**ARTYKUŁ POGLĄDOWY / REVIEW PAPER**
Otrzymano/Submitted: 11.01.2026 • Zaakceptowano/Accepted: 07.05.2026



# *Biological treatment for inflammatory bowel disease – review of current knowledge*

**Grzegorz Zaborowski[1], Jacek Wysoczański[2], Antoni Anczyk[1], Karolina Handzel[1], Dominik Kret[3], Wiktoria Szlachta[3], Miłosz Tworek[4], Filip Basta[5]**

[1] St. Barbara Hospital, Regional Specialist Hospital No. 5, Sosnowiec
[2] St. John Paul II Western Specialist Hospital, Grodzisk Mazowiecki
[3] University Clinical Center of the Silesian Medical University in Katowice
[4] University Hospital in Krakow, Krakow
[5] Gabriel Narutowicz Municipal Specialist Hospital, Krakow

## Abstract

Inflammatory bowel diseases (IBD) represent a significant challenge for modern medicine. Despite the wide availability of numerous conventional therapies, remission cannot be achieved in a substantial proportion of patients, particularly those with severe forms of IBD. The still incompletely understood etiology of these disorders and the need for lifelong treatment underscore the necessity for intensive research into novel therapeutic strategies. A breakthrough in treatment has been achieved with the introduction of monoclonal antibodies, whose more precise mechanisms of action have significantly improved patients' quality of life. Given the currently crucial role of modern therapies in IBD, we have presented and discussed current knowledge on the biological treatment of these diseases. We hope that, in the era of globally increasing incidence, personalized selection of modern therapies and further research will enable patients to achieve longer periods of life free from disease symptoms. *(Farm Współ 2026; 19: 3-12) doi: 10.53139/FW.20261910*

*Keywords: inflammatory bowel disease, Crohn's disease, ulcerative colitis, biological treatment, monoclonal antibodies*

## Introduction

Inflammatory bowel diseases (IBD) comprise a group of disorders represented by Crohn's disease (CD) and ulcerative colitis (UC). IBD are complex, chronic conditions characterized by relapsing periods of disease activity and remission. These disorders are progressive in nature, leading to cumulative tissue damage and the development of complications, which are often responsible for recurrent hospitalizations [1]. In addition to intestinal manifestations, extraintestinal manifestations are frequently observed in IBD, significantly affecting patients' quality of life and complicating the therapeutic process [2].

Despite the broad availability of conventional treatments, including corticosteroids, aminosalicylates, small-molecule agents such as tofacitinib and filgotinib, and immunosuppressive drugs such as azathioprine and cyclosporine, a substantial proportion of patients fail to achieve remission. Moreover, long-term use of these therapies is associated with an increasing risk of serious adverse events [1,3].

In recent years, significant progress in the treatment of IBD has been achieved through the introduction of biological therapies, including monoclonal antibodies targeting specific molecular targets. Inhibition of selected cytokines or receptors enables a more targeted therapeutic approach by modulating disease-related pathophysiological pathways [4]. Although biological agents have revolutionized IBD therapy, challenges related to their use remain, including an increased risk of infections, including opportunistic infections, an elevated risk of malignancy, and high treatment costs [5].

ORCID: Grzegorz Zaborowski 0009-0004-6977-7616, Jacek Wysoczański 0009-0005-1983-486X, Antoni Anczyk 0009-0008-3817-3675, Karolina Handzel 0009-0004-5765-0458, Dominik Kret 0009-0007-6218-027X, Wiktoria Szlachta0009-0009-3739-4211, Miłosz Tworek 0009-0000-5202-9364, Filip Basta 0009-0008-4685-7778

Currently, research is ongoing into novel agents aimed at improving therapeutic efficacy, offering safer adverse event profiles, and more patient-friendly routes of administration [6]. In this article, we briefly summarize current knowledge of the epidemiology and etiopathogenesis of IBD and describe contemporary biological therapies, focusing on the advantages and limitations of each available monoclonal antibody, their mechanisms of action, and the differences between them. Finally, we present a range of novel molecules that are still under investigation for efficacy but demonstrate promising therapeutic potential.

## Methodology

To conduct a literature review of the current state of knowledge regarding biological treatment in IBD, widely used scientific databases, including PubMed and Google Scholar, were searched. During the search process, the following terms and keywords were used: biological treatment, inflammatory bowel disease, pathogenesis, infliximab, adalimumab, golimumab, certolizumab, natalizumab, vedolizumab, and ustekinumab.

## Epidemiology

IBD are diagnosed worldwide; however, the highest incidence is observed among Caucasian populations in developed countries of Europe, North America, and Australia [7]. In South American and African countries with a low development index, a lower incidence of IBD is reported. Nevertheless, a continuous increase in disease incidence is being observed in these regions, and many cases may remain undiagnosed due to limited access to adequate diagnostic facilities [8,9].

In Asian countries, the prevalence of IBD is lower compared with Western countries; however, it is characterized by a high growth rate. The highest projected increase in incidence has been reported in India [10,11]. In Poland, according to data from the National Health Fund, the prevalence of IBD is estimated at 0.25% of the total population, which represents a relatively high rate compared with other countries. However, a stabilizing or declining trend has been observed. The incidence of ulcerative colitis is lower than that of Crohn's disease and amounts to 12.5 per 100,000 compared with 4.7 per 100,000, respectively. The incidence of IBD is highest in the 20-29-year age group and is higher in males than in females, which contrasts with trends observed in the global population [12].

