HEALTH TECHNOLOGY ASSESSMENT REPORT

ON

Cost-effectiveness of Vedolizumab for the Management of Inflammatory Bowel Diseases

RESOURCE CENTRE FOR

HEALTH TECHNOLOGY ASSESSMENT IN INDIA (HTAIn)

ICMR – NATIONAL INSTITUTE OF EPIDEMIOLOGY

CHENNAI

INDIA

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Abbreviations

AE	- Adverse Event
CE	- Cost-effectiveness
CEA	- Cost-effectiveness Analysis
CUA	- Cost-utility Analysis
GDP	- Gross Domestic Product
HICs	- Higher income countries
ICER	- Incremental Cost-effectiveness Ratio
INB	- Incremental Net Benefit
INR	- Indian Rupees
LICs	- Less income countries
LMICs	- Lower middle-income countries
NHA	-National Health Authority
NICE	-National Institute for Health and Care Excellence
PGIMER	- Post Graduate Institute of Medical Education and Research
PSA	- Probabilistic sensitivity analysis
QALY	- Quality Adjusted Life Years
SRMA	- Systematic Review and Meta-analysis
WTP	- willingness to pay threshold

1. Executive Summary

Vedolizumab, a biologic therapy targeting gut-specific inflammation, has demonstrated clinical efficacy in managing Inflammatory Bowel Disease (IBD), which includes Ulcerative Colitis (UC) and Crohn's Disease (CD). However, its high cost challenges its adoption in resource-constrained settings like India. This Health Technology Assessment evaluates the cost-effectiveness of Vedolizumab IV 300 mg compared to conventional therapies for managing UC/CD for the mixed population (anti–TNF alpha naive and anti–TNF alpha failure) within the Indian healthcare context.

The study employed a Markov decision-analytic model to analyze costs and health outcomes over a lifetime horizon from the health system perspective. Direct medical costs were considered, including drug acquisition, administration, and adverse event management. Quality-Adjusted Life Years (QALYs) were used as the primary measure of effectiveness. Scenario analyses were conducted for specific subgroups, such as anti–TNF alpha naive and anti–TNF alpha failure populations, to explore variations in cost-effectiveness. Sensitivity and threshold analyses were also performed to assess model robustness and determine the price reductions required for cost-effectiveness.

Key Findings:

The Vedolizumab IV 300 mg is not cost-effective at its current market price for managing UC or CD in India. The Incremental Cost-Utility Ratios (ICURs) for all analyzed populations, including the mixed, anti–TNF alpha naive, and anti–TNF alpha failure groups, exceeded the willingness-to-pay (WTP) threshold of one-time India's GDP per capita. Sensitivity analyses confirmed the robustness of these findings. Threshold analysis indicated that substantial price reductions—approximately 70% for UC and 76% for CD—are necessary for Vedolizumab to be considered cost-effective in the Indian context.

Conclusion:

In conclusion, while Vedolizumab offers clinical benefits, it is not cost-effective at its current market price in India. Significant price reductions are required to align its economic value with the healthcare priorities of the Indian population. These findings provide critical insights for policymakers to ensure equitable and cost-effective management of IBD in the country.

Recommendations:

- Vedolizumab IV 300 mg is not cost-effective in India for treating moderate-to-severe active ulcerative colitis and Crohn's disease; hence, it is not recommended at the current market price in the Indian context.
- Strategies such as price negotiations with manufacturers, tiered pricing for India to make Vedolizumab a cost-effective treatment option in the Indian context, a price reduction of approximately 70%, 76% in the market price of Vedolizumab IV 300 mg is recommended for ulcerative colitis and Crohn's disease respectively.
- There is a need for longitudinal, real-world studies in India to assess Vedolizumab's effectiveness, safety, and adherence patterns among patients with ulcerative colitis and Crohn's disease.
- It is essential to develop local utility values for ulcerative colitis and Crohn's disease health states in India, as these values are crucial for improving the precision of economic evaluations.

2. Background

Inflammatory bowel disease (IBD) is a chronic, systemic, immune-mediated inflammation of the gastrointestinal tract. It can be subdivided into Crohn's disease (CD) and ulcerative colitis (UC). (1) Chronic diseases, such as CD and UC, can cause significant impairments in quality of life. (2) Evidence shows that incidences of both diseases are rising globally. (3) Epidemiological studies from India have shown UC to be more prevalent than CD and a trend towards an increasing incidence of CD. (4) Khosla et al. (1986) reported the prevalence of UC as 42.8/100,000 patients from Haryana. (5) A similar prevalence of 44.3/100,000 was reported by Sood *et al.* in 2003. (6) In a 2012 national survey, UC was equally prevalent in the northern and southern States of the country.(7) Genetic predisposition,(8) Smoking,(9) animal protein, fats, sugar, meat(10) and excess tea or coffee(11) consumption are consistently associated with IBD. The age distribution in India is similar to that of other Asian countries, with the mean age at the time of diagnosis of UC and CD being closer to 40 years. (12) While IBS is more prevalent among females in Western countries,(13) most studies from India have shown a male preponderance for both UC and CD.(7, 14) With community-based studies show a closer male-to-female ratio, the observed disparity in gender representation in studies may be influenced by referral bias, as male patients are more likely to seek healthcare, particularly at advanced centres where many studies are conducted. (15) The national IBD registry has been formulated to bring out the diversities in the four geographical zones of India, aiming to aid research on IBD and improve the quality of patient care. (16)

IBD patients have relapsing and remitting conditions that may require multiple therapies over the course of their lives. (13, 14) Treatment of IBD is aimed at decreasing inflammation. Current therapies include aminosalicylates, corticosteroids, immunomodulators (e.g., azathioprine or 6-mercaptopurine), and biologic agents. (17-19) Flares of disease activity are common in patients with CD and UC despite the usage of 5-aminosalicylic acid compounds as

maintenance therapy. Corticosteroids are typically used to treat these flares, although they can have major side effects. (15,16) Furthermore, despite the use of immunosuppressant medications to try and lower corticosteroid requirements, 20–40% of IBD patients either develop a dependence on them to maintain remission of disease activity or develop resistance to their positive effects. (17,18) Compared to conventional therapies, biological regimens (e.g., anti-TNF alpha agents, anti-integrins) are effective in achieving clinical response and remission and are treatment alternatives, especially for patients who fail conventional treatment in patients with IBD.

Biologic agents currently approved for use in CD or UC can be divided into two main categories: anti-tumour necrosis factor (TNF) agents (e.g., infliximab, adalimumab, golimumab, and certolizumab pegol and anti-integrins (e.g., natalizumab, which targets α4, and Vedolizumab, which specifically targets the gastrointestinal-selective integrin α4β7). (20, 21) The rising use of biologic agents has led to an increase in the cost of IBD management. (22) The surgical treatment rates in India vary widely across different series for UC and CD, ranging from 4 to 12 percent for UC and 19 to 100 percent for CD. (23) In a nationwide IBD survey in India, approximately two-thirds of all UC patients received steroids, a third were on azathioprine (30%), and less than one per cent received biologicals. (7) The infrequent use of biologicals in India may reflect either a less severe disease or economic constraints. Diagnostic and treatment expenses comprise a significant portion of the cost of IBD management. (24) CD and UC impose significant economic burdens on individual patients and the health care system. (25)

Vedolizumab is a fully humanized monoclonal antibody that selectively targets α4β7 integrin. Based on the results of the clinical GEMINI trials, (26, 27) vedolizumab was approved for the treatment of adult patients with moderately to severely active ulcerative colitis (UC) and Crohn's disease (CD) refractory or intolerant to either CT or TNFα inhibitors. (28)

Vedolizumab inhibits the pathological T-cell migration into the gut without impacting the systemic immune response, making it a safer option concerning the risk of infections and central nervous system (CNS) complications. (29-31) In contrast to TNF inhibitors such as infliximab, which are associated with secondary loss of response in 30–40% of patients due to factors like antibody formation or accelerated drug clearance (32, 33), Vedolizumab offers a more gut-targeted approach. This makes it particularly suitable for patients who need a treatment that minimizes systemic immune suppression, reducing risks like opportunistic infections and CNS involvement. (29)

Many studies have assessed the cost-effectiveness of Vedolizumab for IBD types across different countries, showing mixed findings. Most of the analyses used Markov models with time horizons ranging from 1 year to lifetime and were conducted from the payer's perspective. In the USA, Vedolizumab was reported as cost-effective for ulcerative colitis patients of mixed population (TNF-Naïve and TNFα-failure) (34) and adalimumab non-responders with Crohn's disease (35) but not cost-effective, when used as a first-line treatment for CD compared to other biologics (36). In Europe, Vedolizumab was not cost-effective for fistulizing CD (37) or luminal CD (38). In the UK, it was found to be cost-effective for CD after TNFα-failure (39), but not consistently for both UC and CD (40). Studies from Asia indicated Vedolizumab was cost-effective for anti-TNF-alpha naïve CD in both Japan (41) and China (42). Overall, Vedolizumab's cost-effectiveness varied based on IBD type, patient population, country, and comparator treatments.

Despite the effectiveness of biologics, their cost has become a significant factor in IBD management, particularly in countries like India, where economic constraints limit their widespread use. (43, 44) In India, less than 1% of UC patients are treated with biologics, often due to financial limitations.(45) As new therapies are approved for IBD, it's crucial to balance

the cost increase and the effectiveness gained. The economic burden of IBD is substantial and being mindful of costs when selecting appropriate therapy is a necessary aspect of management. A cost-effectiveness analysis is imperative for systematically exploring Vedolizumab's economic and practical implications for managing IBD within the Indian healthcare system. This informs policy development and healthcare resource allocation for IBD management in India.

Research Question

What is the cost-effectiveness of Vedolizumab drug for the management of Inflammatory Bowel Disease in India?

Objectives

- To conduct model based economic evaluation study to evaluate the Cost effectiveness for Vedolizumab drug for management of Inflammatory Bowel Disease (Ulcerative colitis disease and Crohn's disease) for India.
- To conduct Budget impact analysis on use Vedolizumab for Inflammatory Bowel Disease for Indian health care system, if found cost-effective.

3. Methods

A Health Technology Assessment (HTA) was conducted to analyze the use of Vedolizumab for managing Inflammatory Bowel Disease (Ulcerative colitis and Crohn's disease) in India.

PICO

Population	Moderately-to-severely active Inflammatory Bowel Disease (ulcerative colitis or Crohn's) disease population (includes both anti-TNF alpha naïve and anti-TNF alpha failure)
Intervention	Vedolizumab IV 300mg
Comparator	Conventional therapy (includes 5-ASAs, steroids, immunomodulators)
Outcome	Incremental Cost-effectiveness Ratio (ICUR) or Incremental Net Benefit (INB)
Study type	Economic model-based Cost-Utility Analysis (CUA)

Inclusion Criteria

Adults aged 18 years and older diagnosed with IBD, irrespective of previously received treatment with at least one standard IBD therapy, including corticosteroids, immunomodulators, or TNF inhibitors, have demonstrated either partial response, non-response, or intolerance to these treatments or drug-naive patients. Conventional therapy includes 5-ASAs, steriods,immunomodulators such as methotrexate (46, 47).

Exclusion Criteria

Patients diagnosed with indeterminate colitis or other forms of IBD do not meet the diagnostic criteria for either ulcerative colitis or Crohn's disease.

Perspective

Health system perspective.

Time Horizon

The model was developed over a lifetime year time horizon.

Discounting

All future costs and consequences were discounted at 3% as per WHO guidelines.

Willingness to Pay Threshold

The willingness to pay threshold (WTP) is considered for determining the cost-effectiveness. A formally recognized cost-effectiveness threshold (CET) for India is not available. However, for this analysis, we used the one-time gross domestic product (GDP) per capita for 2024, as suggested by the Indian reference case for conducting economic evaluations in health technology assessments. (48)

Data Collection

Transition probabilities and Proportions

Data on input parameters and transitional probabilities were systematically collected from published, peer-reviewed literature, following a hierarchy of evidence. The highest priority was given to systematic reviews and meta-analyses of randomized controlled trials (49) followed by vedolizumab trials. (26, 27) When multiple studies were available, we conducted a meta-analysis to pool the input parameters. The probability of age-specific all-cause mortality was obtained from Sample Registration System (SRS) data (50).

