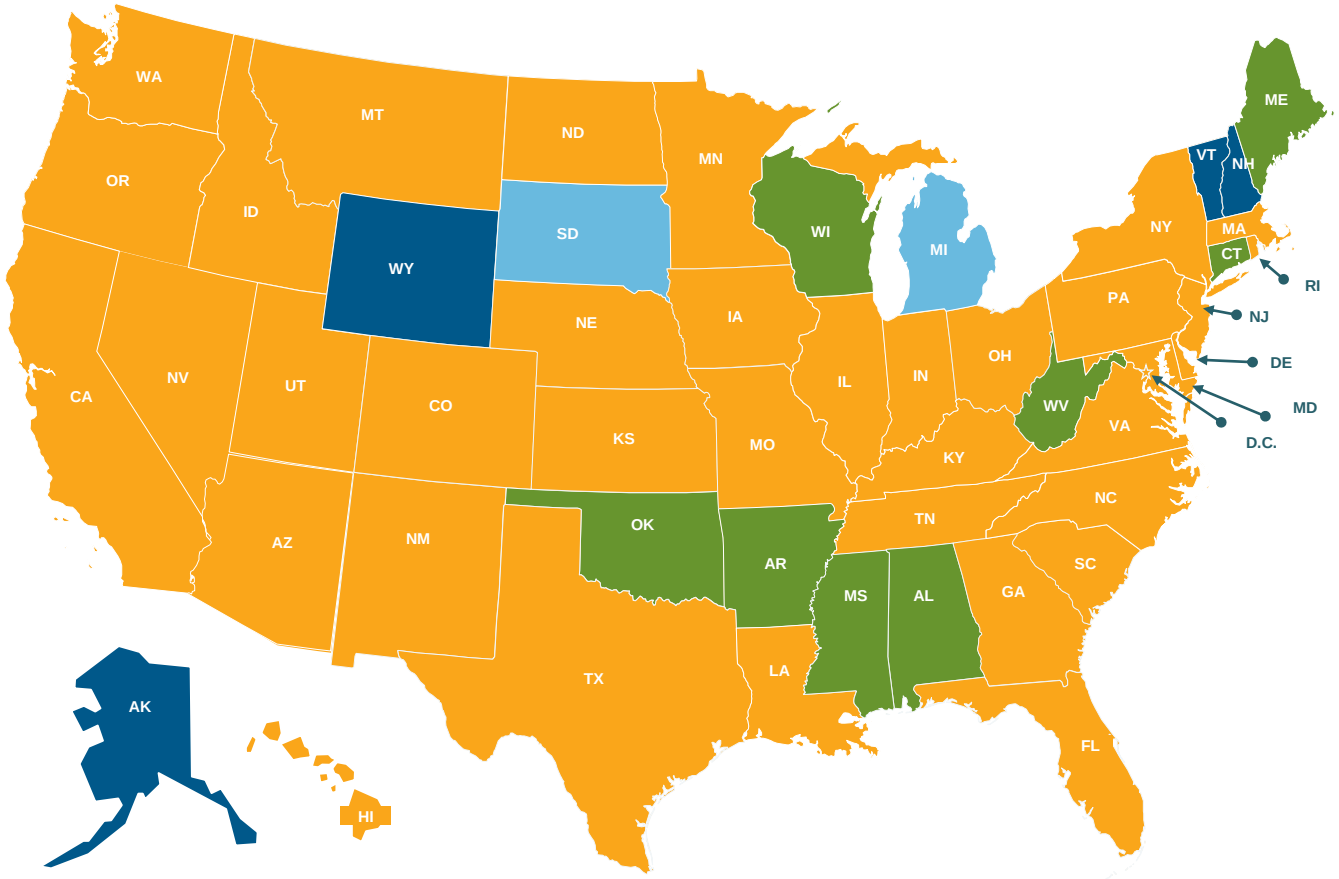
Interchangeability varies by state



- FDA has not granted interchangeability of any biologic for IBD
- Issue has been legislated in the U.S. on a state-by-state basis
- De facto interchangeability will be forced by 3rd party payers

Enacted Legislation (38)
Enacted Legislation in 2018 (2)
Active Legislation (4)
No Legislative Activity (8)

*Note: Map includes all states in which biosimilar switching legislation has been enacted or introduced, as of April 3, 2018. Source: Avalere State Reform 360.