## Types of IBD and etiopathogenesis

Despite differences in disease course and histopathological findings between Crohn's disease (CD) and ulcerative colitis (UC), their etiopathogenesis, certain clinical manifestations, and endoscopic features are very similar in both conditions [13].

CD is a segmental, transmural inflammatory process that may involve any part of the gastrointestinal tract. The disease most commonly begins in the terminal ileum. The most frequent symptoms include anemia, fever, diarrhea, and abdominal pain-most often localized to the right lower quadrant. The presence of blood in the stool is observed relatively rarely [14]. Owing to the extensive areas that may be affected, clinical manifestations can be specific to the involved region, such as aphthous ulcers in the oral cavity, esophageal dysphagia and odynophagia, abdominal pain and vomiting, and perianal ulcers and fistulas in cases with anorectal involvement. In addition to gastrointestinal lesions, extraintestinal manifestations, including dermatological and joint involvement, may also occur [14,15].

UC primarily affects the mucosal layer of the colon and rectum and, in severe cases, may extend to the distal ileum. The predominant and often initial symptom is blood in the stool. Diarrhea, abdominal pain, anemia, and fever are also commonly observed. The severity of symptoms depends on the extent of colonic mucosal involvement. Complications of UC include inflammatory polyps, colonic perforation, toxic megacolon, and colorectal cancer [14].

IBD are diseases with an etiology that remains incompletely understood. Due to their multifactorial nature, several factors contribute to their etiopathogenesis, which can be categorized into four main groups:

- Genetic.
- Enviromental.
- Intestinal barrier-related.
- Immunological [16].

## Classification for biological treatment

The classification of patients eligible for biological therapy is evolving as knowledge advances, diagnostic methods improve, and inflammatory bowel disease (IBD) is better controlled. According to the European Crohn's and Colitis Organization and the guidelines of the Polish Society of Gastroenterology, biological therapy for Crohn's disease (CD) and ulcerative colitis (UC) should be considered in patients with a

moderate to severe disease course. Patients who are steroid-refractory or steroid-dependent, those with recurrent disease—particularly involving the entire colon in CD-those with extensive disease (defined as involvement of more than 100 cm of the gastrointestinal tract in CD), as well as patients with a lack of response after 3 days of intravenous steroid therapy in UC, may also benefit from the initiation of biological treatment [14,17-19].

## Biological treatment

Biological therapy is based on the use of monoclonal antibodies-therapeutic proteins composed of four polypeptide chains. Owing to the presence of a hypervariable region, monoclonal antibodies bind to their specific antigens in the body, thereby modulating the immune system response. Murine, human, chimeric, and humanized antibodies are distinguished. These agents fall into the following groups: anti-TNF-α (tumor necrosis factor), anti-integrin, and anti-cytokine therapies [4].

### Anti-TNF- α

TNF-α is a cytokine secreted predominantly by macrophages. It is involved in numerous physiological processes in the body, including cell proliferation, survival, and cell death. Under normal conditions, it plays a key role in the proper functioning of the immune system [20]. However, TNF-α is also implicated in pathological immune-mediated conditions such as rheumatoid arthritis, psoriasis, and inflammatory bowel disease (IBD). In the course of IBD, elevated levels of TNF-α have been observed in serum, stool, and mucosal biopsy specimens. Moreover, TNF-α inhibitors have been shown to reduce disease symptoms, directly indicating TNF-α's involvement in the pathogenesis and clinical course of IBD. The TNF-α inhibitor group includes infliximab, adalimumab, golimumab, and certolizumab [21].

#### *Infliximab*

Infliximab was the first biological agent approved for the treatment of inflammatory bowel disease (IBD) and is supported by the largest body of published data. It is a chimeric monoclonal immunoglobulin G1 antibody directed against TNF. It is administered intravenously or subcutaneously at intervals of 4–8 weeks, with doses adjusted to body weight. Studies have shown that infliximab is an effective and safe treatment for both Crohn's disease (CD) and ulcerative colitis (UC); however, approximately 30% of patients do not exhibit a therapeutic response, and up to half of treated patients are forced to discontinue therapy due to loss of response or the development of severe adverse effects [22].

Despite the establishment of a universal infliximab dose of 5 mg/kg, this dosing strategy often fails to achieve its intended effect because of interindividual variability in factors influencing drug clearance. These factors include serum C-reactive protein (CRP) concentration, sex, and body weight. Approaches based on monitoring serum drug concentrations, such as therapeutic drug monitoring (TDM), proactive therapeutic drug monitoring (PTDM), and dashboard-guided infliximab dosing, may significantly improve treatment efficacy by enabling patient-specific dose adjustments [23-25].

An additional factor contributing to loss of response to infliximab therapy is the development of antibodies directed against the drug molecule. It has been demonstrated that combination therapy with infliximab and mercaptopurine or azathioprine (antineoplastic and immunosuppressive agents from the thiopurine group) reduces the formation of anti-infliximab antibodies, thereby prolonging the duration of therapeutic effectiveness [26].

#### *Adalimumab*

Adalimumab is a fully humanized monoclonal antibody directed against TNF-α and belongs to the immunoglobulin G1 class. Its administration regimen includes an induction dose of 160 mg given subcutaneously, followed by a second dose of 80 mg after 14 days. Subsequent maintenance doses are 40 mg every 14 days. Remission induction lasts 12 weeks [27].