Estimation of Costs and health outcomes

Cost

The cost analysis was undertaken from the health system perspective. Direct medical costs (DMC) such as cost of drugs, monitoring and administration, common adverse drug reactions, outpatient visits, inpatient care and hospital readmission costs were included. The costing information was taken from India-specific primary costing studies,(46) databases such as the National Health System Cost Database for India developed by the Post Graduate Institute of

Medical Education and Research (PGIMER), the Ayushman Bharat Package, Jan Aushadhi drug prices, and from market prices search. All the previous year's costs were adjusted and reported for 2024 in Indian Rupees (INR). The cost data are provided in Table 2.2.1.

Utility

The health state utility values used in the model were obtained from a systematic search of published peer-reviewed literature and from Tuff's registry. The details of utility data are provided in Table 2.2.1.

Table 2.2.1 Model input parameters

Input Parameters	Mean	SE	Distribution	Reference
UC				
Transition probabilities- Induction phase				
P_UC_VDZ_Indu_Mixed_Mod_response	0.471	0.033	Beta	(26)
P_UC_VDZ_Indu_Mixed_Mod_No-response	0.530	0.033	Beta	(26)
P_UC_CT_Indu_Mixed_total_response	0.255	0.036	Beta	(26)
P_UC_CT_Indu_Mixed_total_No-response	0.744	0.036	Beta	(26)
P_UC_VDZ_Indu_Remission	0.169	0.008	Beta	(26)
P_UC_VDZ_Indu_Clinical_response	0.301	0.015	Beta	(26)
P_UC_CT_Indu_Remission	0.054	0.003	Beta	(26)
P_UC_CT_Indu_Clinical_response	0.201	0.010	Beta	(26)
P_UC_sur	0.300	0.015	Beta	Expert opinion
P_UC_Indu_CNr	0.700	0.035	Beta	Expert opinion
Transition probabilities- Maintenance phase				
p_uc_mx_v_rtom	0.073	0.004	Beta	(51)
p_uc_mx_v_rtor	0.927	0.046	Beta	(51)
p_uc_mx_v_mtom	0.574	0.029	Beta	(51)
p_uc_mx_v_mtomds	0.164	0.008	Beta	(51)
p_uc_mx_v_mdstom	0.212	0.011	Beta	(51)

p_uc_mx_v_mtor	0.262	0.013	Beta	(51)
p_uc_mx_v_mdstosur	0.008	0.000	Beta	(51)
p_uc_mx_v_mdstomds	0.780	0.039	Beta	(51)
p_uc_mx_c_rtom	0.084	0.004	Beta	(51)
p_uc_mx_c_rtor	0.916	0.046	Beta	(51)
p_uc_mx_c_mtom	0.542	0.027	Beta	(51)
p_uc_mx_c_mtomds	0.438	0.022	Beta	(51)
p_uc_mx_c_mtor	0.020	0.001	Beta	(51)
p_uc_mx_c_mdstom	0.013	0.001	Beta	(51)
p_uc_mx_c_mdstomds	0.979	0.049	Beta	(51)
p_uc_mx_c_mdstosur	0.008	0.000	Beta	(51)
p_uc_sur_psurc	0.500	0.025	Beta	(51)
p_uc_sur_postsurr	0.450	0.023	Beta	(51)
p_uc_sur_sur	0.050	0.003	Beta	(51)
p_uc_psurr_sur	0.050	0.003	Beta	(51)
p_uc_psurr_psurr	0.777	0.039	Beta	(51)
p_uc_psurr_psurc	0.173	0.009	Beta	(51)
p_uc_psurc_sur	0.050	0.003	Beta	(51)
p_uc_psurc_psurc	0.705	0.035	Beta	(51)
p_uc_psurc_psurr	0.245	0.012	Beta	(51)
p_uc_mx_cnr_mdstomds	0.982	0.049	Beta	(51)
Utility				
u_uc_mild	0.760	0.038	Beta	(52)
u_uc_mds	0.420	0.021	Beta	(52)
u_uc_r	0.860	0.043	Beta	(52)
u_uc_sur	0.420	0.021	Beta	NICE Report for UC 2015
u_uc_psur	0.600	0.030	Beta	(52)
u_uc_psuc	0.420	0.021	Beta	(52)
Adverse events probability				
p_sae_uc_vdz_induc	0.125	0.006	Beta	(53-58)
p_sae_uc_ct_induc	0.124	0.006	Beta	(53-58)
p_sae_uc_vdz_main	0.081	0.004	Beta	(53-58)
p_sae_uc_ct_main	0.226	0.011	Beta	(53-58)
p_ae_uc_vdz_main	0.055	0.003	Beta	(53-58)
p_ae_uc_ct_main	0.132	0.007	Beta	(53-58)
Adverse events utility				
u_sae_uc_VDZ_main	0.480	0.024	Beta	(59-67)
u_sae_UC_ct_main	0.480	0.024	Beta	(59-67)
u_ae_uc_vdz	0.766	0.038	Beta	(59-67)

u_ae_uc_ct	0.739	0.037	Beta	(59-67)
Costs				
Cost_UC_CT_Relapse	₹ 84,943	₹ 16,989	Gamma	(46)
Cost_UC_CT_Remission	₹ 69,883	₹ 13,977	Gamma	(46)
Cost_UC_postsurcomp	₹ 27,320	₹ 5,464	Gamma	PGIMER database
Cost_UC_postsurrem	₹ 69,883	₹ 13,977	Gamma	PGIMER database
Cost_UC_VDZ_Relapse	₹ 670,451	₹ 134,090	Gamma	(46), Market price search
Cost_UC_VDZ_Remission	₹ 665,369	₹ 133,074	Gamma	(46), Market price search
Cost_UC_VDZ_Induc	₹ 238,815	₹ 47,763	Gamma	(46), Expert opinion, PGIMER database, Market price search
Cost_UC_CT_Induc	₹ 19,164	₹ 3,833	Gamma	Expert opinion, PGIMER database, Market price search
CD				
Transition probabilities- Induction phase				
P_CD_VDZ_Indu_Mixed_Mod_response	0.320	0.041	Beta	(49)
P_CD_VDZ_Indu_Mixed_Mod_No-response	0.680	0.033	Beta	(49)
P_CD_CT_Indu_Mixed_Mod_response	0.210	0.038	Beta	(49)
P_CD_CT_Indu_Mixed_Mod_No-response	0.790	0.202	Beta	(49)
P_CD_VDZ_Indu_Remission	0.160	0.038	Beta	(49)
P_CD_CT_Indu_Remission	0.100	0.020	Beta	(49)
P_CD_VDZ_Indu_Clinical_response	0.160	0.142	Beta	(49)
P_CD_CT_Indu_Clinical_response	0.110	0.006	Beta	(49)
P_CD_sur	0.300	0.015	Beta	Expert opinion
P_CD_Indu_CNr	0.700	0.035	Beta	Expert opinion
Transition probabilities- Maintenance phase				
p_cd_mx_v_rtom	0.021	0.001	Beta	(27, 68)
p_cd_mx_v_rtor	0.979	0.049	Beta	(27, 68)
p_cd_mx_v_mtom	0.531	0.027	Beta	(27, 68)
p_cd_mx_v_mtomds	0.240	0.012	Beta	(27, 68)
p_cd_mx_v_mdstom	0.137	0.007	Beta	(27, 68)
p_cd_mx_v_mtor	0.229	0.011	Beta	(27, 68)
p_cd_mx_v_mdstosur	0.027	0.001	Beta	(27, 68)

p_cd_mx_v_mdstomds	0.836	0.042	Beta	(27, 68)
p_cd_mx_c_rtom	0.121	0.006	Beta	(27, 68)
p_cd_mx_c_rtor	0.879	0.044	Beta	(27, 68)
p_cd_mx_c_mtom	0.600	0.030	Beta	(27, 68)
p_cd_mx_c_mtomds	0.400	0.020	Beta	(27, 68)
p_cd_mx_c_mdstom	0.020	0.001	Beta	(27, 68)
p_cd_mx_c_mdstomds	0.953	0.048	Beta	(27, 68)
p_cd_mx_c_mdstosur	0.027	0.001	Beta	(27, 68)
p_cd_mx_surtor	0.775	0.039	Beta	(27, 68)
p_cd_mx_surtom	0.113	0.006	Beta	(27, 68)
p_cd_mx_surtomds	0.085	0.004	Beta	(27, 68)
p_cd_mx_surtosur	0.027	0.001	Beta	(27, 68)
Utility				
u_cd_medr	0.830	0.042	Beta	(69, 70)
u_cd_mild	0.760	0.092	Beta	(69, 70)
u_cd_mds	0.420	0.092	Beta	(69, 70)
u_cd_s	0.420	0.092	Beta	(69)
u_cd_r	0.880	0.031	Beta	(69, 70)
Adverse events probability				
p_sae_cd_vdz_induc	0.077	0.004	Beta	(49, 54-58, 71)
p_sae_cd_ct_induc	0.070	0.004	Beta	(49, 54-58, 71)
p_sae_cd_vdz_main	0.081	0.004	Beta	(49, 54-58, 71)
p_sae_cd_ct_main	0.318	0.016	Beta	(49, 54-58, 71)
p_ae_cd_vdz_main	0.083	0.004	Beta	(49, 54-58, 71)
p_ae_cd_ct_main	0.181	0.009	Beta	(49, 54-58, 71)
p_ae_sur	0.584	0.029	Beta	(49, 54-58, 71)
Adverse events utility				
u_sae_cd_VDZ_main	0.480	0.024	Beta	(59-67)
u_sae_cd_ct_main	0.480	0.024	Beta	(59-67)
u_ae_cd_vdz	0.762	0.038	Beta	(59-67)
u_ae_cd_ct	0.744	0.037	Beta	(59-67)
u_ae_sur	0.584	0.029	Beta	(27, 68)
Costs				
Cost_CD_VDZ_Induc	₹ 251,459	₹ 50,292	Gamma	Expert opinion, PGIMER database, Market price search
Cost_CD_CT_Induc	₹ 31,808	₹ 6,362	Gamma	Expert opinion, PGIMER database, Market price search
Cost_surgical	₹ 100,000	₹ 20,000	Gamma	PGIMER database
Cost_SAE	₹ 93,500	₹ 18,700	Gamma	HBP 2022

Cost_AE	₹ 8,018	₹ 1,604	Gamma	HBP 2022
Cost_CD_VDZ_Relapse	₹ 676,542	₹ 135,308	Gamma	(46), Market price search
Cost_CD_VDZ_Remission	₹ 662,871	₹ 132,574	Gamma	(46), Market price search
Cost_CD_CT_Relapse	₹ 116,869	₹ 23,374	Gamma	(46), Market price search
Cost_CD_CT_Remission	₹ 70,893	₹ 14,179	Gamma	(46), Market price search
Cost_AE_sur	₹ 27,320	₹ 5,464	Gamma	Expert opinion and PGIMER database
Cost_surgical_CD	₹ 25,000	₹ 5,000	Gamma	Expert opinion, PGIMER database

Model Framework

A Markov decision-analytic model was developed to evaluate the cost-effectiveness of VDZ compared to Conventional treatment for patients with Inflammatory Bowel Disease. We build two separate similar models to include two separate populations, patients having UC or CD in India. The decision-analytic model was based on models developed by Wilson et al. 2017 (51) and Zhou et al. 2021(42). The model includes a decision tree and a Markov framework (Figure 1).