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Avoiding the nocebo effect when switching

- Nocebo effect: AEs produced by negative expectations of a drug[a,b]
- Not a direct result of specific pharmacologic action of a drug[c]
- Can occur with nonplacebo drugs[b]
- Low patient expectations of treatment or reluctance to switch from their current therapy can negatively affect clinical outcomes

Screening and education can mitigate potential "nocebo effects" and ensure patient comfort with switch in therapy.

a. Kristensen LE et al. BioDrugs, 2018;32:397-404; b. Colloca L et al. JAMA, 2012;307:567-568; c. Barsky AJ,et al. JAMA, 2002;287:622-627.

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Possible clinical scenarios for biosimilars use

New Start	• Prescriber choice of reference product or biosimilar
Primary Responder	• Prescriber elects to switch to biosimilar • Prescriber elects to switch to another biologic
Stabilized Responder	• Prescriber elects to maintain original biologic • Prescriber elects to switch to biosimilar (Non-medical SWITCH)
Loss of Response	• If attributed to high titer of ADA, switch to biosimilar is not supported • Prescriber elects to switch to another therapy

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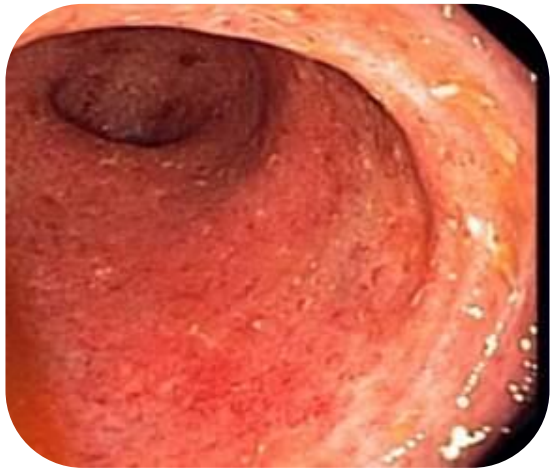
Positioning biosimilars within IBD treatment paradigms:

- Same positioning as reference products for infliximab or adalimumab naive patients
- If clinically significant antibodies present to adalimumab, infliximab do not use the biosimilar
- If primary non-response to adalimumab, infliximab, 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

Case 1: (New Start) Moderate to severe disease, what should we use?

- 29-year-old woman diagnosed with extensive ulcerative colitis 4 months ago presents for a second opinion
- Prior non-responder to mesalamines
- Steroid-dependent with increased symptoms upon decreasing prednisone < 20mg
- Brother has UC, in sustained remission with Remicade
- Anti-TNF therapy is recommended with infliximab but her insurance approved infliximab-dyyb



Question: How would you talk to this patient about therapeutic options?

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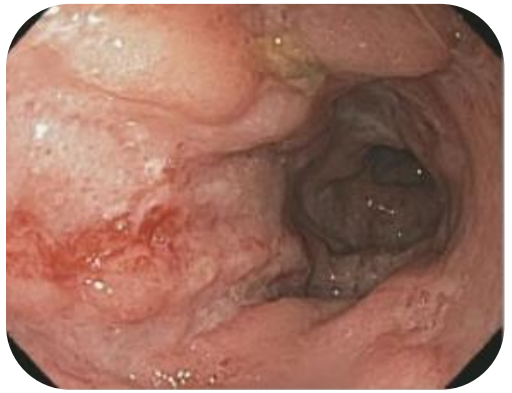
Case 2: Primary non-responder

- 20-year-old male with moderate-severe Crohn's disease
- Failed steroids + azathioprine
- Treated with infliximab reference product with 5mg/kg at weeks 0,2,6,14 but remains with CDAI 350, c-reactive protein 15, Fecal calprotectin 800
- Infliximab level 10 with no antibodies



Question: Should patient be switched to biosimilar?

