## Journal

BioDrugs

## Title

Maintaining Clinical Freedom Whilst Achieving Value in Biologics Prescribing: An Integrated Cross-Specialty Consensus of UK Dermatologists, Rheumatologists and Gastroenterologists

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Supplementary Table

Phase III, randomised controlled trials of biologics targeting IL-12/23, IL-23, IL-17 and integrins that have shown superiority versus TNF inhibitors

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Indication** | **Study** | **Treatment comparisons** | **Duration** | **Outcomes superior to TNFi** |
| Psoriasis | ACCEPT [1] | UST vs ETN | 12 weeks | PASI 75, PASI 90, PGA 0/1, PGA 0 |
| FIXTURE [2] | SEC vs ETN | 52 weeks | PASI 75, PASI 90, PASI 100, IGA 0/1 |
| IMMvent [3] | RIS vs ADA | 16 weeks | PASI 75, PASI 90, PASI 100, sPGA 0/1, sPGA 0, DLQI |
| reSURFACE 2 [4] | TIL vs ETN | 12 weeks | PASI 75, PASI 90, PASI 100, PGA 0/1, DLQI |
| UNCOVER-2 and -3 [5] | IXE vs ETN | 12 weeks | sPGA 0/1, sPGA 0, PASI 75, PASI 90, PASI 100, DLQI |
| VOYAGE 1 [6] | GUS vs ADA | 48 weeks | IGA 0/1, IGA 0, PASI 75, PASI 90, PASI 100, DLQI |
| VOYAGE 2 [7] | GUS vs ADA | 24 weeks | IGA 0/1, IGA 0, PASI 75, PASI 90, PASI 100, DLQI |
| PsA | SPIRIT-H2H [8] | IXE vs ADA | 24 weeks | ACR 50 and PASI 100 responses |
| Axial spondyloarthritis | COAST-V [9] | IXE vs ADA | 16 weeks | ASAS20, ASAS 40, BASDAI 50, MRI SPARCC spine score, MRI SPARCC sacroiliac joint score, SF-36 PCS, ASAS Health Index |
| Ulcerative colitis | VARSITY [10] | VDZ vs ADA | 52 weeks | Clinical remission, endoscopic improvement  |

ACR, American College of Rheumatology; ADA, adalimumab; ASAS, Assessment in Ankylosing Spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; DLQI, Dermatology Life Quality Index; ETN, etanercept; GUS, guselkumab; IBD, inflammatory bowel disease; IGA, Investigator’s Global Assessment; IL, interleukin; IXE, ixekizumab; MRI, magnetic resonance imaging; PASI, Psoriasis Area and Severity Index; (s)PGA, (static) Physician’s Global Assessment; PsA, psoriatic arthritis; RIS, risankizumab; SEC, secukinumab; SF-36 PCS, 36-Item Short Form Survey physical component score; SPARCC, Spondyloarthritis Research Consortium of Canada; TIL, tildrakizumab; TNF(i), tumour necrosis factor (inhibitor); UST, ustekinumab; VDZ, vedolizumab.

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Literature Search

# Objectives

* To review available literature and relevant guidelines in order to support clinical opinion and guide the modified Delphi consensus process

# Key Research Questions

## Clinical Freedom

* 1. What is the principle of “clinical freedom”, and how does it differ from clinical judgement?
	2. What is the importance of the principle of “clinical freedom” to clinicians, patients and to the healthcare system?
	3. To what extent would greater understanding of the Biologic Commissioning Framework permit greater clinical freedom?
	4. Are population-based pathways always applicable to individual patient-level treatment decisions? If not, which patient factors should be considered when deviating from the pathway?

## Value of Biologics

* 1. What is the difference between “value” and “price”, and how should these factor into patient-level treatment decisions for psoriasis, PsA, and IBD?
	2. Which drug-related factors can impart additional value on both the patient with psoriasis, PsA, and/or IBD and the healthcare system?
	3. What added value can novel biologics provide for patients with psoriasis, PsA, and/or IBD, beyond that offered by a TNFi? Is this specific to certain patient types or does it apply to the full patient spectrum?
	4. Does any additional value to patients with psoriasis, PsA, and/or IBD offered by novel biologics affect their positioning in the treatment pathway relative to TNFis?