The clinical response to adalimumab is closely associated with the therapeutic serum drug concentration. Serum antibody levels below 0.33 μg/mL, recorded at least once, are associated with a lower rate of remission and sustained clinical benefit. To achieve the greatest therapeutic benefit from adalimumab therapy, serum drug concentrations should be maintained between 4.8 and 5.9 μg/mL. Higher serum drug levels reduce the risk of developing antibodies against adalimumab molecules and, consequently, the risk of loss of response to treatment [28].

Adalimumab may be used as first-line biological therapy on par with infliximab. During long-term tre-

atment, no significant differences have been observed between adalimumab and infliximab, with both agents demonstrating comparable efficacy in remission induction [29,30]. Combination therapy with adalimumab and thiopurines does not show the same effectiveness as observed with infliximab. It has been demonstrated that combination therapy may only slightly reduce the risk of antibody formation against the drug molecule; therefore, in patients for whom thiopurine therapy is contraindicated due to adverse effects, adalimumab should be considered [31].

***Golimumab***

Golimumab is also a fully human IgG1 anti–TNF-α antibody. In 2013, it was approved by the FDA (United States Food and Drug Administration) and the EMA (European Medicines Agency) for the treatment of patients with moderate to severe ulcerative colitis (UC). For remission induction, golimumab is administered via subcutaneous injections at an initial dose of 200 mg in the first week of therapy, followed by 100 mg in the second week. Maintenance dosing ranges from 50 mg to 100 mg, administered every 4 weeks (according to EMA recommendations, in patients with a body weight below 80 kg, the maintenance dose should be reduced by half) [32].

Similarly to infliximab, an association has been observed between increased golimumab clearance and low serum albumin levels, leading to rapid loss of response after induction therapy. Moreover, fecal loss of golimumab has been demonstrated, increasing in proportion to the severity of intestinal inflammation present at the time of drug administration, which may necessitate higher doses of the monoclonal antibody [33].

In combination therapy, only methotrexate has been shown to increase drug levels. Thiopurines, nonsteroidal anti-inflammatory drugs, corticosteroids, or sulfasalazine did not affect golimumab clearance. The immunogenicity of golimumab remains under investigation due to the limited availability of reliable assays to detect and quantify antibodies against the drug. Nevertheless, studies indicate that golimumab is less immunogenic than infliximab [34].

The safety and efficacy profile of golimumab is comparable to that of infliximab and adalimumab. The advantages of golimumab include a 4-week dosing regimen, the possibility of subcutaneous administration, potentially reduced immunogenicity, and the lowest cost to achieve a full year of remission [35,36]. There are no formal clinical trials based on which the efficacy of golimumab in Crohn's disease (CD) can be definitively assessed; however, available retrospective studies demonstrate a satisfactory safety profile and efficacy of golimumab in the treatment of CD [37].

***Certolizumab***

Certolizumab is a humanized monoclonal antibody fragment lacking the Fc region, to which polyethylene glycol (PEG) is attached-specifically, a Fab fragment. This structure enables more effective penetration into tissues affected by inflammatory processes while not inducing complement activation or antibody-dependent cell apoptosis. All studies involving certolizumab have focused exclusively on Crohn's disease (CD).

Remission induction with certolizumab consists of subcutaneous administration of 400 mg at weeks 0, 2, and 4, followed by continued treatment at 4-week intervals. Owing to its modified structure, certolizumab is less likely to induce antibody formation against the drug. Additionally, the combined use of certolizumab with immunosuppressive agents further reduces the incidence of such antibodies [38].

Certolizumab is more effective at inducing remission in CD, but only in patients who have not been previously treated with other anti–TNF-α agents and who present with high CRP levels; however, it demonstrates lower efficacy in maintaining remission. Due to its molecular structure, certolizumab does not cross the placenta and may therefore be used in pregnant women [39,40]. Certolizumab is not approved for the treatment of Crohn's disease in the European Union [14].

**Anti-integrin**

Integrins are receptors present on the surface of leukocytes and are composed of two subunits, α and β. Different leukocyte populations express integrins characteristic of each cell type. The α4β1 integrin is expressed on the majority of leukocytes, whereas α4β7 is detected exclusively on lymphocytes of the gastrointestinal tract. Integrins enable communication between leukocytes and cells expressing appropriate cell adhesion molecules (CAMs), such as E-cadherin on mucosal epithelial cells or MadCAM-1 on endothelial cells. Excessive CAM expression leads to enhanced leukocyte migration into tissues and the development of inflammatory processes.

Anti-integrin therapy, which includes two monoclonal antibodies—natalizumab and vedolizumab—blocks the interaction between integrins and their ligands, thereby inhibiting leukocyte migration and alleviating inflammation [41]. Integrins may also be involved in the manifestation of extraintestinal symptoms of inflammatory bowel disease (IBD) [42]. Anti-integrin therapy is particularly important for patients who do not respond to, or have lost the therapeutic effect of, anti–TNF-α agents [43].

***Natalizumab***

Natalizumab is a humanized monoclonal immunoglobulin G4 antibody directed against the α4β1 and α4β7 integrins. Natalizumab is administered at a dose of 300 mg as an intravenous infusion every 4 weeks [44]. The drug is more effective as maintenance therapy than as an induction agent; however, due to the high risk of adverse effects, it is used only in selected cases of Crohn's disease, most often in patients with concomitant multiple sclerosis [14,45].