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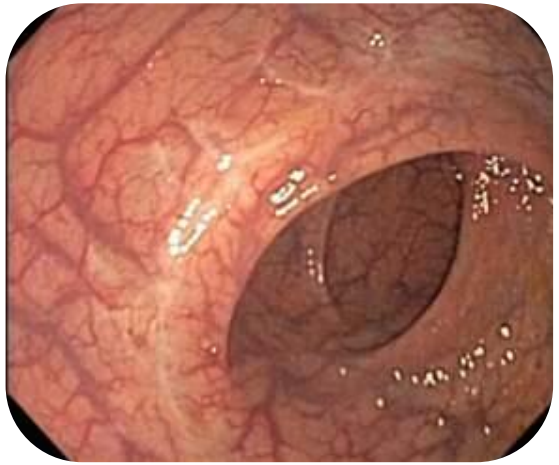
Case 3: (Stabilized responder, non-medical switch) Moderate to severe disease in sustained remission on Infliximab RP

- 43-year-old woman diagnosed with extensive ulcerative colitis 5 years ago
- Previously with steroid-dependent disease
- Treated with infliximab RP induction then maintenance, now in remission for the past 4 years on infliximab RP 5mg/kg every 8 weeks
- No history of infusion reactions
- Therapeutic levels, no antibodies
- Just changed jobs and was told by new insurer she needed to switch to infliximab-abda



Question: What does current research data say about switching to biosimilar infliximab-abda over continuing with infliximab RP in this scenario?

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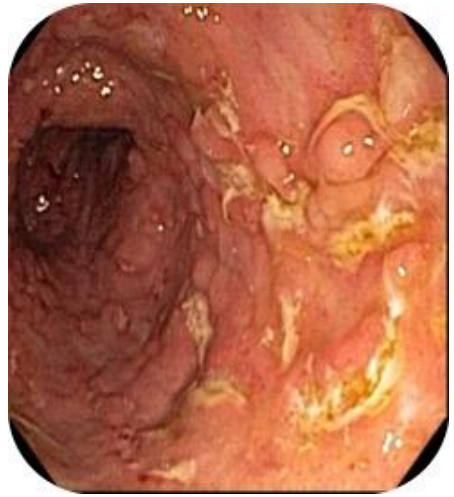
Case 4: Loss of response

- 47-year-old male with 10-year history of UC
- Long-term maintenance with mesalamine but flared 1 year ago. Treatment escalated to adalimumab.
- Induced and maintained in remission for 9 months
- Recent flare with confirmed moderate-severe disease despite dose escalation to 40mg weekly
- Adalimumab levels 0
- Anti-drug antibodies 800



Question: Should patient be switched to biosimilar?