For UC, the model considers three on-treatment health states based on Mayo scores: remission (Mayo <3), mild UC (Mayo 3–5), and moderate-severe UC (Mayo ≥6); three health states related to surgery: surgery; post-surgery remission; and post-surgery complications. (Figure 1 A)

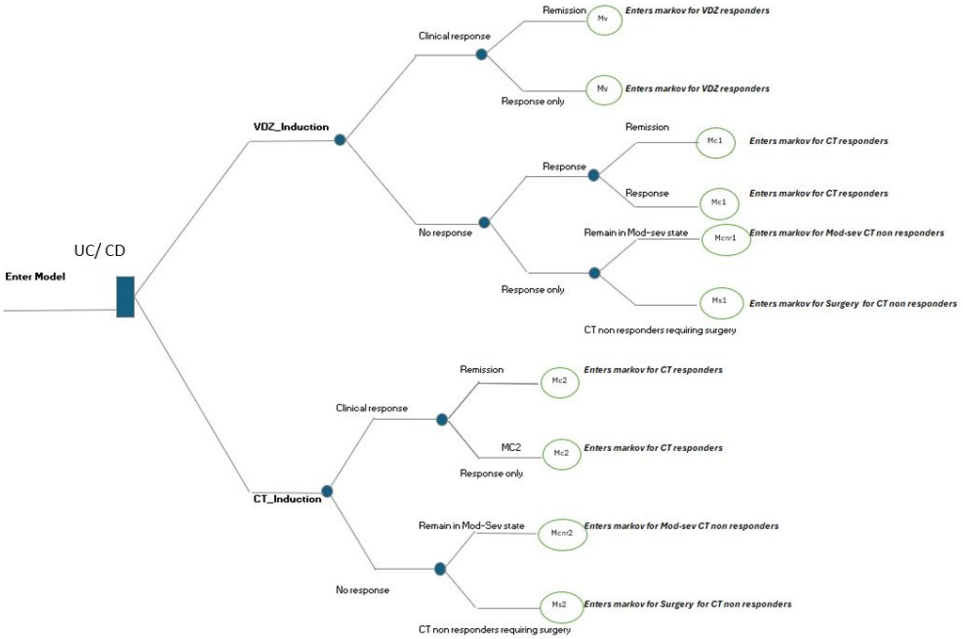
For Crohn's Disease, the model considers three on-treatment health states based on Crohn's Disease Activity Index (CDAI) score: remission (CDAI score less than 150), mild (CDAI score 150–220), and moderate-to-severe (CDAI score 220–600); three health states related to surgery: surgery; post-surgery remission; and post-surgery complications. (Figure 1 B)

Patients with moderate-severe disease initiate treatment with either Vedolizumab or conventional therapy. Patients responding to Vedolizumab in induction and who do not experience discontinuation resulting from adverse event intolerability then enter a long-term

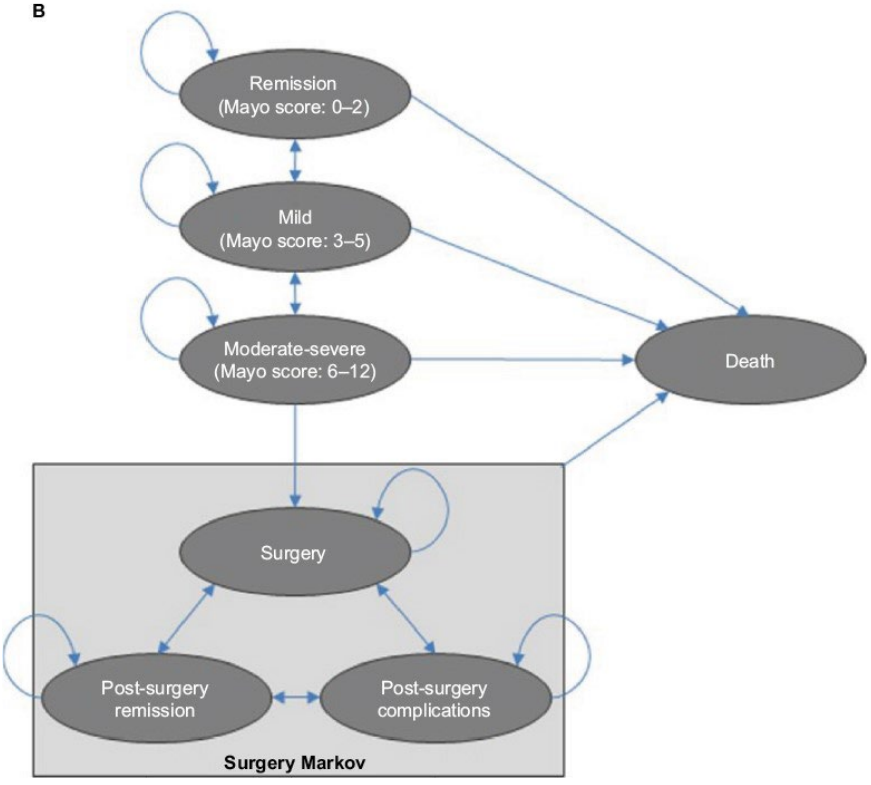
Markov model for maintenance therapy in one of the three treatment health states (Figure 1 B) for UC and (Figure 1 B) for CD Patients who respond to treatment may remain on therapy moving through these health states. Patients who fail to respond in induction, who subsequently lose response, or who experience intolerability to adverse events are assumed to discontinue Vedolizumab and switch to conventional therapy. Patients in the CTarm (whether at the onset of the model or after switching from Vedolizumab) face a similar decision tree for induction as vedolizumab patients. However, those who fail to respond to CTare assumed to remain in the moderate-severe health state until they require surgery.

Patients in either arm of the model in moderate-severe disease incur a risk of surgery. Those who require surgery move to the surgery health state and are assumed to discontinue pharmacotherapy (Figure 1 B). Following surgery, in the UC model, these patients may transition among the surgery-related health states in each subsequent cycle: post-surgery remission (free of complications), post-surgery complications (experiencing complications); or surgery (requiring another surgery). Following surgery, in the CD model, these patients may transition to and among the remission, mild and moderate-severe health states. All patients incur a risk of death in any cycle in the model, regardless of their current health state or pharmacotherapy.

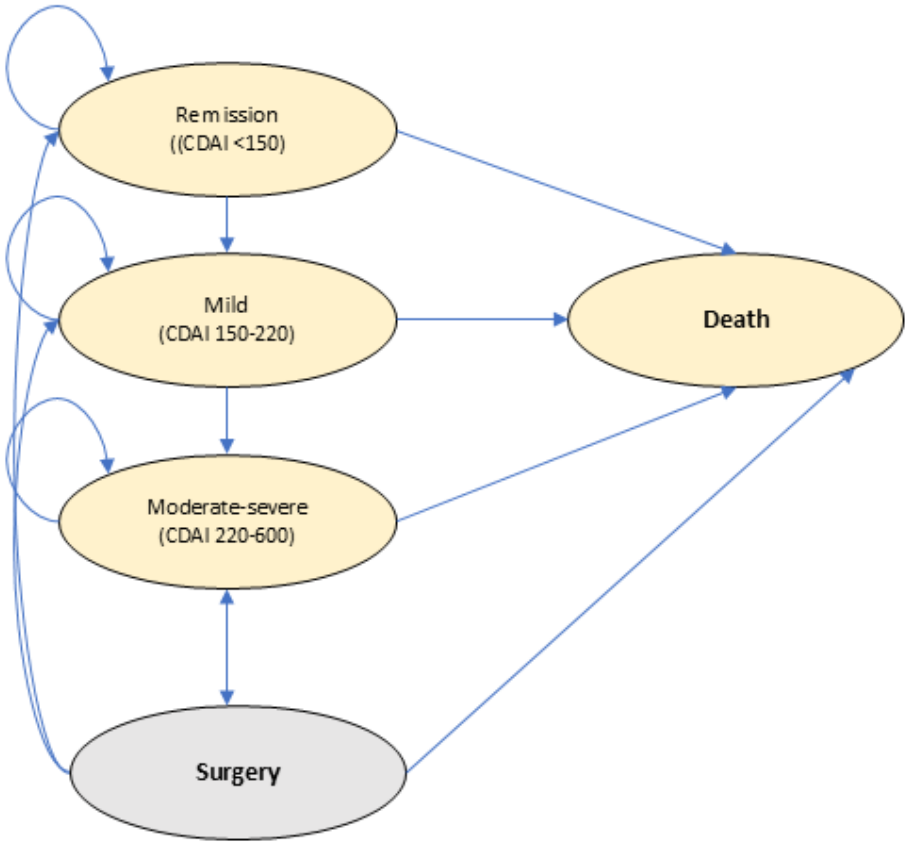
Figure 1. Schematic representation of the decision model


UC/ CD
Enter Model
VDZ_Induction
Clinical response
Remission
Mv
Enters markov for VDZ responders
Response only
Mv
Enters markov for VDZ responders
No response
Response
Remission
Mc1
Enters markov for CT responders
Response
Mc1
Enters markov for CT responders
Response only
Remain in Mod-sev state
Mcnr1
Enters markov for Mod-sev CT non responders
Ms1
Enters markov for Surgery for CT non responders
CT non responders requiring surgery
CT_Induction
Clinical response
Remission
Mc2
Enters markov for CT responders
MC2
Mc2
Enters markov for CT responders
Response only
Remain in Mod-Sev state
Mcn2
Enters markov for Mod-sev CT non responders
No response
Ms2
Enters markov for Surgery for CT non responders
CT non responders requiring surgery

B


Remission
(Mayo score: 0–2)
Mild
(Mayo score: 3–5)
Moderate-severe
(Mayo score: 6–12)
Death
Surgery
Post-surgery
remission
Post-surgery
complications
Surgery Markov

C



Model Assumptions

The assumptions used in the decision analytical model are as follows:

1. Response and Treatment Pathway:
    - Mod-sev. patients are assumed to enter the model at 35 years for both UC and CD
    - Patients who initially respond to Vedolizumab in the maintenance phase continue to respond throughout the model.
    - Non-responders to VDZ are assumed to follow a treatment pathway similar to conventional therapy.

- The entry into the Markov model for VDZ is in the mild to severe health state as well as remission..
- There is no additional mortality risk due to IBD, therefore mortality is modeled as equivalent to only age-specific mortality rate (SRS report 2020).

2. Surgical Interventions:
    - Colectomy is assumed to be the most commonly performed surgical intervention for UC and IPAA for CD (Expert's opinion).
    - The utility value for post-surgical complications, including ileostomy-related complications assumed as adhesive intestinal obstruction. For other surgical complications, the utility value of severe adverse events or serious infections was used.
    - For CD:
        - Proportion of patients who do not respond to therapy will require surgery.
        - After VDZ failure, the probability of transitioning to surgery or remaining in the moderate-to-severe disease state is assumed to be similar to that observed in CT failure.
        - Post-operative complication rates for non-responders after CT or VDZ failure are assumed to be similar.
3. Utility values
    - The utility values are borrowed from meta-analysis (Wu et al.2017) for UC and Buxton et al. 2017, Punekar et al. for CD
    - We have assumed the utility values of TNF-alpha naïve and failure patients to be same as that for mixed population in UC as well as CD
4. AE utility related assumptions

- The utility values for each condition are assumed based on available literature or analogous conditions.
- For nasopharyngitis values were derived from diseases of the respiratory system.
- For Headache values were assumed based on mild migraine.
- For Arthralgia values were assumed based on mild rheumatoid arthritis
- For Vomiting and nausea values were derived from diseases of the digestive system.
- For Pyrexia values were assumed from hypersensitivity-related conditions.

5. Cost Assumptions:
    - The cost of managing mild disease and remission states is assumed to be the same for UC.
    - The cost of managing mild disease and remission states is assumed to be the same for CD.
    - The proportion of requiring surgery among non-responders is assumed to be the same for UC and CD.
    - Based on expert opinion, the cost of remission and mild UC/CD management is assumed to be almost similar.
6. AE cost related assumptions:
    - The cost for serious adverse events was estimated based on the 10-day intensive care unit (ICU) cost for pneumonia, per the 2022 Health Benefits Package (HBP) rates for ICU care without ventilator support.
    - The cost for adverse events (AEs) was determined using the median cost of managing a single event.

- The cost for abdominal pain was considered as the median cost of managing any illness.
- The cost for nasopharyngitis was assumed as that of outpatient treatment for acute respiratory infection (ARI) without hospitalization.
- Upper respiratory tract infection was assumed to have costs similar to ARI with hospitalization.
- The cost for pyrexia was considered as that of undifferentiated fever.
- The cost for vomiting was assumed to be the same as that for nausea.
- Exacerbations of Ulcerative colitis and Crohn's disease were assumed to have costs similar to those for treating Ulcerative colitis and Crohn's disease, respectively.
- Serious infections were costed as hospital-acquired infections.
- Acute hypersensitivity reactions and skin site reactions were costed using moderate and mild atopic dermatitis, respectively.
- All other AEs were costed based on standard treatment assumptions.

Results reporting:

Results were reported as Quality Adjusted Life Years (QALYs) and Life Years (LYs) as the measure of effectiveness. A half-cycle correction was performed for the costs and QALYs. Incremental cost/QALY will be determined as the difference between the total cost/QALY of the intervention and the comparator. ICUR is obtained by taking the ratio of incremental cost over incremental QALY.

$$ICUR = \frac{Cost\ of\ intervention - Cost\ of\ comparator}{QALY of\ intervention - QALY\ of\ comparator}$$

Incremental Net Benefit is calculated using the formula. $INB = K * \Delta E - \Delta C$

Where K is the willingness to pay threshold, which is one time of GDP of India for the year

2023, ΔE the incremental QALY and ΔC is incremental cost.