***Vedolizumab***

Vedolizumab is a human monoclonal antibody directed against the α4β7 integrin. For remission induction, 300 mg of the drug is administered intravenously at weeks 0 and 2, followed by a third dose at week 6, after which a maintenance dose of 108 mg is given every 8 weeks. If remission is not achieved after the third dose, a fourth dose may be administered at week 10. A subcutaneous formulation of the drug is also available; in this form, vedolizumab may be administered starting from the third dose.

Serum albumin levels significantly affect vedolizumab clearance, with lower levels associated with increased clearance [46]. Vedolizumab is also characterized by a lower rate of antibody formation against the drug molecule, and the antibodies that do develop do not cause significant elimination of vedolizumab from the body, which may be related to its gut-selective mechanism of action [47].

Previous use of TNF-α antagonists does not significantly affect vedolizumab therapy, apart from a slightly higher probability of remission when vedolizumab is used as the first biological agent. The use of immunosuppressive drugs, such as thiopurines or methotrexate, in combination therapy with vedolizumab results in a similar increase in plasma drug concentrations as observed with anti–TNF-α monoclonal antibodies. The therapeutic effect of vedolizumab is comparable in patients with Crohn's disease (CD) and ulcerative colitis (UC) [48].

Due to its gut-selective mechanism of action, vedolizumab causes fewer systemic adverse effects than TNF-α antagonists; however, it also does not reduce extraintestinal manifestations of IBD [43]. Although vedolizumab is approved for the treatment of IBD in patients who have failed anti–TNF-α therapy, it should be considered as a first-line treatment in steroid-dependent and steroid-refractory patients, as well as in those with intolerance to immunosuppressive drugs, owing to its favorable safety profile [49].

**Anti-cytokine**

Cytokines are molecules produced by immune system cells, other cells of the body, such as mucosal cells, and the gut microbiota present in every individual. Cytokines perform numerous important pleiotropic functions in communication between the body's cells and immune cells, as well as in maintaining overall homeostasis [50]. Unfortunately, the same cytokines are also involved in pathological processes, often initiating disease mechanisms. In addition to driving chronic inflammatory processes, they can also regulate extraintestinal disease manifestations in IBD. Due to their widespread involvement in intestinal inflammatory processes, molecules have been developed to limit cytokine-mediated inflammation. One such molecule approved for the treatment of IBD is ustekinumab [51,52].

***Ustekinumab***

Ustekinumab is a humanized monoclonal IgG4 antibody targeting the cytokines IL-12 and IL-23, which are involved in the cascade of responses that contribute to the pathogenesis of IBD. Inhibition of these cytokines' interactions with their receptors induces remission of the disease, without affecting immune responses mediated by other cytokines [53].

The induction dose of ustekinumab is 6 mg/kg, administered intravenously. Maintenance doses can be administered subcutaneously at 90 mg every 8–12 weeks. No differences in pharmacokinetics or clinical outcomes have been observed between its use in Crohn's disease (CD) and ulcerative colitis (UC). As with other biological agents, ustekinumab clearance increases with decreasing serum albumin levels and increasing CRP concentrations [54].

Ustekinumab exhibits low immunogenicity, and antibodies developed against the drug do not significantly reduce its efficacy [55]. Combination therapy with immunosuppressive agents does not affect the rate of clinical or endoscopic remission [56]. Ustekinumab has an excellent safety and efficacy profile, with a substantially reduced risk of serious infections compared with TNF-α antagonists [57].

## Adverse reactions to biological drugs

Although monoclonal antibodies are highly effective in the treatment of moderate to severe IBD, they are associated with adverse effects that may complicate or even preclude further therapy. Infection-related adverse events are common across all classes of biological agents, with the highest incidence, including opportunistic infections, observed during TNF-α antagonist therapy. Interstitial lung disease, as well as malignancies such as lymphoma, breast cancer, and gastric cancer, have also been significantly associated with TNF-α antagonist therapy [58].

For anti-integrin antibodies, the main serious adverse effect observed is the risk of progressive multifocal leukoencephalopathy during long-term natalizumab use [59]. In the case of ustekinumab, as a representative of anti-cytokine antibodies, adverse effects, in addition to an increased risk of infections, include musculoskeletal pain accompanied by fatigue [60].

Although these serious adverse events occur in a minority of patients treated with biological agents, it is important to consider their potential occurrence during therapy and to use the lowest effective drug doses recommended. In patients at risk of malignancy, the selection of vedolizumab or ustekinumab, which carry the lowest risk of carcinogenesis, should be promoted [14].

## Treatment costs

The costs of biological agent treatment vary depending on drug prices in a given country [61]. Nevertheless, the prices of biological drugs are significantly higher than the costs of treatment with non-biological preparations. An additional factor contributing to higher treatment costs is the chronic nature of Crohn's disease (CD) and ulcerative colitis (UC), meaning that treatment costs are not one-time expenses. According to an article by J. Burisch in The Lancet Gastroenterology and Hepatology, the average annual cost of IBD treatment per patient in Europe using biological agents is €866 [62].

In Poland, the cost of an 8-week treatment cycle, including both induction and maintenance phases, per patient for infliximab is as follows: 16,240.57 PLN (Induction phase: 12,180.43 PLN; Maintenance phase: 4,060.14 PLN). The total lifetime cost of treatment from the time of diagnosis amounts to 141,300.94 PLN for infliximab [63]. Complex production processes and administrative methods, combined with evolving generic competition, result in biological therapy costs approximately 60% higher than those for conventional IBD treatment [64].