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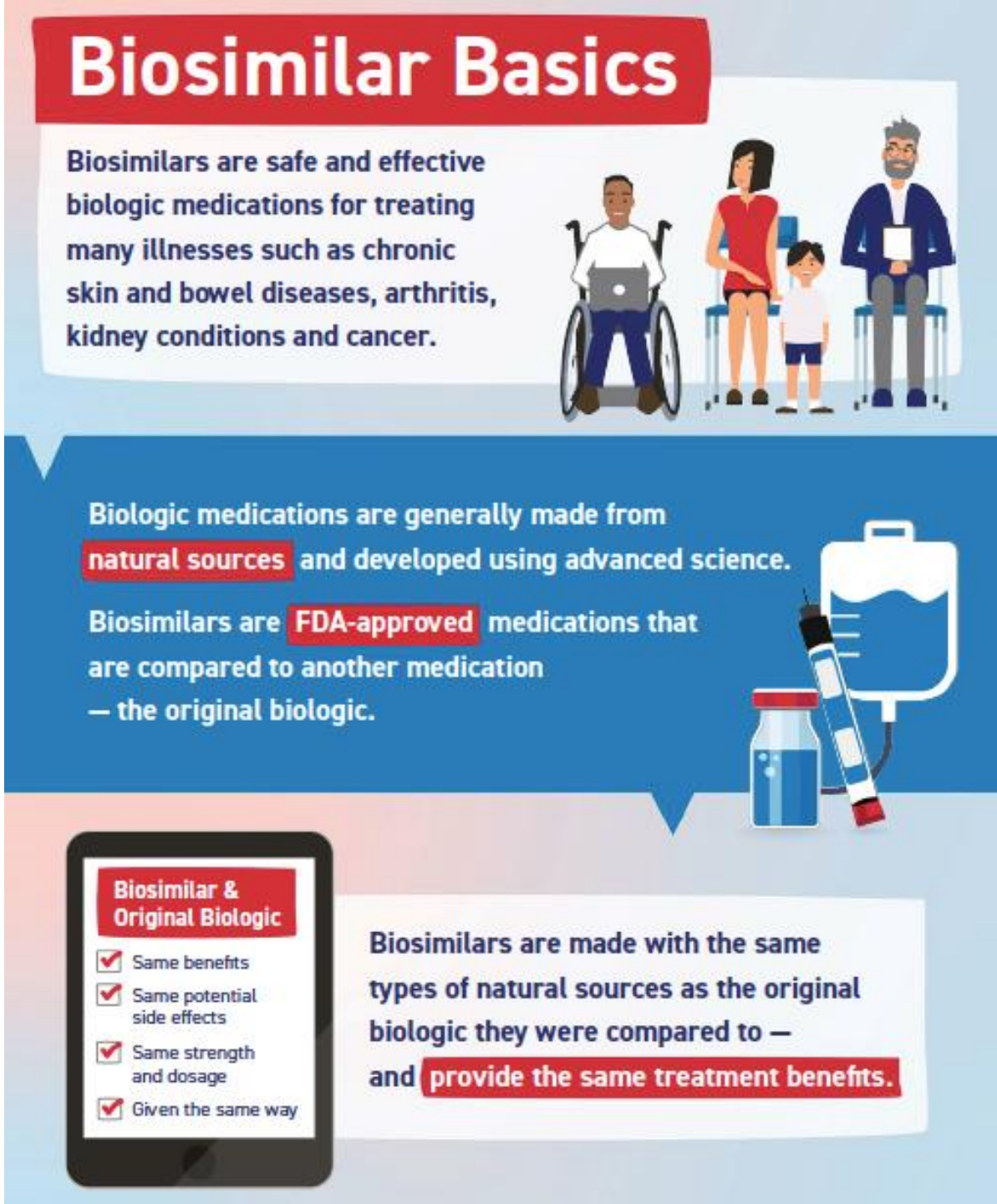
How to approach biosimilars with patients

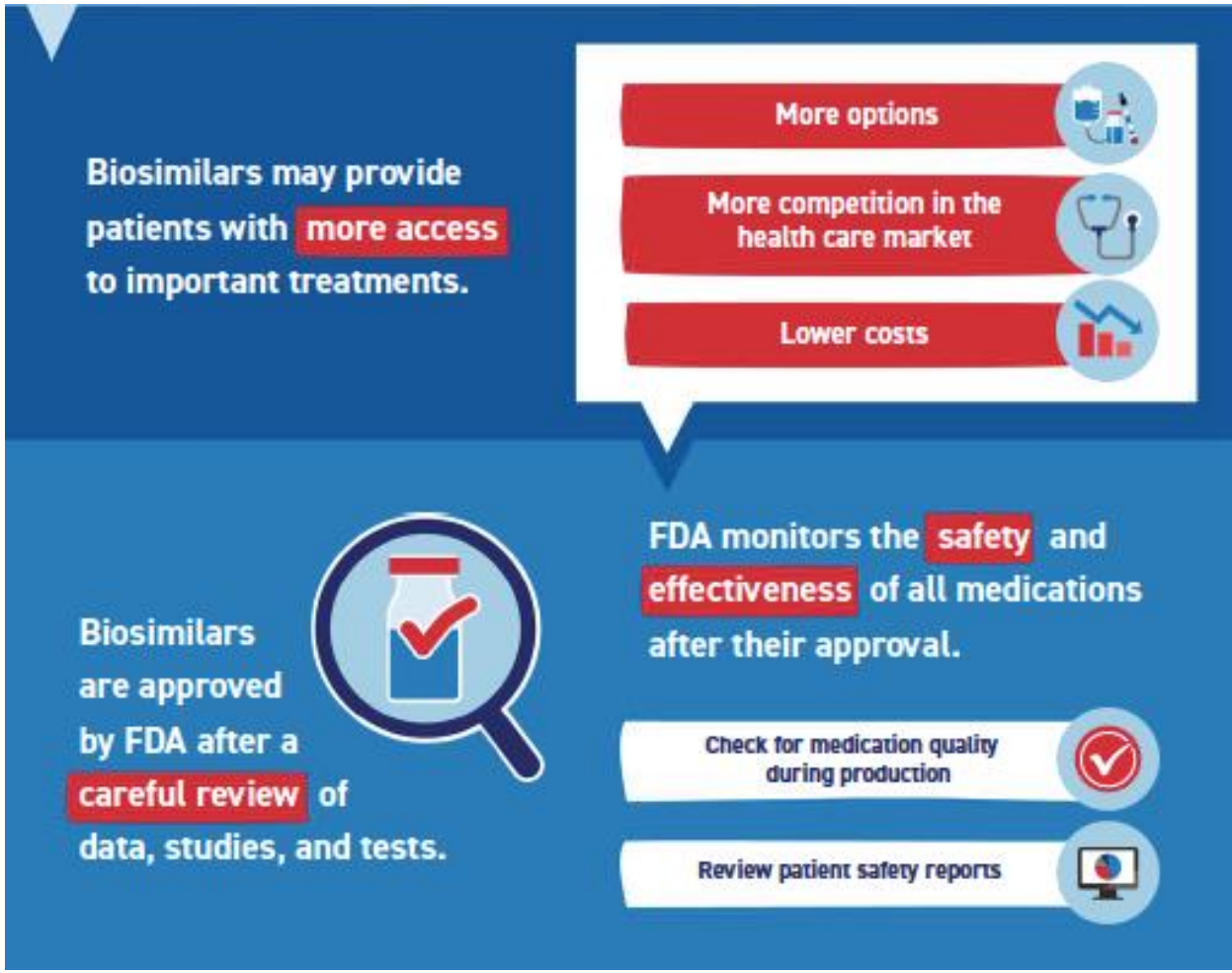
- Inform early about biosimilar use
  - **ESPECIALLY IF SWITCHING**
- Define biosimilars and experience with the agents
- Emphasize biosimilars are not a new mechanism of action
- Same indications and dosing as RP agents (infliximab, adalimumab)