Sensitivity analysis

The robustness of the model will be assessed using sensitivity analysis, which includes one-way sensitivity analysis (OWSA) and probabilistic sensitivity analysis (PSA). In one-way sensitivity analysis with upper and lower limits of 95% confidence interval values of the model inputs depending on the availability, model input parameters were used and reported as tornado diagrams. PSA was performed with Monte Carlo simulation 5000 times based on the data distribution. Cost data was simulated using Gamma distribution and transitional probabilities using beta distribution. Results were reported with a cost-effectiveness plane and CE-acceptability curve.

Scenario analysis

The expected high cost and varying documented benefits of Vedolizumab for treating IBD are concerns. We calculated the ICUR at the current price point (market price) to establish whether Vedolizumab meets the accepted CE threshold. Since Vedolizumab does not meet the accepted CE threshold, we conducted a what-if analysis to determine the price point at which Vedolizumab becomes cost-effective.

Budget impact analysis

We did not conduct a budget impact analysis since Vedolizumab did not meet the accepted CE threshold.

4. Results

4.1 Cost-effectiveness analysis

From a health system perspective, we assessed the cost-effectiveness of adding Vedolizumab 300 mg IV compared to CTfor patients with moderately-to-severely active inflammatory bowel disease (ulcerative colitis or Crohn's disease) for the mixed population (anti-TNF alpha naïve and anti-TNF alpha failure populations), in India.

Ulcerative colitis population

In the base-case/deterministic analysis, VDZ treatment was more expensive for UC but had a higher QALY gain than the conventional therapy. The ICUR of VDZ compared to CT is higher than the WTP threshold of one-time GDP per capita for India; hence, it is not cost-effective. The incremental net monetary benefit is also negative, indicating that VDZ is not economically efficient. (Table 4.1)

Crohn's disease population

In the base-case/deterministic analysis, VDZ treatment was more expensive for CD but had a higher QALY gain than conventional therapy. The ICUR of VDZ compared to CT is higher than the WTP threshold of one-time GDP per capita for India; hence, it is not cost-effective. The incremental net monetary benefit is also negative, indicating that VDZ is not economically efficient. (Table 4.1)

Table 4.1 Cost-effectiveness Analysis: Results in the UC/CD Mixed population (Anti–TNF Alpha Naive and Anti–TNF Alpha Exposed (Deterministic)

	Ulcerative Colitis		**Crohn's disease**	
	Vedolizumab	**Conventional therapy**	**Vedolizumab**	**Conventional therapy**
Total Cost	₹ 4,552,955	₹ 1,597,283	₹ 4,125,865	₹ 2,223,201
Total LY	16.465	16.465	15.975	15.975
Total QALY	8.227	4.806	7.619	5.956
NMB	₹ -2,687,304	₹ -507,357	₹ -2,398,108	₹ -872,514
Incremental Cost	₹ 2,955,671		₹ 1,902,663	
Incremental QALY	3.421		1.663	
ICER per QALY	**₹ 8,64,026**		**₹ 11,44,244**	
INB	₹ -21,79,947		₹ -15,25,594	

4.2 Sensitivity analysis

4.2.1 One-Way Sensitivity Analysis

For the UC model, the model parameters had minimal influence on the ICUR results, as observed in the OWSA. Among them, the probability of response to VDZ in the induction phase had the most significant impact, leading to a nearly 6% increase in ICUR when varied to its lower limit and a 7% decrease when varied to its upper limit.

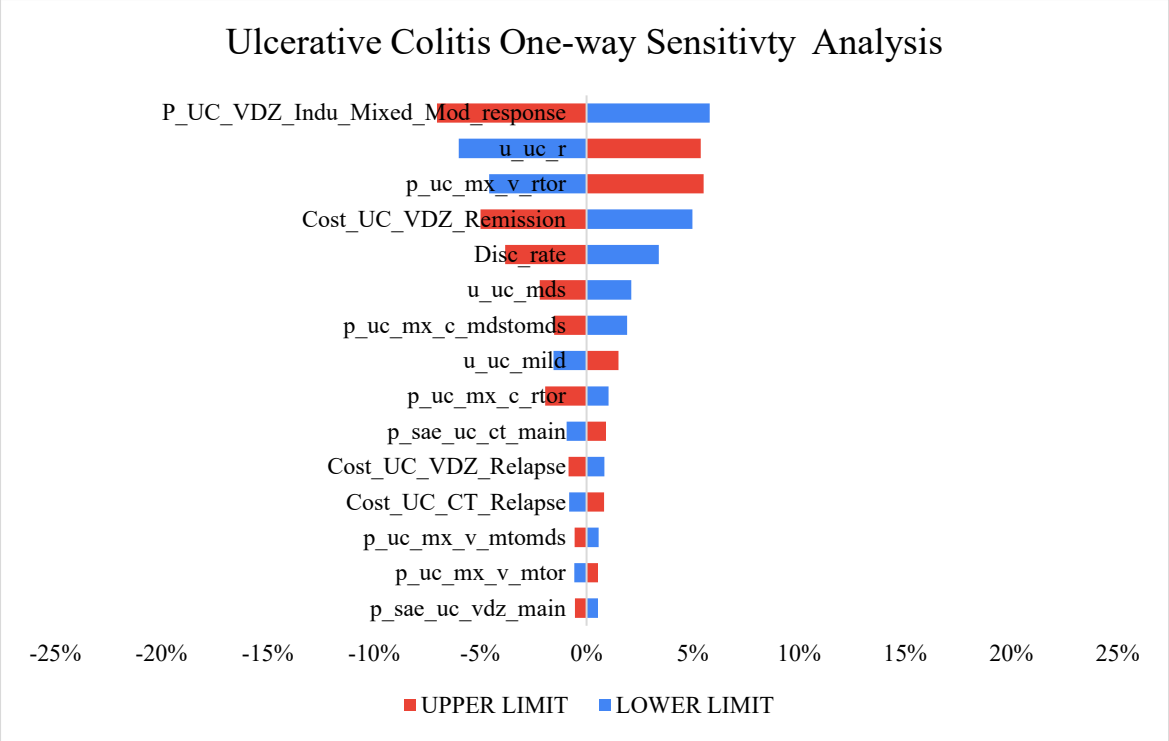


Figure 4.2.1.1 One-way sensitivity analysis for VDZ vs CT among the UC population

One-way sensitivity analysis was conducted using higher and lower values of all the transitional probabilities, cost, and utility values. The red bars show the effect on the ICUR of applying the lower limit of the specific parameter, while the blue bars show the effect on the ICUR of applying the upper limit of the specific parameter.

For the CD model, among the parameters, increasing the probability of no response to CT during the induction phase to its upper limit has the most significant impact, resulting in a 264% increase in the ICUR. Conversely, decreasing the probability of vedolizumab responders remaining in remission to its lower limit reduces the ICUR by nearly 156%.

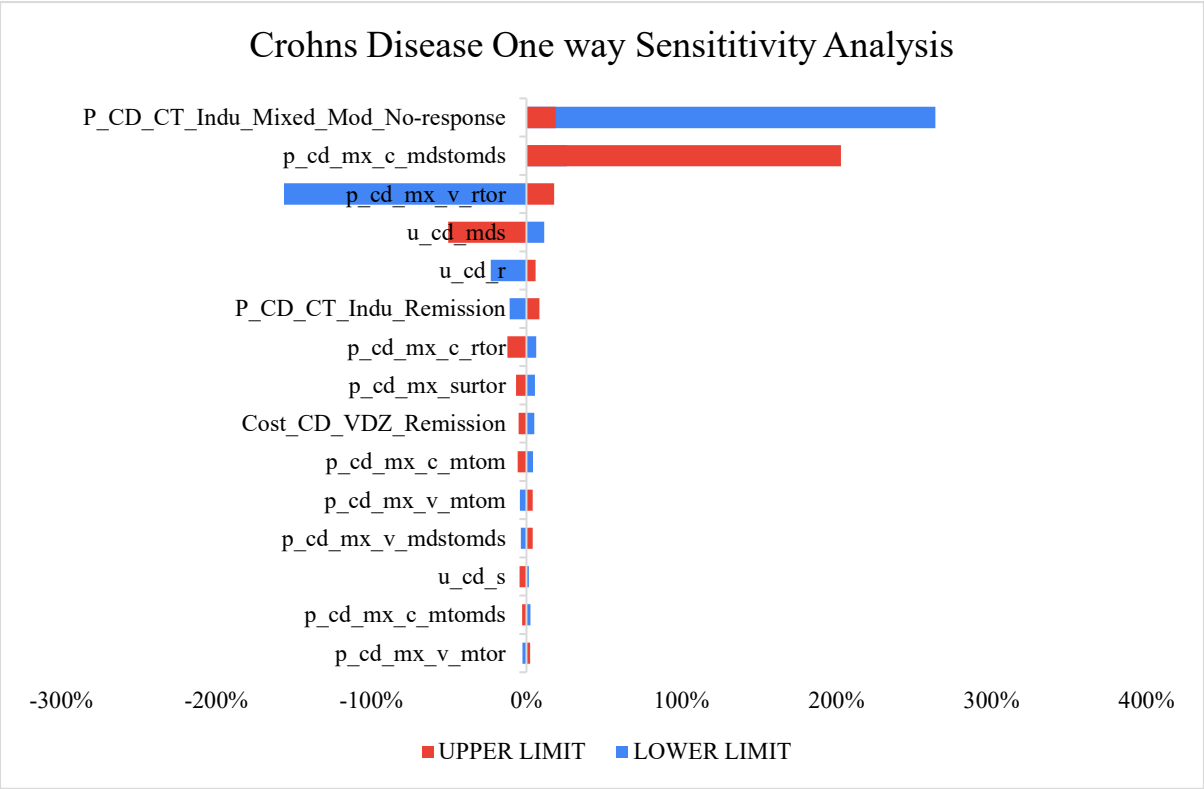


Figure 4.2.1.2 One-way sensitivity analysis for VDZ vs CT among the CD population

One-way sensitivity analysis was conducted using higher and lower values of all the transitional probabilities, cost, and utility values. The red bars show the effect on the ICUR of applying the lower limit of the specific parameter, while the blue bars show the effect on the ICUR of applying the upper limit of the specific parameter.

4.2.2 Probabilistic Sensitivity Analysis

The PSA was performed with 5000 Monte Carlo simulations for Vedolizumab compared to CT for UC and CD populations. The mean stochastic ICURs aligned with the base case result for all the interventions, indicating low uncertainty (Table 4.2).

Table 4.2 Cost-effectiveness Analysis: Results in the UC/CD Mixed population (Anti–TNF Alpha Naive and Anti–TNF Alpha Exposed (Probabilistic)

	Ulcerative colitis		Crohn's disease	
	Vedolizumab	Conventional therapy	Vedolizumab	Conventional therapy
Total Cost	₹ 6,881,656	₹ 2,453,666	₹ 6,783,585	₹ 3,985,704
Total LY	25.608	25.228	26.516	28.421
Total QALY	12.536	7.278	12.801	10.664
NMB	₹ -4,039,014	₹ -803,374	₹ -3,880,760	₹ -1,567,377
Incremental Cost	₹ 4,427,989		₹ 2,797,882	
Incremental QALY	5.258		2.137	
ICER per QALY	**₹ 8,42,133**		**₹ 13,09,527**	
INB	₹ -32,35,639		₹ -23,13,383	

For the UC population, ICUR points are distributed in the upper right quadrant, with very few points (<5%) in the upper left quadrant. All of the ICUR points lie above the WTP threshold line, indicating the chance of VDZ not being cost-effective compared to CT. The mean stochastic ICUR and the INB indicate consistency in the results (Figure 4.2.2.1).