Many patients are unable to personally finance the full course of treatment, particularly when disease exacerbations compromise their earning capacity. Consequently, drug reimbursement programs fully funded by the National Health Fund (NFZ) have been established in Poland. These include:

- Drug Program B.32 – for the treatment of Crohn's Disease.
- Drug Program B.55 – for the treatment of Ulcerative Colitis.

Program B.32 encompasses a 12-month treatment cycle utilizing Adalimumab and Ustekinumab, or a 24-month regimen involving Infliximab and Vedolizumab. In contrast, Program B.55 provides for a 12-month course of Infliximab or Tofacitinib, or a 54-week therapeutic regimen with Vedolizumab [65]. According to 2024 reports from the Medical Technology Assessment Division of the Agency for Health Technology Assessment and Tariffication (AOTMiT), the average annual cost of therapy per patient is 22,129 PLN for Program B.32 and 28,125 PLN for Program B.55 [66,67]. Beyond the direct cost of the biological agents, the total expenditure is further increased by administration costs—associated with either hospitalization or outpatient visits—as well as eligibility screening and treatment monitoring. These components add several hundred or even thousands of PLN to the overall clinical budget per patient [65].

However, studies on treatment efficacy and quality of life in patients receiving biological therapy demonstrate its superiority over conventional IBD therapy. During treatment with non-biological drugs, the percentage of patients reporting deterioration in self-care increased significantly-from 3.09% at the start of observation to 17.52% after 6 months of treatment. This represents approximately 11 percentage points

more compared with patients treated with biological agents (11.86% at baseline and 15.25% after 6 months of observation). Biological therapy is always considerably more expensive but is more effective in improving quality of life in 99.45% of cases [68].

Furthermore, early initiation of biological therapy in IBD, without prior step-up treatment, may be more cost-effective than treatments involving surgical intervention for severe cases of IBD [62]. In the future, the cost-effectiveness of biological drugs may improve as prices decline and biosimilars are introduced. Cost-effectiveness studies indicate that biosimilars can reduce treatment costs by 30–50% compared with original biological drugs, increasing accessibility without compromising clinical outcomes [69].

## New biologics for the treatment of IBD

Currently, research is ongoing on new biological drug molecules with a more patient-friendly route of administration, reduced risk of adverse effects, lower immunogenicity, and decreased susceptibility to loss of disease remission. One such agent currently in Phase II clinical trials is the oral anti–TNF-α preparation AVX-470. This is a polyclonal antibody derived from bovine colostrum. Due to its gut-specific activity and the known safety of IgA, it is considered a promising therapeutic candidate [70].

New anti-integrin agents are also under investigation, such as AJM300, an oral formulation of natalizumab. Attention is drawn to its very short half-life, which reduces the risk of adverse effects. Abrilumab is a humanized antibody targeting the α4β7 integrin, demonstrating very low immunogenicity, a favorable safety profile, and particularly promising outcomes in patients who have failed TNF-α antagonist therapy. Etrolizumab is an antibody that binds the β7 integrin subunit, thereby blocking interactions between α4β7 and MAdCAM-1 as well as αEβ7 and E-cadherin, inhibiting leukocyte migration to the gut and retention in the intraepithelial compartment. PF-00547659 is a humanized antibody directed against the MAdCAM-1 receptor, representing a distinct mechanism of inhibiting integrin-receptor interactions. This strategy is still under investigation for efficacy and potential adverse effects [43].

Research is also ongoing on biological molecules targeting cytokines. Bimekizumab and brodalumab block IL-17 activity by inhibiting, respectively, the ligand and the receptor of this cytokine [71]. Olamkicept is a monoclonal antibody targeting IL-6 trans-signaling, offering a better safety profile than pan–IL-6 inhibitors. Mirkizumab, guselkumab, and brazikumab inhibit IL-23 by binding to its p19 subunit. Although further studies are needed to confirm the efficacy of these agents, the molecules reported to date demonstrate an optimal safety profile and a low infection risk [72].

Conflict of interest
None

Correspondence address
Grzegorz Zaborowski
St. Barbara Hospital, Regional Specialist Hospital
No. 5, Sosnowiec, Poland
Plac Medyków 1, 41-200 Sosnowiec
☎ (+48 32) 368 20 00
g.zab@o2.pl

**References**

1. Nakase H, Uchino M, Shinzaki S, et al. Evidence-based clinical practice guidelines for inflammatory bowel disease. J Gastroenterol. 2021;56(6):489-526.
2. Rogler G, Singh A, Kavanaugh A, et al. Extraintestinal Manifestations of Inflammatory Bowel Disease: Current Concepts, Treatment, and Implications for Disease Management. Gastroenterology. 2021;161(4):1118-32.
3. Magro F, Cordeiro G, Dias AM, et al. Inflammatory Bowel Disease – Non-biological treatment. Pharmacol Res. 2020;160:105075.
4. Moreno LO, Fernández-Tomé S, Abalo R. Biological Treatments in Inflammatory Bowel Disease: A Complex Mix of Mechanisms and Actions. Biologics. 2021;1(2):102.
5. Stallmach A, Hagel S, Bruns T. Adverse effects of biologics used for treating IBD. Best Pract Res Clin Gastroenterol. 2010;24(2):167-82.
6. Danese S, Solitano V, Jairath V, et al. The future of drug development for inflammatory bowel disease: the need to ACT (advanced combination treatment). Gut. 2022;71(12):2380-7.
7. Ananthakrishnan AN. Epidemiology and risk factors for IBD. Nat Rev Gastroenterol Hepatol. 2015;12(4):205-17.