## Current Practices in the Biologic Era

* 1. Which patient factors should impact choice of biologic prescription for psoriasis, PsA, or IBD (e.g. disease severity, location, duration, prior drug exposure, comorbidities, previous AEs or family history thereof, patient preferences and beliefs)?
	2. Has availability of newer biologic options changed prescribing patterns in psoriasis, PsA, and IBD? If so, how? What effect has this had on patient outcomes?
	3. To what extent is there room for variation in interpretation of NICE guidelines for biologic prescription in psoriasis, PsA, and IBD, and how well does this align with the Biologic Commissioning Framework?
	4. At what point in the treatment of psoriasis, PsA, and IBD should a clinician consider a switch from one biologic class to another? Which factors should go into making this decision?

# Process

A literature search was performed ahead of the e-survey and group meeting. Search terms were identified and collated from PubMed Central and the European, UK national and NICE clinical guidelines. Articles that did not contribute to the key research questions were excluded. Including the NICE clinical guidelines, 144 unique references were summarised into key themes and used to highlight research gaps or considerations.

*Supplementary Table 1: Search Terms Used in PubMed Central*

|  |  |  |
| --- | --- | --- |
| Key research question | Search query | Hits after exclusions |
| 1. *Clinical freedom*
 |
| * 1. What is the principle of “clinical freedom”, and how does it differ from clinical judgement?
 | (("clinical freedom") OR (“clinical freedom” AND "clinical judgement")) | 62 |
| * 1. What is the importance of the principle of “clinical freedom” to clinicians, patients and to the healthcare system?
 | (“clinical freedom”) AND ((relevance) OR (importance)) AND ((clinicians) OR (physicians) OR (doctors) OR (patients) OR (“healthcare system”)) NOT (prostate) | 14 |
| * 1. To what extent would greater understanding of the Biologic Commissioning Framework permit greater clinical freedom?
 | N/A | – |
| * 1. Are population-based pathways always applicable to individual patient-level treatment decisions? If not, which patient factors should be considered when deviating from the pathway?
 | (biologic) AND (((population) AND (pathway)) OR ("patient factors") OR ("treatment decisions") OR ("prescribing decisions") OR ("individualized care") OR ("personalized care") OR ("patient-centric")) AND ((psoriasis) OR (PsA) OR (“psoriatic arthritis”) OR (IBD) OR (“inflammatory bowel disease”) OR (“Crohn’s disease”) OR (“ulcerative colitis”)) NOT (prostate) | 11 |
| 1. *Value of biologics*
 |
| * 1. What is the difference between “value” and “price”, and how should these factor into patient-level treatment decisions for psoriasis, PsA, and IBD?
 | (biologic) AND ((drug) OR (healthcare) OR (medicine) OR (treatment) OR (therapy)) AND ((value) AND (price) AND (defined)) NOT (cost) NOT (analysis) | 2 |
| * 1. Which drug-related factors can impart additional value on both the patient with psoriasis, PsA, and/or IBD and the healthcare system? (e.g. clinical efficacy, patient adherence, safety, tolerability and immunogenicity profiles, dosing regimen)
 | ((drug) OR (healthcare) OR (medicine) OR (treatment) OR (therapy)) AND (value) AND ("healthcare system") AND (factors) AND ((psoriasis) OR (PsA) OR (“psoriatic arthritis”) OR (IBD) OR (“inflammatory bowel disease”) OR (“Crohn’s disease”) OR (“ulcerative colitis”)) NOT (prostate) | 10 |