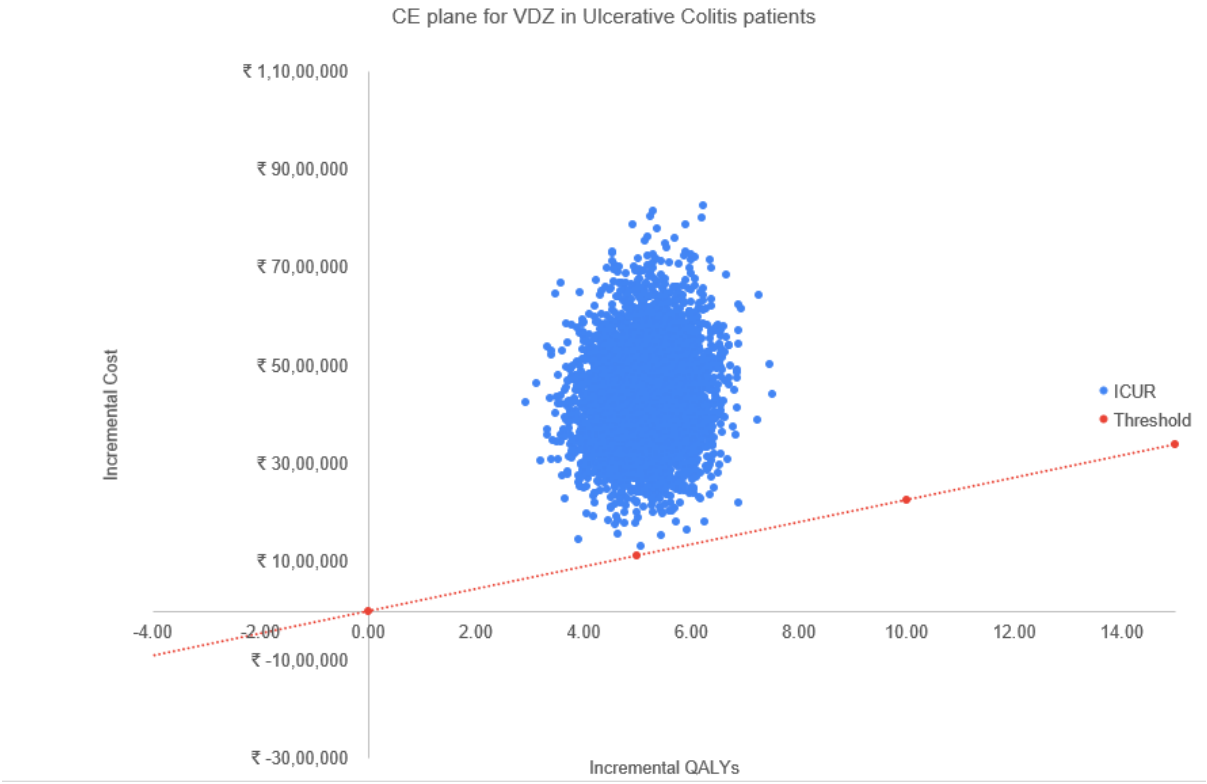


Figure 4.2.2.1 CE-plane for VDZ vs CT among the UC population

For the CD population, ICUR points are distributed in the upper right quadrants and left quadrants, with most of the points in the upper right quadrant. All the ICUR points in the upper right quadrant lie above the WTP threshold line, indicating the chance of VDZ being not cost-effective compared to CT. The mean stochastic ICUR and the INB indicate consistency in the results (Figure 4.2.2.2).

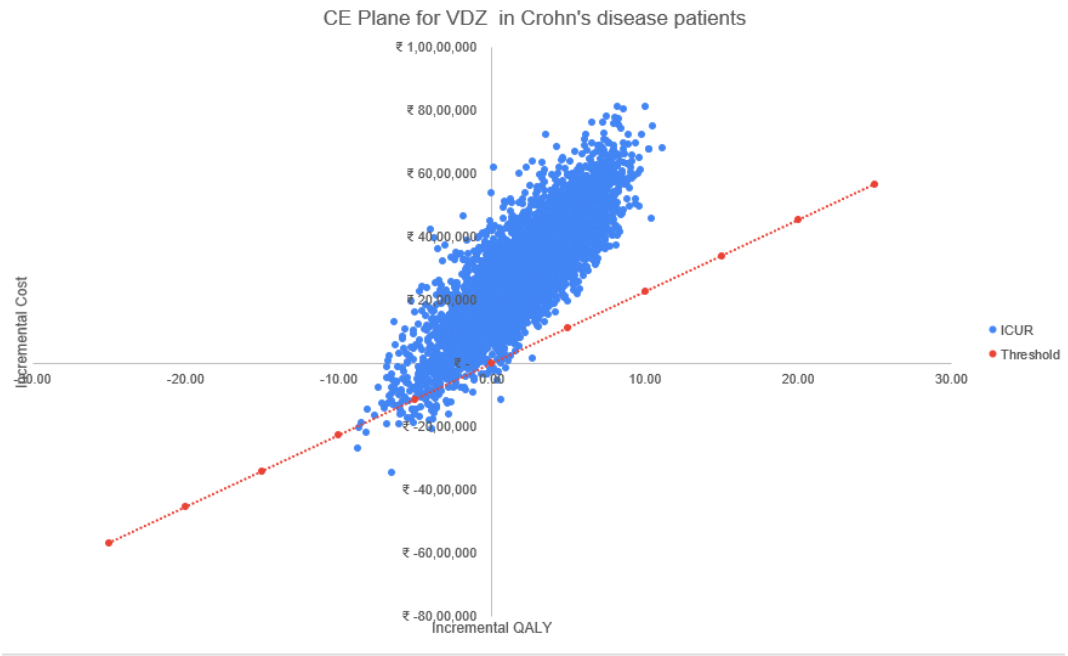


Figure 4.2.2.2 CE-plane for VDZ vs CT among the CD population

The CEAC, considering the WTP threshold, the probability that VDZ is cost-effective compared to CT among the UC population and CD population is given in Figure 4.2.2.3 and Figure 4.2.2.4, respectively.

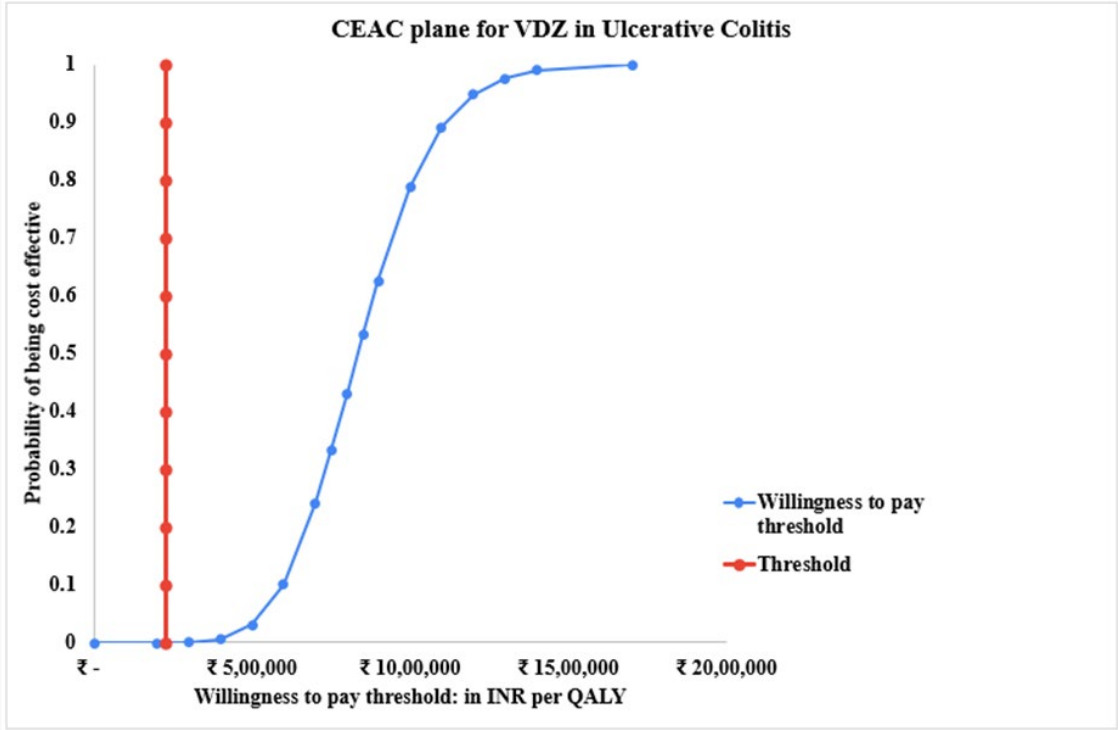


Figure 4.2.2.3 CEAC for VDZ vs CT among the UC population

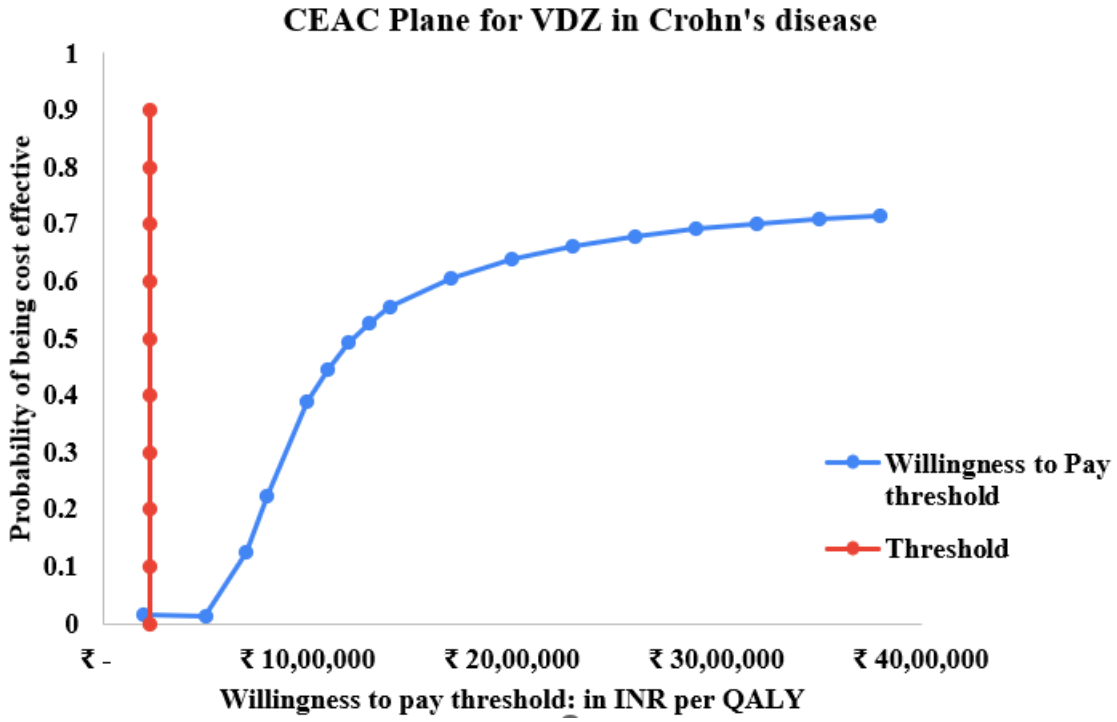


Figure 4.2.2.4 CEAC for VDZ vs CT among the CD population

4.3 Threshold analysis

For both the UC and CD populations, VDZ is not cost-effective in terms of market drug prices. Hence, a threshold analysis was conducted to determine the market drug price at which VDZ would be cost-effective. With a 70% reduction in the drug price (at ₹ 21,239), VDZ will be cost-effective for UC patients. Also, with a 76% reduction in the drug price (at ₹ 16,847), VDZ will be cost-effective for CD patients.

4.4 Scenario analysis

Since VDZ is not cost-effective for both UC and CD mixed population, which includes both anti-TNF-alpha naïve and anti-TNF alpha failure patients, we conducted scenario analyses for the anti-TNF alpha naïve population and the anti-TNF alpha failure population with UC/CD.

4.4.1 Anti-TNF alpha naïve population with moderately to severely active ulcerative colitis/Crohn's disease

In the scenario analysis, for the Anti-TNF alpha naïve population with moderately to severely active UC and CD, the ICUR of VDZ compared to CT is higher than the WTP threshold of one-time GDP per capita for India; hence, it is not cost-effective. (Table 4.4.1)

Table 4.4.1 Scenario Analysis: Results in the UC/CD Anti–TNF Alpha naïve

	Ulcerative colitis		Crohn's disease	
	Vedolizumab	Conventional therapy	Vedolizumab	Conventional therapy
Total Cost	₹ 49,03,776	₹ 15,90,548	₹ 41,02,305	₹ 21,61,917
Total LY	16.465	16.465	15.975	15.975
Total QALY	8.689	4.847	7.800	6.357
NMB	₹ -29,33,306	₹ -4,91,415	₹ -23,33,596	₹ -7,20,434
Incremental Cost	₹ 33,13,228		₹ 19,40,389	
Incremental QALY	3.842		1.443	
ICER per QALY	₹ 8,62,270		₹ 13,44,675	
INB	₹ -24,41,891		₹ -16,13,161	

4.4.2 Anti-TNF alpha failure population with moderately to severely active ulcerative colitis/Crohn's disease

In the scenario analysis, for the Anti-TNF alpha failure population with moderately to severely active UC and CD, the ICUR of VDZ compared to CT is higher than the WTP threshold of one-time GDP per capita for India; hence, it is not cost-effective. (Table 4.4.1)

Table 4.4.2 Scenario Analysis: Results in the UC/CD Anti–TNF Alpha failure

	Ulcerative colitis		Crohn's disease	
	Vedolizumab	Conventional therapy	Vedolizumab	Conventional therapy
Total Cost	₹ 41,07,580	₹ 16,27,786	₹ 41,37,562	₹ 22,63,339
Total LY	16.465	16.465	15.975	15.975
Total QALY	7.856	4.896	7.898	5.668
NMB	₹ -23,26,028	₹ -5,17,592	₹ -23,46,530	₹ -9,78,072
Incremental Cost	₹ 24,79,794		₹ 18,74,223	
Incremental QALY	2.961		2.230	
ICER per QALY	₹ 8,37,606		₹ 8,40,332	
INB	₹ -18,08,436		₹ -13,68,459	

5. Discussion

The Health Technology Assessment evaluated the cost-effectiveness of Vedolizumab IV 300 mg compared to conventional therapies for managing moderately to severely active inflammatory bowel diseases, including ulcerative colitis and Crohn's disease, within the Indian healthcare context using a health system perspective. The analysis revealed that VDZ is not cost-effective at its current market price for UC or CD populations (mixed, naïve, failure), as its incremental cost-utility ratios exceed the willingness-to-pay threshold of one-time India's gross domestic product per capita.