8. Selvaratnam S, Gullino S, Shim L, et al. Epidemiology of inflammatory bowel disease in South America: A systematic review. World J Gastroenterol. 2019;25(47):6866-75.
9. Watermeyer G, Katsidzira L, Setshedi M, et al. Inflammatory bowel disease in sub-Saharan Africa: epidemiology, risk factors, and challenges in diagnosis. Lancet Gastroenterol Hepatol. 2022;7(10):952-61.
10. Aniwan S, Santiago P, Loftus EV, et al. The epidemiology of inflammatory bowel disease in Asia and Asian immigrants to Western countries. United European Gastroenterol J. 2022;10(10):1063-76.
11. Park SH. Update on the epidemiology of inflammatory bowel disease in Asia: where are we now? Intest Res. 2022;20(2):159-64.
12. Zagórowicz E, Walkiewicz D, Kucha P, et al. Nationwide data on epidemiology of inflammatory bowel disease in Poland between 2009 and 2020. Pol Arch Intern Med. 2022;132(5):16194.
13. Yeshi K, Ruscher R, Hunter L, et al. Revisiting Inflammatory Bowel Disease: Pathology, Treatments, Challenges and Emerging Therapeutics Including Drug Leads from Natural Products. J Clin Med. 2020;9(5):1273.
14. Gomollón F, Dignass A, Annese V, et al. 3rd European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease 2016: Part 1: Diagnosis and Medical Management. J Crohns Colitis. 2017;11(1):3-25.
15. Laube R, Liu K, Schifter M, et al. Oral and upper gastrointestinal Crohn's disease. J Gastroenterol Hepatol. 2018;33(2):355-64.
16. Ramos GP, Papadakis KA. Mechanisms of Disease: Inflammatory Bowel Diseases. Mayo Clin Proc. 2019;94(1):155-65.
17. Harbord M, Dignass A, Danese S, et al. Third European Evidence-based Consensus on Diagnosis and Management of Ulcerative Colitis. Part 2: Current Management. J Crohns Colitis. 2017;11(7):769-84.
18. Łodyga M, Eder P, Gawron-Kiszka M, et al. Guidelines for the management of patients with Crohn's disease. Recommendations of the Polish Society of Gastroenterology and the Polish National Consultant in Gastroenterology. Prz Gastroenterol. 2021;16(4):257-96.
19. Eder P, Łodyga M, Gawron-Kiszka M, et al. Guidelines for the management of ulcerative colitis. Recommendations of the Polish Society of Gastroenterology and the Polish National Consultant in Gastroenterology. Prz Gastroenterol. 2023;18(1):1-42.
20. Levin AD, Wildenberg ME, van den Brink GR. Mechanism of Action of Anti-TNF Therapy in Inflammatory Bowel Disease. J Crohns Colitis. 2016;10(8):989-97.
21. Perše M, Unkovič A, et al. The Role of TNF in the Pathogenesis of Inflammatory Bowel Disease. IntechOpen. 2019;1(1):84375.
22. Papamichael K, Lin S, Moore M, et al. Infliximab in inflammatory bowel disease. Ther Adv Chronic Dis. 2019;10:20406223198384443.
23. Strik AS, Löwenberg M, Mould DR, et al. Efficacy of dashboard driven dosing of infliximab in inflammatory bowel disease patients; a randomized controlled trial. Scand J Gastroenterol. 2021;56(2):145-54.
24. Fuentes-Valenzuela E, García-Alonso FJ, Maroto-Martín C, et al. Influence of HLADQA1*05 Genotype in Adults With Inflammatory Bowel Disease and Anti-TNF Treatment With Proactive Therapeutic Drug Monitoring: A Retrospective Cohort Study. Inflamm Bowel Dis. 2023;29(10):1586-93.
25. Desai DC, Dherai AJ, Strik A, et al. Personalized Dosing of Infliximab in Patients With Inflammatory Bowel Disease Using a Bayesian Approach: A Next Step in Therapeutic Drug Monitoring. J Clin Pharmacol. 2023;63(4):480-9.
26. Mogensen DV, Brynskov J, Ainsworth MA, et al. A Role for Thiopurine Metabolites in the Synergism Between Thiopurines and Infliximab in Inflammatory Bowel Disease. J Crohns Colitis. 2018;12(3):298-305.
27. Roblin X, Rinaudo-Gaujous M, Del Tedesco E, et al. Development of an Algorithm Incorporating Pharmacokinetics of Adalimumab in Inflammatory Bowel Diseases. Am J Gastroenterol. 2014;109(8):1250.
28. Paul S, Moreau AC, Del Tedesco E, et al. Pharmacokinetics of Adalimumab in Inflammatory Bowel Diseases: A Systematic Review and Meta-analysis. Inflamm Bowel Dis. 2014;20(7):1288-95.
29. Gil-Candel M, Gascón-Cánovas JJ, Urbieta-Sanz E, et al. Comparison of drug survival between infliximab and adalimumab in inflammatory bowel disease. Int J Clin Pharm. 2020;42(2):500-7.
30. Ungar B, Levy I, Yavne Y, et al. Optimizing Anti-TNF-α Therapy: Serum Levels of Infliximab and Adalimumab Are Associated With Mucosal Healing in Patients With Inflammatory Bowel Diseases. Clin Gastroenterol Hepatol. 2016;14(4):550-7.
31. Kopylov U, Al-Taweel T, Yaghoobi M, et al. Adalimumab monotherapy versus combination therapy with immunomodulators in patients with Crohn's disease: A systematic review and meta-analysis. J Crohns Colitis. 2014;8(12):1632-41.
32. Dragoni G, Le Grazie M, Orlandini B, et al. Golimumab in inflammatory bowel diseases: present and future scenarios. Clin J Gastroenterol. 2019;12(1):1-9.
33. Berends SE, Strik AS, Jansen JM, et al. Pharmacokinetics of golimumab in moderate to severe ulcerative colitis: the GO-KINETIC study. Scand J Gastroenterol. 2019;54(6):700-6.
34. Harzallah I, Rigaill J, Williet N, et al. Golimumab pharmacokinetics in ulcerative colitis: a literature review. Ther Adv Gastroenterol. 2017;10(1):89-100.
35. Danese S, Fiorino G, Peyrin-Biroulet L, et al. Biological Agents for Moderately to Severely Active Ulcerative Colitis. Ann Intern Med. 2014;160(10):704-11.
36. Trigo-Vicente C, Gimeno-Ballester V, Montoiro-Allué R, et al. Cost-effectiveness analysis of infliximab, adalimumab, golimumab and vedolizumab for moderate to severe ulcerative colitis in Spain. Expert Rev Pharmacoecon Outcomes Res. 2018;18(3):321-9.
37. Martineau C, Flourie B, Wils P, et al. Efficacy and safety of golimumab in Crohn's disease: a French national retrospective study. Aliment Pharmacol Ther. 2017;46(11-12):1077-84.
38. Tun GS, Lobo AJ. Evaluation of pharmacokinetics and pharmacodynamics and clinical efficacy of certolizumab pegol for Crohn's disease.