https://www.fda.gov/media/130918/download



How to approach biosimilars with patients

- Not compromising quality of care for costs of care
- Same monitoring strategy applies:
  - “Treat to target”
  - Therapeutic drug monitoring
  - Adverse events



https://www.fda.gov/media/130918/download

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Reimbursement and Economic Considerations for Biosimilars

Who will Benefit from ~20-30% Cost Savings

Will this be a cost savings or cost shifting?

- If total biologic market continues to expand there will be no overall cost-savings on national basis

If cost per patient falls who will benefit?

- Third party payers (including government)
- Not likely individual patients

Individual patient costs may increase for originator products depending on insurance plan

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Outstanding questions and concerns

- Pathway to biosimilars in U.S. remains a “work in progress”
  - Interchangeability is most critical issue for patients and physicians (bears careful monitoring)
  - More IBD-centric biosimilar data should increase acceptance of biosimilar use in clinical practice
  - No published data on mucosal healing
- Continued reliance primarily on extrapolations rather than direct IBD comparisons
- Unclear if repeated switching between biosimilars will impact response/immunogenicity
- Pending data on mucosal healing
- Unclear how managed care and other insurers will determine substitution/interchangeability (No biosimilar in the U.S. yet has interchangeable designation for patients with IBD)

Managing patients using biosimilars: Clinical considerations

- Help patients understand the difference between biologics to biosimilars.
- Help patients feel comfortable using or switching to biosimilars.
- Understand that living with chronic illness is expensive, so cost-savings may matter to many patients.
- Show confidence about treatment choices.
- Remember the nocebo effect (patient doing fine on biologic, so any change is going to be attributed to biosimilar).
- Know patient PK status before making any non-medical changes.
- Lack of data regarding risks of non-medical switching across multiple biosimilars.

Resources

For providers:

- https://www.gastro.org/practice-guidance/practice-updates/biosimilars
- https://www.crohnscolitisfoundation.org/science-and-professionals/education-resources/whitepapers/biosimilars
- https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/biosimilars
- https://www.fda.gov/drugs/biosimilars/health-care-provider-materials

For patients:

- http://www.aga-resources.com/biologics/guide/pubData/mobile/index.htm
- https://www.fda.gov/drugs/biosimilars/patient-materials
- https://www.crohnscolitisfoundation.org/what-is-ibd/medication/biosimilars

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