Sensitivity analyses demonstrated minimal variability in ICURs across a range of plausible model inputs for UC, and the probability of no response to CT during the induction phase has the most significant impact on ICURs for CD. Probabilistic sensitivity analysis affirmed

consistency with base-case results, further substantiating the drug's lack of cost-effectiveness at the current market price. Threshold analysis indicated that a price reduction of approximately 70% for UC and 76% for CD would be required for VDZ to meet cost-effectiveness criteria for the mixed population.

The cost-effectiveness of VDZ for UC shows substantial variation across studies based on patient subgroups and healthcare contexts. Most of the model-based studies CUAs were from HICs and the health system's perspective, limiting results to other contexts. For biologic-naïve populations, Wilson et al. (2017) demonstrated cost-effectiveness in the UK when compared to standard care under a health system perspective (51), aligning with findings from Japan by Hernandez et al. (2020) (41), where VDZ was cost-effective against infliximab and golimumab. However, results from Canada (72) and Poland (73) indicate Vedolizumab is non-cost-effective for TNF-naïve UC populations. Additionally, evidence from the USA emphasizes limited feasibility for broader adoption due to higher drug acquisition costs and WTP thresholds. (74) In CD, evidence points to a similar trend of variability. Zhou et al. (2021) in China highlighted cost-effectiveness for mixed and TNF-naïve populations, demonstrating potential affordability in MICs. (42) Conversely, findings from across Europe (37) and in luminal CD populations (38) reported consistent non-cost-effectiveness for Vedolizumab in TNF-naïve patients due to high costs and limited incremental benefits. For TNF-i exposed CD populations, evidence, such as Petryszyn et al. (2020) in Poland, suggests cost-effectiveness under societal perspectives but highlights limited generalizability.

The findings in this study emphasize the limited affordability and financial feasibility of Vedolizumab in India without substantial price reductions and underscore the significant role of pricing strategies. Vedolizumab holds promise for select subgroups, but its broader adoption requires substantial price reductions to align with affordability thresholds, particularly in LMICs like India.

This study adopted a comprehensive approach, employing a Markov decision-analytic model validated against international standards. The study ensured contextual relevance by incorporating India-specific cost data and market searches. Including multiple scenarios, price reductions, and sensitivity analyses enhances the study's applicability for policymakers. The absence of India-specific utility values for health states related to IBD necessitated reliance on international data, potentially limiting the precision of QALY estimations. The study relied on clinical trial data for efficacy inputs, which may not fully capture real-world effectiveness and adherence patterns in the Indian context. Although justified by the lack of cost-effectiveness at current prices, the absence of a budget impact analysis limits insights into the financial implications of broader adoption. Also, the study did not explicitly address equity implications, crucial in LMICs where socioeconomic disparities significantly affect healthcare access.

The findings underscore the necessity of price negotiations or alternative pricing mechanisms for Vedolizumab in India. Policymakers should consider strategies such as volume-based discounts, encouraging manufacturers to offer reduced pricing based on procurement volumes, and tailored pricing models, which align costs with India's economic conditions through differential pricing. Vedolizumab could serve as a treatment option for select patient subgroups, such as those with severe disease refractory to conventional therapies or at high risk of adverse events from TNF inhibitors. However, its adoption should be guided by cost-sharing arrangements or availability through health insurance schemes. Improved accessibility to biologic therapies like Vedolizumab could substantially enhance the quality of life for patients with severe UC or CD. However, the current cost barriers highlight the need for supportive policies to ensure equitable access.

In the future, conducting primary research to derive utility values specific to Indian populations would enhance the accuracy of future economic evaluations. Longitudinal studies capturing Vedolizumab's real-world effectiveness, adherence, and safety in India could refine cost-

effectiveness estimates. Future HTAs should explicitly incorporate equity considerations, assessing the distributional impact of Vedolizumab across socioeconomic groups. A detailed assessment of the financial implications of Vedolizumab adoption under various pricing scenarios would provide actionable insights for policymakers.

6. Conclusion

Vedolizumab IV 300 mg, while clinically effective, is not cost-effective at its current market price as compared to conventional therapy in the management of moderate to severe active ulcerative colitis and Crohn's disease in India. Even within specific subgroups of IBD, such as the anti–TNF alpha naive population, the anti–TNF alpha failure population, and the mixed population based on prior exposure, VDZ remains not cost-effective. Substantial price reductions are essential to align its economic value with the WTP threshold.

With a reduction of about 70% in the VDZ market price for the mixed UC population, VDZ will become more cost-effective than conventional therapy. Similarly, with a 76% reduction in market price, VDZ will be cost-effective for the mixed CD population. These findings provide a foundation for informed decision-making and highlight critical areas for policy decisions and future drug price negotiations to ensure equitable and economically efficient management of IBD in India.

7. Study Recommendations

- Vedolizumab IV 300 mg is not cost-effective in India for treating moderate-to-severe active Ulcerative colitis and Crohn's disease; hence, it is not recommended at the current market price in the Indian context.
- Strategies such as price negotiations with manufacturers, tiered pricing for India to make Vedolizumab a cost-effective treatment option in the Indian context, a price reduction of approximately 70%, 76% in the market price of Vedolizumab IV 300 mg is recommended for Ulcerative colitis and Crohn's Disease respectively.
- There is a need for longitudinal, real-world studies in India to assess Vedolizumab's effectiveness, safety, and adherence patterns among patients with Ulcerative colitis and Crohn's disease.
- It is essential to develop local utility values for Ulcerative colitis and Crohn's disease health states in India, as these values are crucial for improving the precision of economic evaluations.

8. Appendix

Appendix I: Model input parameters for TNF alpha naïve and failure population UC/CD

Input Parameters	Mean	SE	Distribution	Reference
Naive				
P_UC_VDZ_Indu_Mixed_Mod_response	0.531	0.044	Beta	(75)
P_UC_VDZ_Indu_Mixed_Mod_No-response	0.469	0.033	Beta	(75)
P_UC_CT_Indu_Mixed_total_response	0.263	0.036	Beta	(75)
P_UC_CT_Indu_Mixed_total_No-response	0.737	0.036	Beta	(75)
P_CD_VDZ_Indu_Mixed_Mod_response	0.321	0.041	Beta	(76)
P_CD_VDZ_Indu_Mixed_Mod_No-response	0.679	0.033	Beta	(76)
P_CD_CT_Indu_Mixed_Mod_response	0.206	0.038	Beta	(76)
P_CD_CT_Indu_Mixed_Mod_No-response	0.794	0.202	Beta	(76)
P_CD_VDZ_Indu_Remission	0.161	0.038	Beta	(76)
P_CD_CT_Indu_Remission	0.100	0.020	Beta	(76)
P_CD_VDZ_Indu_Clinical_response	0.160	0.142	Beta	(76)
P_CD_CT_Indu_Clinical_response	0.105	0.005	Beta	(76)
P_UC_VDZ_Indu_Remission	0.231	0.012	Beta	(75)
P_UC_VDZ_Indu_Clinical_response	0.300	0.015	Beta	(75)
P_UC_CT_Indu_Remission	0.066	0.003	Beta	(75)
P_UC_CT_Indu_Clinical_response	0.197	0.010	Beta	(75)
P_CD_sur	0.300	0.015	Beta	(76)
P_CD_Indu_CNr	0.700	0.035	Beta	(76)
P_UC_sur	0.300	0.015	Beta	(75)
P_UC_Indu_CNr	0.700	0.035	Beta	(75)
p_uc_mx_v_rtom	0.073	0.004	Beta	(75)
p_uc_mx_v_rtor	0.927	0.046	Beta	(75)
p_uc_mx_v_mtom	0.574	0.029	Beta	(75)
p_uc_mx_v_mtomds	0.164	0.008	Beta	(75)
p_uc_mx_v_mdstom	0.212	0.011	Beta	(75)
p_uc_mx_v_mtor	0.262	0.013	Beta	(75)
p_uc_mx_v_mdstosur	0.008	0.000	Beta	(75)
p_uc_mx_v_mdstomds	0.780	0.039	Beta	(75)
p_uc_mx_c_rtom	0.979	0.049	Beta	(75)
p_uc_mx_c_rtor	0.916	0.046	Beta	(75)
p_uc_mx_c_mtom	0.542	0.027	Beta	(75)
p_uc_mx_c_mtomds	0.438	0.022	Beta	(75)
p_uc_mx_c_mtor	0.020	0.001	Beta	(75)

p_uc_mx_c_mdstom	0.013	0.001	Beta	(75)
p_uc_mx_c_mdstomds	0.979	0.049	Beta	(75)
p_uc_mx_c_mdstosur	0.008	0.000	Beta	(75)
p_uc_sur_psurc	0.500	0.025	Beta	(75)
p_uc_sur_postsurr	0.450	0.023	Beta	(75)
p_uc_sur_sur	0.050	0.003	Beta	(75)
p_uc_psurr_sur	0.050	0.003	Beta	(75)
p_uc_psurr_psurr	0.777	0.039	Beta	(75)
p_uc_psurr_psurc	0.173	0.009	Beta	(75)
p_uc_psurc_sur	0.050	0.003	Beta	(75)
p_uc_psurc_psurc	0.705	0.035	Beta	(75)
p_uc_psurc_psurr	0.245	0.012	Beta	(75)
p_cd_mx_v_rtom	0.031	0.002	Beta	(76)
p_cd_mx_v_rtor	0.969	0.048	Beta	(76)
p_cd_mx_v_mtom	0.560	0.028	Beta	(76)
p_cd_mx_v_mtomds	0.208	0.010	Beta	(76)
p_cd_mx_v_mdstom	0.180	0.009	Beta	(76)
p_cd_mx_v_mtor	0.232	0.012	Beta	(76)
p_cd_mx_v_mdstosur	0.027	0.001	Beta	(76)
p_cd_mx_v_mdstomds	0.793	0.040	Beta	(76)
p_cd_mx_c_rtom	0.080	0.004	Beta	(76)
p_cd_mx_c_rtor	0.920	0.046	Beta	(76)
p_cd_mx_c_mtom	0.588	0.029	Beta	(76)
p_cd_mx_c_mtomds	0.387	0.019	Beta	(76)
p_cd_mx_c_mdstom	0.054	0.003	Beta	(76)
p_cd_mx_c_mdstomds	0.919	0.046	Beta	(76)
p_cd_mx_c_mdstosur	0.027	0.001	Beta	(76)
p_cd_mx_surtor	0.775	0.039	Beta	(76)
p_cd_mx_surtom	0.113	0.006	Beta	(76)
p_cd_mx_surtomds	0.085	0.004	Beta	(76)
p_cd_mx_surtosur	0.027	0.001	Beta	(76)
Failure				
P_UC_VDZ_Indu_Mixed_Mod_response	0.390	0.054	Beta	(75)
P_UC_VDZ_Indu_Mixed_Mod_No-response	0.610	0.033	Beta	(75)
P_UC_CT_Indu_Mixed_total_response	0.206	0.036	Beta	(75)
P_UC_CT_Indu_Mixed_total_No-response	0.794	0.036	Beta	(75)
P_CD_VDZ_Indu_Mixed_Mod_response	0.320	0.041	Beta	(76)
P_CD_VDZ_Indu_Mixed_Mod_No-response	0.680	0.033	Beta	(76)
P_CD_CT_Indu_Mixed_Mod_response	0.220	0.038	Beta	(76)