| * 1. Can novel biologics add value for patients with psoriasis, PsA, and/or IBD beyond that offered by a TNFi? Is this specific to certain patient types or does it apply to the full patient spectrum?
 | ((IL-17 inhibitor) OR (anti-IL-17) OR (ixekizumab) OR (Taltz) OR (secukinumab) OR (Cosentyx) OR (brodalumab) OR (Kyntheum) OR (IL-12/23 inhibitor) OR (anti-IL-12/23) OR (ustekinumab) OR (Stelara) OR (IL-23 inhibitor) OR (anti-IL-23) OR (guselkumab) OR (Tremfya) OR (risankizumab) OR (Skyrizi) OR (tildrakizumab) OR (Ilumetri) OR (Ilumya) OR (“novel biologics”)) AND (value) AND ((psoriasis) OR (PsA) OR (“psoriatic arthritis”) OR (IBD) OR (“inflammatory bowel disease”) OR (“Crohn’s disease”) OR (“ulcerative colitis”)) NOT (prostate) | 11 |
| * 1. Does any additional value to patients with psoriasis, PsA, and/or IBD offered by novel biologics affect their positioning in the treatment pathway relative to TNFis?
 | ((IL-17 inhibitor) OR (anti-IL-17) OR (ixekizumab) OR (Taltz) OR (secukinumab) OR (Cosentyx) OR (brodalumab) OR (Kyntheum) OR (IL-12/23 inhibitor) OR (anti-IL-12/23) OR (ustekinumab) OR (Stelara) OR (IL-23 inhibitor) OR (anti-IL-23) OR (guselkumab) OR (Tremfya) OR (risankizumab) OR (Skyrizi) OR (tildrakizumab) OR (Ilumetri) OR (“novel biologics”)) AND ((value) OR (additional benefits)) AND (position) AND ((psoriasis) OR (PsA) OR (“psoriatic arthritis”) OR (IBD) OR (“inflammatory bowel disease”) OR (“Crohn’s disease”) OR (“ulcerative colitis”)) NOT (prostate) | 0 |
| 1. *Current practices in the biologic era*
 |
| * 1. Which patient factors should impact choice of TNFi vs. novel biologic prescription for psoriasis, PsA, or IBD (e.g. disease severity, location, duration, prior drug exposure, comorbidities, previous AEs or family history thereof, patient preferences and beliefs)?
 | ((TNFi) OR (TNF inhibitor) OR (anti-TNF)) AND (patient) AND ((suitability) OR (suitable) OR (appropriate)) AND ((psoriasis) OR (PsA) OR (“psoriatic arthritis”) OR (IBD) OR (“inflammatory bowel disease”) OR (“Crohn’s disease”) OR (“ulcerative colitis”)) NOT (prostate) | 23 |
| * 1. Has TNFi biosimilar availability changed prescribing patterns in psoriasis, PsA, and IBD? If so, how? What effect has this had on patient outcomes?
 | (biosimilars) AND (("patient outcomes") OR ("prescribing patterns") OR ("prescribing habits")) AND ((psoriasis) OR (PsA) OR (“psoriatic arthritis”) OR (IBD) OR (“inflammatory bowel disease”) OR (“Crohn’s disease”) OR (“ulcerative colitis”)) NOT (prostate) | 7 |
| * 1. To what extent is there room for variation in interpretation of NICE guidelines for biologic prescription in psoriasis, PsA, and IBD, and how well does this align with the Biologic Commissioning Framework on biosimilar prescription?
 | N/A | – |
| * 1. At what point in the treatment of psoriasis, PsA, and IBD should a clinician consider a switch from one biologic class to another, and which factors should go into making this decision? (e.g. time on therapy, clinical response, anti-drug antibodies, adverse events, unit cost, potential costs to the healthcare system, patient satisfaction, comorbidity development)
 | ((TNFi) OR (TNF inhibitor) OR (anti-TNF) OR (biosimilar) OR (biologic)) AND (switch) AND (class) AND ((psoriasis) OR (PsA) OR (“psoriatic arthritis”) OR (IBD) OR (“inflammatory bowel disease”) OR (“Crohn’s disease”) OR (“ulcerative colitis”)) NOT (prostate) | 4 |

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