





## GUIDELINES

# Belgian recommendations for managing psoriasis in a changing treatment landscape

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## Abstract

Targeted biologic drugs and small molecules have transformed the psoriasis treatment landscape in recent years. The Belgian healthcare system, in common with many others across Europe, must balance the burgeoning use of these transformative, yet expensive, drugs with the sustainable use of limited resources. Drawing on recent updates to the EuroGuiDerm and the German S2 psoriasis guidelines, eight Belgian dermatologists experienced in treating patients with psoriasis undertook a quasi-Delphi initiative to provide perspectives on the current opportunities and challenges in psoriasis. This update focuses on responsible ways to rationalize the use of innovative treatments (e.g. biologics and small molecules). Inherently, this required viewpoints on the International Psoriasis Council's new definition of severe psoriasis, defining psoriasis severity and the concept of treating to target. It discusses the appropriateness of using older biologics classes, biosimilars and personalized dosing and lastly, how teledermatology may play a role in providing sustainable, patient-centric psoriasis care. In addition, this manuscript includes the updated Belgian evidence-based treatment advice in psoriasis (BETA-PSO) to reflect recent data and drug approvals. The recommendations reflect the best practices for clinicians when using systemic and biologic therapies to treat patients with psoriasis and offer guidance on how they may prescribe these drugs sustainably and efficiently.

## INTRODUCTION

Targeted therapies have transformed psoriasis management, as well as patients' and clinicians' expectations of treatment and its outcomes.<sup>1</sup> However, they are expensive: their burgeoning use challenges healthcare budgets.

Without action, these costs are becoming unsustainable, yet current systems may underserve patients, with some patients lacking access to them while others may receive them unnecessarily. To address this, disease endpoints and treatment targets are needed to measure the impact of targeted therapies, define their success and enable judicious prescribing. Indeed, international proposals advocate departing from traditional psoriasis classifications

based on objective measures such as Psoriasis Area and Severity Index (PASI), towards 'test-to-treat' classifications based on treatment requirements.<sup>2</sup> A related approach is 'treating-to-target', in which treatment, follow-up and assessment are tightly controlled to achieve predefined outcomes within specified time frames.<sup>3</sup> This concept is well established in rheumatology, in which it improves outcomes and reduces costs,<sup>1</sup> yet similar approaches for psoriasis are less widespread.<sup>4</sup>

Different governments contain costs differently. Some mandate using old medications before considering biologics; some advocate using biosimilars. Still others advocate personalized dosing, which recognizes that costs vary temporally and that better understanding the cost-effectiveness of

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different treatment sequences could offer savings at various timepoints along the patient's journey.

Medications represent only part of the cost of psoriasis care: cost containment must also streamline its other aspects. One example is by applying teledermatology, which uses photographs to diagnose and monitor skin conditions remotely.<sup>5</sup> Evidence suggests teledermatology is directly and indirectly cost-effective,<sup>6–9</sup> associating with high satisfaction among patients and clinicians<sup>10</sup>; yet how best to integrate this into Belgian care pathways is unclear, as are the implications for patient care, dermatologists' workload and costs.

The Belgian evidence-based treatment advice in psoriasis (BETA-PSO) was published in 2020.<sup>11,12</sup> Since then, evidence has evolved and additional guidelines (EuroGuiDerm)<sup>13</sup> have been adopted across Europe.<sup>14,15</sup> Additionally, Belgian treat-to-target recommendations have been published.<sup>3</sup> We BETA-PSO authors therefore reconvened to update our recommendations, adopting elements of the EuroGuiDerm 2022 guidelines. Here, we expand our guidelines to address disease severity classification, treat-to-target recommendations and teledermatology, and suggest responsible cost containment and reimbursement measures for policymakers. We consider general recommendations for optimal psoriasis care and for tailoring treatment for special populations and those with comorbidities.

## MATERIALS AND METHODS

The 2020 BETA-PSO<sup>11,12</sup> was reviewed in light of recent EuroGuiDerm<sup>13</sup> and German guidelines<sup>14,15</sup> publication and updated to reflect recent data. This involved including or adapting parts of the EuroGuiDerm or German guidelines, as well as including new recommendations. Therapies approved since the previous BETA-PSO iteration were considered and guidance adapted accordingly.

Eight expert Belgian dermatologists, experienced in treating psoriasis, used a quasi-Delphi methodology. The experts outlined the scope in a 2-hour virtual meeting (August 2022). Two experts organized voting topics (June to September 2022) and all participated in two online voting rounds (Round 1, September to October 2022; Round 2, February 2023), discussing virtually between rounds (January 2023).

Voting took two forms. First, the experts voted whether to adopt statements from the EuroGuiDerm or German guidelines or retain those from BETA-PSO 2020. The experts indicated their agreement with each statement plus its published strength.<sup>16</sup> Second, the experts voted on new statements, indicating their strength of agreement with them, as shown in Table 1. Both statement types were categorized by level of consensus<sup>17</sup> between experts, as shown in Table 2.