P_CD_CT_Indu_Mixed_Mod_No-response	0.780	0.202	Beta	(76)
P_CD_VDZ_Indu_Remission	0.170	0.038	Beta	(76)
P_CD_CT_Indu_Remission	0.080	0.020	Beta	(76)
P_CD_VDZ_Indu_Clinical_response	0.190	0.142	Beta	(76)
P_CD_CT_Indu_Clinical_response	0.140	0.007	Beta	(76)
P_UC_VDZ_Indu_Remission	0.231	0.012	Beta	(75)
P_UC_VDZ_Indu_Clinical_response	0.159	0.008	Beta	(75)
P_UC_CT_Indu_Remission	0.032	0.002	Beta	(75)
P_UC_CT_Indu_Clinical_response	0.175	0.009	Beta	(75)
P_CD_sur	0.300	0.015	Beta	(76)
P_CD_Indu_CNr	0.700	0.035	Beta	(76)
P_UC_sur	0.300	0.015	Beta	(75)
P_UC_Indu_CNr	0.700	0.035	Beta	(75)
p_uc_mx_v_rtom	0.073	0.004	Beta	(75)
p_uc_mx_v_rtor	0.927	0.046	Beta	(75)
p_uc_mx_v_mtom	0.574	0.029	Beta	(75)
p_uc_mx_v_mtomds	0.164	0.008	Beta	(75)
p_uc_mx_v_mdstom	0.212	0.011	Beta	(75)
p_uc_mx_v_mtor	0.262	0.013	Beta	(75)
p_uc_mx_v_mdstosur	0.008	0.000	Beta	(75)
p_uc_mx_v_mdstomds	0.780	0.039	Beta	(75)
p_uc_mx_c_rtom	0.084	0.004	Beta	(75)
p_uc_mx_c_rtor	0.916	0.046	Beta	(75)
p_uc_mx_c_mtom	0.542	0.027	Beta	(75)
p_uc_mx_c_mtomds	0.438	0.022	Beta	(75)
p_uc_mx_c_mtor	0.020	0.001	Beta	(75)
p_uc_mx_c_mdstom	0.013	0.001	Beta	(75)
p_uc_mx_c_mdstomds	0.979	0.049	Beta	(75)
p_uc_mx_c_mdstosur	0.008	0.000	Beta	(75)
p_uc_sur_psurc	0.500	0.025	Beta	(75)
p_uc_sur_postsurr	0.450	0.023	Beta	(75)
p_uc_sur_sur	0.050	0.003	Beta	(75)
p_uc_psurr_sur	0.050	0.003	Beta	(75)
p_uc_psurr_psurr	0.777	0.039	Beta	(75)
p_uc_psurr_psurc	0.173	0.009	Beta	(75)
p_uc_psurc_sur	0.050	0.003	Beta	(75)
p_uc_psurc_psurc	0.705	0.035	Beta	(75)
p_uc_psurc_psurr	0.245	0.012	Beta	(75)
p_uc_mx_cnr_mdstomds	0.982	0.049	Beta	(75)

p_cd_mx_v_rtom	0.021	0.001	Beta	(76)
p_cd_mx_v_rtor	0.979	0.049	Beta	(76)
p_cd_mx_v_mtom	0.531	0.027	Beta	(76)
p_cd_mx_v_mtomds	0.240	0.012	Beta	(76)
p_cd_mx_v_mdstom	0.137	0.007	Beta	(76)
p_cd_mx_v_mtor	0.229	0.011	Beta	(76)
p_cd_mx_v_mdstosur	0.027	0.001	Beta	(76)
p_cd_mx_v_mdstomds	0.836	0.042	Beta	(76)
p_cd_mx_c_rtom	0.121	0.006	Beta	(76)
p_cd_mx_c_rtor	0.879	0.044	Beta	(76)
p_cd_mx_c_mtom	0.600	0.030	Beta	(76)
p_cd_mx_c_mtomds	0.400	0.020	Beta	(76)
p_cd_mx_c_mdstom	0.020	0.001	Beta	(76)
p_cd_mx_c_mdstomds	0.953	0.048	Beta	(76)
p_cd_mx_c_mdstosur	0.027	0.001	Beta	(76)
p_cd_mx_surtor	0.775	0.039	Beta	(76)
p_cd_mx_surtom	0.113	0.006	Beta	(76)
p_cd_mx_surtomds	0.085	0.004	Beta	(76)
p_cd_mx_surtosur	0.027	0.001	Beta	(76)

Appendix II: CHEERS 2022 Checklist (Model-based economic evaluation of VDZ vs CT)

Topic	No.	Item	Location where item is reported
	1	Identify the study as an economic evaluation and specify the interventions being compared.	Yes
	2	Provide a structured summary that highlights context, key methods, results, and alternative analyses.	NA
Introduction			
Background and objectives	3	Give the context for the study, the study question, and its practical relevance for decision-making in policy or practice.	Yes
Methods			
Health economic analysis plan	4	Indicate whether a health economic analysis plan was developed and where available.	Yes
Study population	5	Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).	Yes
Setting and location	6	Provide relevant contextual information that may influence findings.	Yes
Comparators	7	Describe the interventions or strategies being compared and why chosen.	Yes
Perspective	8	State the perspective(s) adopted by the study and why chosen.	Yes
Time horizon	9	State the time horizon for the study and why appropriate.	Yes
Discount rate	10	Report the discount rate(s) and reason chosen.	Yes
Selection of outcomes	11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).	Yes
Measurement of outcomes	12	Describe how outcomes used to capture benefit(s) and harm(s) were measured.	Yes
Valuation of outcomes	13	Describe the population and methods used to measure and value outcomes.	Yes
Measurement and valuation of resources and costs	14	Describe how costs were valued.	Yes
Currency, price date, and conversion	15	Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion.	Yes
Rationale and description of model	16	If modelling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed.	Yes
Analytics and assumptions	17	Describe any methods for analyzing or statistically transforming data, any extrapolation methods, and approaches for validating any model used.	Yes
Characterizing heterogeneity	18	Describe any methods used for estimating how the results of the study vary for subgroups.	Yes
Characterizing distributional effects	19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.	Yes
Characterizing uncertainty	20	Describe methods to characterize any sources of uncertainty in the analysis.	Yes
Approach to engagement with patients and others affected by the study	21	Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (such as clinicians or payers) in the design of the study.	Yes
Results			
Study parameters	22	Report all analytic inputs (such as values, ranges, references) including uncertainty or distributional assumptions.	Yes
Summary of main results	23	Report the mean values for the main categories of costs and outcomes of interest and summarise them in the most appropriate overall measure.	Yes
Effect of uncertainty	24	Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable.	Yes
Effect of engagement with patients and others affected by the study	25	Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study	Yes
Discussion			

Topic	No.	Item	Location where item is reported
Study findings, limitations, generalisability, and current knowledge	26	Report key findings, limitations, ethical or equity considerations not captured, and how these could affect patients, policy, or practice.	Yes
Other relevant information			
Source of funding	27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis	NA
Conflicts of interest	28	Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.	NA

9. References

1. Adolph TE, Meyer M, Schwärzler J, Mayr L, Grabherr F, Tilg H. The metabolic nature of inflammatory bowel diseases. Nat Rev Gastroenterol Hepatol. 2022;19(12):753-67.
2. Irvine JE. Quality of life of patients with ulcerative colitis: past, present, and future. Inflammatory bowel diseases. 2008;14(4):554-65.
3. Molodecky NA, Soon S, Rabi DM, Ghali WA, Ferris M, Chernoff G, et al. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. Gastroenterology. 2012;142(1):46-54. e42.
4. Prideaux L, Kamm MA, De Cruz PP, Chan FK, Ng SC. Inflammatory bowel disease in Asia: a systematic review. Journal of gastroenterology and hepatology. 2012;27(8):1266-80.
5. Khosla S, Girdhar N, Lal S, Mishra D. Epidemiology of ulcerative colitis in hospital and select general population of northern India. The Journal of the Association of Physicians of India. 1986;34(6):405-7.
6. Sood A, Midha V, Sood N, Bhatia A, Avasthi G. Incidence and prevalence of ulcerative colitis in Punjab, North India. Gut. 2003;52(11):1587-90.
7. Makharia GK, Ramakrishna BS, Abraham P, Choudhuri G, Misra SP, Ahuja V, et al. Survey of inflammatory bowel diseases in India. Indian Journal of Gastroenterology. 2012;31:299-306.
8. Liu JZ, Van Sommeren S, Huang H, Ng SC, Alberts R, Takahashi A, et al. Association analyses identify 38 susceptibility loci for inflammatory bowel disease and highlight shared genetic risk across populations. Nature genetics. 2015;47(9):979-86.
9. Jantchou P, Morois S, Clavel-Chapelon F, Boutron-Ruault M-C, Carbonnel F. Animal protein intake and risk of inflammatory bowel disease: The E3N prospective study. Official journal of the American College of Gastroenterology| ACG. 2010;105(10):2195-201.
10. Jowett S, Seal C, Pearce M, Phillips E, Gregory W, Barton J, et al. Influence of dietary factors on the clinical course of ulcerative colitis: a prospective cohort study. Gut. 2004;53(10):1479-84.
11. Ng SC, Tang W, Leong RW, Chen M, Ko Y, Studd C, et al. Environmental risk factors in inflammatory bowel disease: a population-based case-control study in Asia-Pacific. Gut. 2015;64(7):1063-71.
12. Makharia GK, Sachdev V, Gupta R, Lal S, Pandey R. Anti-Saccharomyces cerevisiae antibody does not differentiate between Crohn's disease and intestinal tuberculosis. Digestive diseases and sciences. 2007;52:33-9.
13. Brandt LJ, Chey WD, Foxx-Orenstein AE, Quigley EM, Schiller LR, Schoenfeld PS, et al. An evidence-based position statement on the management of irritable bowel syndrome. American Journal of Gastroenterology (Springer Nature). 2009;104.
14. Das K, Ghoshal UC, Dhali GK, Benjamin J, Ahuja V, Makharia GK. Crohn’s disease in India: a multicenter study from a country where tuberculosis is endemic. Digestive diseases and sciences. 2009;54:1099-107.
15. Ghoshal UC, Abraham P, Bhatt C, Choudhuri G, Bhatia SJ, Shenoy KT, et al. Epidemiological and clinical profile of irritable bowel syndrome in India: report of the Indian Society of Gastroenterology Task Force. Indian J Gastroenterol. 2008;27(1):22-8.
16. Sood A, Kaur K, Mahajan R, Midha V, Singh A, Sharma S, et al. Colitis and Crohn’s Foundation (India): a first nationwide inflammatory bowel disease registry. Intestinal research. 2021;19(2):206.
17. Bressler B, Marshall JK, Bernstein CN, Bitton A, Jones J, Leontiadis GI, et al. Clinical practice guidelines for the medical management of nonhospitalized ulcerative colitis: the Toronto consensus. Gastroenterology. 2015;148(5):1035-58. e3.
18. Sood A, Kaur K, Mahajan R, Midha V, Singh A, Sharma S, et al. Colitis and Crohn's Foundation (India): a first nationwide inflammatory bowel disease registry. Intest Res. 2021;19(2):206-16.

