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Brazilian Expert Consensus on the Use of Biosimilars in Inflammatory Bowel Disease

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1. Introduction

The advent of biologic therapies has significantly improved outcomes for patients with inflammatory bowel diseases (IBD). Beyond their clinical benefits, biologics have the potential to reduce the overall economic burden of IBD by decreasing indirect costs, such as hospitalizations, surgeries, complications, and lost work productivity. However, the high cost of originator biologics limits access and compromises the sustainability of healthcare systems. Biosimilars—biologic products that are highly similar to their reference agents in terms of quality, efficacy, and safety—represent an essential strategy for reducing treatment costs, increasing accessibility, and promoting the long-term sustainability of IBD care.

Accumulating evidence from systematic reviews and real-world studies demonstrates comparable efficacy, safety, and immunogenicity of anti-TNF biosimilars in both bio-naïve patients and after switching from the originator biologic. The European Crohn's and Colitis Organization (ECCO) endorsed the use of biosimilars in IBD management in its 2017 position statement, emphasizing their role in improving cost-effectiveness without compromising clinical outcomes.

Nevertheless, essential uncertainties remain regarding issues such as multiple switches between biosimilars, the potential impact on immunogenicity, nocebo effect, and the availability of data in specific subgroups, including pediatric patients and mucosal healing outcomes. In this context, expert consensus documents play a crucial role in guiding clinical practice by synthesizing the best available evidence and addressing knowledge gaps. The current consensus aims to provide clear, evidence-based answers to the most pertinent questions surrounding the use of biosimilars in inflammatory bowel disease, thereby supporting clinicians in informed decision-making and promoting the safe and effective integration of these agents into clinical care.

2. Method

The *GEDIIB (Brazilian Crohn's and Colitis Organization) Guidelines on the Use of Biosimilars in Inflammatory Bowel Disease (IBD)* relied on a formal and explicit **systematic review** organized around eight clinical questions using the PICO format [Population, Intervention, Comparator, Outcomes].

The recommendations of this consensus comprehensively address the main issues and challenges related to the use of biosimilars in the treatment of Inflammatory Bowel Diseases (IBD), focusing on clinical, therapeutic, and cost-related aspects. To formulate these recommendations, PICO (Patient, Intervention, Comparison, and Outcome) structured questions were employed, a widely recognized method for developing robust scientific evidence that allows for a systematic analysis of best practices in the use of biosimilars. Each PICO question was carefully discussed by the experts, considering the available clinical evidence, the safety, and efficacy profiles of biosimilars. The results are summarized in Table 1. Additionally, for each of these questions, levels of evidence were assigned based on the quality of the reviewed studies, and practice points were provided to guide the implementation of these recommendations in clinical practice.

Following the systematic review, the Delphi process was employed to construct consensus, a structured and iterative approach that gathered expert judgments through controlled feedback across two rounds to refine opinions. The statement was considered consensual when the voting reached an 85% or higher level of agreement.

The recommendations presented here aim to provide a solid foundation for informed decision-making by healthcare professionals, promoting the rational and safe use of biosimilars in IBD patients. Confidence in the use of biosimilars has grown as more scientific data accumulates, and this consensus seeks to consolidate these advancements, addressing the primary concerns of clinicians and specialists in the field.

Table 1: Patient, intervention, comparison, outcome questions, recommendations and level of evidence:

Questions	Statements	Agreement
1. In patients with IBD, what is the effect on remission of treatment with biosimilar biologics compared to the originator biologics?	Biosimilars are effective during maintenance and do not result in increased rates of loss of response or discontinuation. Low quality of evidence.	100%

2. In patients with IBD, what is the effect on maintenance or discontinuation of treatment with biosimilar biologicals compared to the originating biologicals?	Infliximab and adalimumab biosimilars are effective during maintenance and do not result in increased rates of loss of response or discontinuation. Very low quality of evidence.	100%
3. In patients with IBD, what are the adverse effects of treatment with biosimilar biologics compared to the originator biologics?	There is no difference in adverse effects between therapy with biosimilar and originator biologics in patients with IBD. Low quality of evidence.	91%
4. In patients with IBD and undergoing treatment with biosimilar biologicals, what is the role of the serum level of biological and anti-drug antibodies?	In patients with IBD treated with biosimilar anti-TNF biologics, measuring serum levels and anti-drug antibodies can support decisions regarding dose escalation or reduction, or even change the drug treatment or regimen. Low quality of evidence.	100%
5. In patients with IBD, what is the effect on maintenance or discontinuation of treatment with biosimilar biologicals compared to the original biologicals after multiple switches?	The number of switches was not independently associated with persistence in the biological treatment, nor was it related to clinical remission or loss of response. Therefore, although the evidence is limited, multiple switches cannot be stated to be ineffective or unsafe. Due to the evidence's low quality, it is not possible to recommend for or against multiple switches. Low quality of evidence.	95.6%
6. In pediatric patients with IBD, what is the efficacy and safety of treatment with biosimilar biologics compared to the originator biologics?	In pediatric patients with IBD, biosimilar biologics demonstrate efficacy and safety comparable to those of originator biologics; however, current evidence is insufficient to quantify these outcomes precisely. Very low quality of evidence	100%
7. In patients with IBD, what is the impact on the cost of treatment with biosimilar biologics compared to the originator biologics?	In patients with IBD, the use of biosimilar biologics for maintenance therapy is associated with lower treatment costs compared with originator biologics. Low quality of evidence.	91%

8. In patients with IBD, what is the effect on mucosal healing of treatment with biosimilar biologics compared to the originator biologics?	In patients with IBD, treatment with biosimilar biologics results in mucosal healing rates comparable to those achieved with originator biologics. No significant differences are observed between switch and non-switch groups. Low quality of evidence.	100%

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