Expert Opin Drug Metab Toxicol. 2015;11(2):317-27.
39. Ferrante M, Vermeire S, Rutgeerts P. Certolizumab pegol in the treatment of Crohn's disease. Expert Opin Biol Ther. 2013;13(4):595-605.
40. Gisbert JP, Chaparro M. Predictors of Primary Response to Biologic Treatment [Anti-TNF, Vedolizumab, and Ustekinumab] in Patients With Inflammatory Bowel Disease: From Basic Science to Clinical Practice. J Crohns Colitis. 2020;14(5):694-709.
41. Dotan I, Allez M, Danese S, et al. The role of integrins in the pathogenesis of inflammatory bowel disease: Approved and investigational anti-integrin therapies. Med Res Rev. 2020;40(1):245-62.
42. Kim JM, Cheon JH. Pathogenesis and clinical perspectives of extraintestinal manifestations in inflammatory bowel diseases. Intest Res. 2020;18(3):249-64.
43. Park SC, Jeen YT. Anti-integrin therapy for inflammatory bowel disease. World J Gastroenterol. 2018;24(17):1868-80.
44. Sakuraba A, Keyashian K, Correia C, et al. Natalizumab in Crohn's disease: results from a US tertiary inflammatory bowel disease center. Inflamm Bowel Dis. 2013;19(3):621-6.
45. Scott FI, Osterman MT. Natalizumab for Crohn's Disease: Down but Not Out. Clin Gastroenterol Hepatol. 2015;13(11):1926-8.
46. Rosario M, Dirks NL, Gastonguay MR, et al. Population pharmacokinetics-pharmacodynamics of vedolizumab in patients with ulcerative colitis and Crohn's disease. Aliment Pharmacol Ther. 2015;42(2):188-202.
47. Ungar B, Kopylov U, Yavzori M, et al. Association of Vedolizumab Level, Anti-Drug Antibodies, and α4β7 Occupancy With Response in Patients With Inflammatory Bowel Diseases. Clin Gastroenterol Hepatol. 2018;16(5):697-705.
48. Scribano ML. Vedolizumab for inflammatory bowel disease: From randomized controlled trials to real-life evidence. World J Gastroenterol. 2018;24(23):2457-67.
49. Macaluso FS, Ventimiglia M, Orlando A. Effectiveness and Safety of Vedolizumab in Inflammatory Bowel Disease: A Comprehensive Meta-analysis of Observational Studies. J Crohns Colitis. 2023;17(8):1217-27.
50. Bamias G, Corridoni D, Pizarro TT, et al. New insights into the dichotomous role of innate cytokines in gut homeostasis and inflammation. Cytokine. 2012;59(3):451-9.
51. Neurath MF. Cytokines in inflammatory bowel disease. Nat Rev Immunol. 2014;14(5):329-42.
52. Leppkes M, Neurath MF. Cytokines in inflammatory bowel diseases – Update 2020. Pharmacol Res. 2020;158:104835.
53. Gutiérrez A, Rodríguez-Lago I. How to Optimize Treatment With Ustekinumab in Inflammatory Bowel Disease: Lessons Learned From Clinical Trials and Real-World Data. Front Med (Lausanne). 2021;8:640813.
54. Adedokun OJ, Xu Z, Gasink C, et al. Population Pharmacokinetics and Exposure–Response Analyses of Ustekinumab in Patients With Moderately to Severely Active Crohn's Disease. Clin Ther. 2022;44(10):1336-55.
55. Strand V, Balsa A, Al-Saleh J, et al. Immunogenicity of Biologics in Chronic Inflammatory Diseases: A Systematic Review. BioDrugs. 2017;31(4):299-316.
56. Hu A, Kotze PG, Burgevin A, et al. Combination Therapy Does Not Improve Rate of Clinical or Endoscopic Remission in Patients with Inflammatory Bowel Diseases Treated With Vedolizumab or Ustekinumab. Clin Gastroenterol Hepatol. 2021;19(7):1366-76.
57. Honap S, Meade S, Ibraheim H, et al. Effectiveness and Safety of Ustekinumab in Inflammatory Bowel Disease: A Systematic Review and Meta-Analysis. Dig Dis Sci. 2022;67(3):1018-35.