19. Iskandar HN, Dhere T, Farraye FA. Ulcerative Colitis: Update on Medical Management. Curr Gastroenterol Rep. 2015;17(11):44.
20. Iskandar HN, Dhere T, Farraye FA. Ulcerative colitis: update on medical management. Current gastroenterology reports. 2015;17:1-11.
21. Wyant T, Fedyk E, Abhyankar B. An overview of the mechanism of action of the monoclonal antibody vedolizumab. Journal of Crohn's and Colitis. 2016;10(12):1437-44.
22. Danese S, Vuitton L, Peyrin-Biroulet L. Biologic agents for IBD: practical insights. Nature reviews Gastroenterology & hepatology. 2015;12(9):537-45.
23. Ray G. Inflammatory bowel disease in India—changing paradigms. International journal of colorectal disease. 2011;26:635-44.
24. Jain M, Venkataraman J. Inflammatory bowel disease: An Indian perspective. Indian J Med Res. 2021;153(4):421-30.
25. Park K, Bass D. Inflammatory bowel disease-attributable costs and cost-effective strategies in the United States: a review. Inflammatory bowel diseases. 2011;17(7):1603-9.
26. Feagan BG, Rutgeerts P, Sands BE, Hanauer S, Colombel JF, Sandborn WJ, et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2013;369(8):699-710.
27. Sandborn WJ, Feagan BG, Rutgeerts P, Hanauer S, Colombel JF, Sands BE, et al. Vedolizumab as induction and maintenance therapy for Crohn's disease. N Engl J Med. 2013;369(8):711-21.
28. Scribano ML. Vedolizumab for inflammatory bowel disease: From randomized controlled trials to real-life evidence. World J Gastroenterol. 2018;24(23):2457-67.
29. Soler D, Chapman T, Yang LL, Wyant T, Egan R, Fedyk ER. The binding specificity and selective antagonism of vedolizumab, an anti-alpha4beta7 integrin therapeutic antibody in development for inflammatory bowel diseases. J Pharmacol Exp Ther. 2009;330(3):864-75.
30. Milch C, Wyant T, Xu J, Kent W, Berger J, Fox IH. P234 Vedolizumab does not reduce the CD4+:CD8+ ratio in the CSF of healthy volunteers. Journal of Crohn's and Colitis. 2012;6(Supplement_1):S102-S3.
31. Fedyk E, Csizmadia V, Shyu W, Yang L, Wyant T, Kadambi V. The gastrointestinal-selective biologic vedolizumab does not impair immune surveillance of the central nervous system in non-human primates.: O-015. Inflammatory Bowel Diseases. 2011;17(suppl_1):S4-S5.
32. Leung Y, Panaccione R. Anti-adhesion molecule strategies for Crohn disease. BioDrugs. 2008;22(4):259-64.
33. Ben-Horin S, Chowers Y. Review article: loss of response to anti-TNF treatments in Crohn's disease. Aliment Pharmacol Ther. 2011;33(9):987-95.
34. Wilson M, Mody R, Ursan I, Carr S. Sa1019 Cost-Effectiveness of Vedolizumab Compared With Conventional Therapy and Biologics for Treatment of Moderately to Severely Active Ulcerative Colitis in the United States. Gastroenterology. 2015;148(4):S-198-S-9.
35. Erim DO, Mahendraratnam N, Okafor PN, Wheeler SB. The value of vedolizumab as rescue therapy in moderate-severe Crohn’s disease patients with adalimumab non-response in the USA. Journal of Crohn's and Colitis. 2015;9(8):669-75.
36. Bounthavong M, Bae Y, Devine B, Veenstra D. A cost-utility analysis of biologics for moderate-to-severe Crohn’s disease: evidence synthesis using a Bayesian network meta-analysis. Value in Health. 2015;18(3):A224-A5.
37. Baji P, Gulácsi L, Brodszky V, Végh Z, Danese S, Irving PM, et al. Cost-effectiveness of biological treatment sequences for fistulising Crohn’s disease across Europe. United European Gastroenterology Journal. 2018;6(2):310-21.
38. Rencz F, Gulácsi L, Péntek M, Gecse KB, Dignass A, Halfvarson J, et al. Cost-utility of biological treatment sequences for luminal Crohn’s disease in Europe. Expert Review of Pharmacoeconomics & Outcomes Research. 2017;17(6):597-606.

39. Holko P, Kawalec P, Pilc A. Cost-effectiveness analysis of Crohn's disease treatment with vedolizumab and ustekinumab after failure of tumor necrosis factor-α antagonist. PharmacoEconomics. 2018;36:853-65.
40. Bouhnik Y, Atreya R, Casey D, Górecki M, Baik D, Yoon SW, et al. Cost-effectiveness Analysis of Subcutaneous Infliximab for Inflammatory Bowel Diseases in Sequential Biologic Treatment. Inflammatory Bowel Diseases. 2022;29(6):898-913.
41. Hernandez L, Kuwabara H, Shah A, Yamabe K, Burnett H, Fahrbach K, et al. Cost-effectiveness analysis of vedolizumab compared with other biologics in anti-TNF-naïve patients with moderate-to-severe ulcerative colitis in Japan. Pharmacoeconomics. 2020;38:69-84.
42. Zhou T, Sheng Y, Guan H. Cost-Effectiveness of Vedolizumab in the Treatment of Moderate-to-Severe Crohn's Disease in China. Adv Ther. 2021;38(8):4233-45.
43. Agace WW. Tissue-tropic effector T cells: generation and targeting opportunities. Nature Reviews Immunology. 2006;6(9):682-92.
44. Sandborn WJ, Colombel JF, Enns R, Feagan BG, Hanauer SB, Lawrance IC, et al. Natalizumab induction and maintenance therapy for Crohn's disease. N Engl J Med. 2005;353(18):1912-25.
45. Kappelman MD, Rifas-Shiman SL, Porter CQ, Ollendorf DA, Sandler RS, Galanko JA, et al. Direct health care costs of Crohn's disease and ulcerative colitis in US children and adults. Gastroenterology. 2008;135(6):1907-13.
46. Kamat N, Ganesh Pai C, Surulivel Rajan M, Kamath A. Cost of Illness in Inflammatory Bowel Disease. Dig Dis Sci. 2017;62(9):2318-26.
47. Sood A, Ahuja V, Midha V, Sinha SK, Pai CG, Kedia S, et al. Colitis and Crohn's Foundation (India) consensus statements on use of 5-aminosalicylic acid in inflammatory bowel disease. Intest Res. 2020;18(4):355-78.
48. Sharma D, Prinja S, Aggarwal AK, Rajsekar K, Bahuguna P. Development of the Indian Reference Case for undertaking economic evaluation for health technology assessment. The Lancet Regional Health-Southeast Asia. 2023.
49. Hui S, Sinopoulou V, Gordon M, Aali G, Krishna A, Ding NS, et al. Vedolizumab for induction and maintenance of remission in Crohn's disease. Cochrane Database Syst Rev. 2023;7(7):Cd013611.
50. SRS. ABRIDGED LIFE TABLES 2020 [updated Nov 1, 2022. Available from: https://censusindia.gov.in/census.website/data/SRSALT.
51. Wilson MR, Azzabi Zouraq I, Chevrou-Severac H, Selby R, Kerrigan MC. Cost-effectiveness of vedolizumab compared with conventional therapy for ulcerative colitis patients in the UK. ClinicoEconomics and Outcomes Research. 2017:641-52.
52. Wu B, Wang Z, Zhang Q. Cost-Effectiveness of Different Strategies for the Treatment of Moderate-to-Severe Ulcerative Colitis. Inflammatory Bowel Diseases. 2018;24(11):2291-302.
53. Mosli MH, MacDonald JK, Bickston SJ, Behm BW, Tsoulis DJ, Cheng J, et al. Vedolizumab for Induction and Maintenance of Remission in Ulcerative Colitis: A Cochrane Systematic Review and Meta-analysis. Inflammatory Bowel Diseases. 2015;21(5):1151-9.
54. Hoshino N, Hida K, Yoshida S, Ueno K, Noguchi T, Ishihara S, et al. Postoperative complications and prognosis based on type of surgery in ulcerative colitis patients with colorectal cancer: A multicenter observational study of data from the Japanese Society for Cancer of the Colon and Rectum. Annals of Gastroenterological Surgery. 2023;7(4):626-36.
55. Kim JY, Zaghiyan K, Lightner A, Fleshner P. Risk of postoperative complications among ulcerative colitis patients treated preoperatively with vedolizumab: a matched case-control study. BMC Surgery. 2020;20(1):46.
56. Baker DM, Folan A-M, Lee MJ, Jones GL, Brown SR, Lobo AJ. A systematic review and meta-analysis of outcomes after elective surgery for ulcerative colitis. Colorectal Disease. 2021;23(1):18-33.
57. Pal S, Sahni P, Pande GK, Acharya SK, Chattopadhyay TK. Outcome following emergency surgery for refractory severe ulcerative colitis in a tertiary care centre in India. BMC Gastroenterology. 2005;5(1):39.

58. Macaluso FS, Ventimiglia M, Orlando A. Effectiveness and Safety of Vedolizumab in Inflammatory Bowel Disease: A Comprehensive Meta-analysis of Observational Studies. Journal of Crohn's and Colitis. 2023;17(8):1217-27.
59. Arseneau KO, Sultan S, Provenzale DT, Onken J, Bickston SJ, Foley E, et al. Do Patient Preferences Influence Decisions on Treatment for Patients With Steroid-Refractory Ulcerative Colitis? Clinical Gastroenterology and Hepatology. 2006;4(9):1135-42.
60. Porco TC, Lewis B, Marseille E, Grinsdale J, Flood JM, Royce SE. Cost-effectiveness of tuberculosis evaluation and treatment of newly-arrived immigrants. BMC Public Health. 2006;6(1):157.
61. Hornberger J, Reyes C, Lubeck D, Valente N. Economic evaluation of rituximab plus cyclophosphamide, vincristine and prednisolone for advanced follicular lymphoma. Leukemia & Lymphoma. 2008;49(2):227-36.
62. Beusterien KM, Szabo SM, Kotapati S, Mukherjee J, Hoos A, Hersey P, et al. Societal preference values for advanced melanoma health states in the United Kingdom and Australia. British Journal of Cancer. 2009;101(3):387-9.
63. Beusterien KM, Davies J, Leach M, Meiklejohn D, Grinspan JL, O'Toole A, et al. Population preference values for treatment outcomes in chronic lymphocytic leukaemia: a cross-sectional utility study. Health and Quality of Life Outcomes. 2010;8(1):50.
64. Xu R, Insinga RP, Golden W, Hu XH. EuroQol (EQ-5D) health utility scores for patients with migraine. Quality of Life Research. 2011;20(4):601-8.
65. Brown RE, Hutton J, Burrell A. Cost Effectiveness of Treatment Options in Advanced Breast Cancer in the UK. PharmacoEconomics. 2001;19(11):1091-102.
66. Haridoss M, Bagepally BS, Natarajan M. Health-related quality of life in rheumatoid arthritis: Systematic review and meta-analysis of EuroQoL (EQ-5D) utility scores from Asia. International Journal of Rheumatic Diseases. 2021;24(3):314-26.
67. Falk Hvidberg M, Hernández Alava M. Catalogues of EQ-5D-3L Health-Related Quality of Life Scores for 199 Chronic Conditions and Health Risks for Use in the UK and the USA. PharmacoEconomics. 2023;41(10):1287-388.
68. Sands BE, Feagan BG, Rutgeerts P, Colombel JF, Sandborn WJ, Sy R, et al. Effects of vedolizumab induction therapy for patients with Crohn's disease in whom tumor necrosis factor antagonist treatment failed. Gastroenterology. 2014;147(3):618-27.e3.
69. Buxton MJ, Lacey LA, Feagan BG, Niecko T, Miller DW, Townsend RJ. Mapping from Disease-Specific Measures to Utility: An Analysis of the Relationships between the Inflammatory Bowel Disease Questionnaire and Crohn's Disease Activity Index in Crohn's Disease and Measures of Utility. Value in Health. 2007;10(3):214-20.
70. Punekar YS, Hawkins N. Cost-effectiveness of infliximab for the treatment of acute exacerbations of ulcerative colitis. Eur J Health Econ. 2010;11(1):67-76.
71. Colombel JF, Sands BE, Rutgeerts P, Sandborn W, Danese S, D'Haens G, et al. The safety of vedolizumab for ulcerative colitis and Crohn's disease. Gut. 2017;66(5):839-51.
72. Fenu E, Lukyanov V, Acs A, Radu X, Stypa S, Fischer A, et al. Cost Effectiveness of Subcutaneous Vedolizumab for Maintenance Treatment of Ulcerative Colitis in Canada. Pharmacoecon Open. 2022;6(4):519-37.
73. 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. Therap Adv Gastroenterol. 2020;13:1756284820941179.
74. Yokomizo L, Limketkai B, Park KT. Cost-effectiveness of adalimumab, infliximab or vedolizumab as first-line biological therapy in moderate-to-severe ulcerative colitis. BMJ Open Gastroenterology. 2016;3(1):e000093.
75. Vickers AD, Ainsworth C, Mody R, Bergman A, Ling CS, Medjedovic J, et al. Systematic Review with Network Meta-Analysis: Comparative Efficacy of Biologics in the Treatment of Moderately to Severely Active Ulcerative Colitis. PLoS One. 2016;11(10):e0165435.
76. Moćko P, Kawalec P, Smela-Lipińska B, Pilc A. Effectiveness and safety of vedolizumab for treatment of Crohn's disease: a systematic review and meta-analysis. Arch Med Sci. 2016;12(5):1088-96.