58. Wakabayashi T, Hosohata K, Oyama S, et al. Comparison of Adverse Event Profiles of Tumor Necrosis Factor-Alfa Inhibitors: Analysis of a Spontaneous Reporting Database. Ther Clin Risk Manag. 2020;16:741-7.
59. Pérez-Jeldres T, Tyler CJ, Boyer JD, et al. Cell Trafficking Interference in Inflammatory Bowel Disease: Therapeutic Interventions Based on Basic Pathogenesis Concepts. Inflamm Bowel Dis. 2019;25(2):270-82.
60. Dayan JR, Dolinger M, Benkov K, et al. Real World Experience With Ustekinumab in Children and Young Adults at a Tertiary Care Pediatric Inflammatory Bowel Disease Center. J Pediatr Gastroenterol Nutr. 2019;69(1):61-7.
61. Baji P, Gulácsi L, Brodszky V, et al. Cost-effectiveness of biological treatment sequences for fistulising Crohn's disease across Europe. United European Gastroenterol J. 2018;6(2):310-21.
62. Burisch J, Vardi H, Schwartz D, et al. Health-care costs of inflammatory bowel disease in a pan-European, community-based, inception cohort during 5 years of follow-up: a population-based study. Lancet Gastroenterol Hepatol. 2020;5(5):454-64.
63. Petryszyn P, Ekk-Cierniakowski P, Zurakowski G. Infliximab, adalimumab, golimumab, vedolizumab and tofacitinib in moderate to severe ulcerative colitis: comparative cost-effectiveness study in Poland. Ther Adv Gastroenterol. 2020;13:1756284820941179.
64. Makurvet FD. Biologics vs. small molecules: Drug costs and patient access. Med Drug Discov. 2021;9:100075.
65. Pod red. prof. Grażyny Rydzewskiej. Analiza wpływu na budżet leczenia nieswoistych chorób zapalnych jelit. Proponowane zmiany w zapisach programów lekowych B.32 i B.55 oraz ich wpływ na budżet płatnika publicznego. CEESTAHC / towarzystwo , Kraków, 2021.
66. Agencja Oceny Technologii Medycznych i Taryfikacji. Wprowadzenie kompleksowych zmian w dotychczasowym opisie programu lekowego: B.32 „Leczenie pacjentów z chorobą Leśniowskiego – Crohna (ICD-10: K50)". Warszawa: AOTMiT; 2024. Raport nr OT.422.X.2024. Dostępne na: https://bip.aotm.gov.pl/assets/files/zlecenia_mz/2023/056/RPT/OT.422.0.1.2024_zmiany_PL_B.32_BIP_REOPTR.pdf.
67. Agencja Oceny Technologii Medycznych i Taryfikacji. Opracowanie dotyczące oceny zasadności wprowadzenia kompleksowych zmian dotychczasowej treści programu lekowego B.55: Leczenie pacjentów z wrzodziejącym zapaleniem jelita grubego (WZJG) (ICD-10: K51). Warszawa: AOTMiT; 2024. Raport nr OT.422.0.2.2024. Dostępne na: https://bip.aotm.gov.pl/assets/files/zlecenia_mz/2024/057/RPT/OT.422.0.2.2024_zmiany_PL_B.5 _WZJG_BIP_REOPTR.pdf.

68. AlRuthia Y, Almadi M, Aljebreen A, et al. The cost-effectiveness of biologic versus non-biologic treatments and the health-related quality of life among a sample of patients with inflammatory bowel disease in a tertiary care center in Saudi Arabia. J Med Econ. 2020;23(10):1102-10.
69. Danese S, Bonovas S, Peyrin-Biroulet L. Biosimilars in IBD: from theory to practice. Nat Rev Gastroenterol Hepatol. 2017;14(1):22-31.
70. Misselwitz B, Juillerat P, Sulz MC, et al. Emerging Treatment Options in Inflammatory Bowel Disease: Janus Kinases, Stem Cells, and More. Digestion. 2020;101(1):69-82.
71. Baker KF, Isaacs JD. Novel therapies for immune-mediated inflammatory diseases: What can we learn from their use in rheumatoid arthritis, spondyloarthritis, systemic lupus erythematosus, psoriasis, Crohn's disease and ulcerative colitis? Ann Rheum Dis. 2018;77(2):175-87.
72. Bretto E, Ribaldone DG, Caviglia GP, et al. Inflammatory Bowel Disease: Emerging Therapies and Future Treatment Strategies. Biomedicines. 2023;11(8):2249.