General considerations for managing psoriasis and handling new opportunities (e.g. teledermatology) and challenges (e.g. financial sustainability) are discussed in this manuscript. Recommendations for special populations (i.e. age, pregnancy and psoriasis subtype) and patients with

**TABLE 1** Strength of recommendation.

Strength of recommendation	
Strong recommendation in favour	↑↑
Weak recommendation in favour	↑
Weak strong recommendation against	↓
Strong recommendation against	↓↓
No/open recommendation	-

**TABLE 2** Level of consensus.

Level of consensus	Participants, %	Experts, N
100% consensus	100	8
Consensus	>75–95	6–7
Agreement of the majority	>50–75	4–5

comorbidities are shown in File S1. The full dataset is available in File S2.

## RESULTS AND DISCUSSION

### Treat-to-target and measuring disease activity

A common measure of psoriasis treatment success is  $\geq 90\%$  improvement in PASI (PASI-90); however, this has limitations including its dependency on a baseline severity assessment.<sup>1,13</sup> Various groups have sought to define more stringent treatment goals for a treat-to-target approach.

The European Consensus on Treatment Goals, first defined in 2011, describes an algorithm for effective treatment in clinical practice.<sup>17</sup> A related algorithm from a Spanish working group defines criteria for ideal, acceptable and minimal disease–control targets based on PASI and Dermatology Life Quality Index (DLQI) scores.<sup>18</sup> US and Canadian groups have likewise proposed goals, which utilize measures such as the Physician Global Assessment (PGA) and affected body surface area (BSA).<sup>19,20</sup>

These frameworks are helpful despite their variability, but transferability between countries is limited owing to regional practice variations and reimbursement criteria.<sup>1,3,4</sup> For example, the Spanish consensus<sup>18</sup> permits first-line biologics for moderate-to-severe psoriasis, yet this is not reimbursed in Belgium.

In 2020, a Belgian consensus proposed treat-to-target outcomes for moderate-to-severe psoriasis.<sup>3</sup> This also proposed ideal and acceptable outcomes, accounting for factors that influence outcomes, including disease characteristics, comorbidities, treatment burden and patient well-being. Interestingly, the concept of ‘minimal disease activity’ (MDA; or remission) does not feature explicitly in any psoriasis treat-to-target algorithms, yet MDA is an important concept for rheumatic and metabolic diseases. We found only one paper examining this concept in detail.<sup>21</sup> A panel of Spanish dermatologists and patients systematically reviewed the domains included in psoriasis trials and identified key characteristics indicating a state of MDA. They defined

MDA as the absence of active arthritis, no lesions in special locations, plus any three of the following: itching  $\leq 1/10$ ; scaling  $\leq 2/10$ ; redness  $\leq 2/10$ ; visibility  $\leq 2/10$  (all 10-point visual analogue scales); BSA  $\leq 2$ ; and DLQI  $\leq 2$ .<sup>21</sup> MDA is an efficacy endpoint in trials for psoriatic arthritis,<sup>22</sup> yet its applicability to psoriasis clinical practice remains underevaluated.

We considered the definition of MDA for patients with psoriasis and reached full consensus that this overlaps entirely with the 'ideal' treatment outcomes defined in the Belgian treat-to-target guidelines (Table 3; Figure 1). Almost all experts agreed strongly that an outcome less than this should prompt consideration of changing the patient's therapy. This is a stringent goal, which we recognize may be unachievable for certain patients, such as those who are pregnant or have a history of cancer. For these, it is reasonable to pursue 'acceptable' targets.<sup>3</sup>

As the time needed to reach these targets depends on the specific drugs prescribed, we specify no exact timeline for assessing response, but broadly agree with other guidelines groups including the Belgian treat-to-target working group,<sup>3</sup> EuroGuiDerm<sup>13</sup> and the European Consensus on Treatment Goals,<sup>17</sup> which suggest assessing response after 10–14 weeks. We suggest physicians closely monitor patients starting systemic therapy and allow sufficient time for medications to work, but without unduly prolonging the duration of inadequately controlled symptoms.<sup>23</sup>

## Clinical decision-making on systemic treatments

EuroGuiDerm made recommendations for selecting and initiating systemic treatment for patients with psoriasis.<sup>13</sup> We discussed each of their recommendations and adopted those shown in Table 4 and Figure 2.

We retain our previous recommendation regarding biologic-experienced patients<sup>12</sup>: most experts agreed that for biologic-experienced patients needing to switch treatments, drug survival is better when switching between, not within, biologic classes. However, if a particular class was chosen for its specific characteristics, switching within classes is appropriate. In both cases, consider switching to the treatment exhibiting the highest efficacy in clinical trials.

We also considered the suitability of all systemic psoriasis medications available in Europe for patients of varying age, pregnancy status and psoriasis subtype and for patients with specific comorbidities. Full recommendations are in File S1.

## Challenges for psoriasis management

### Medication access

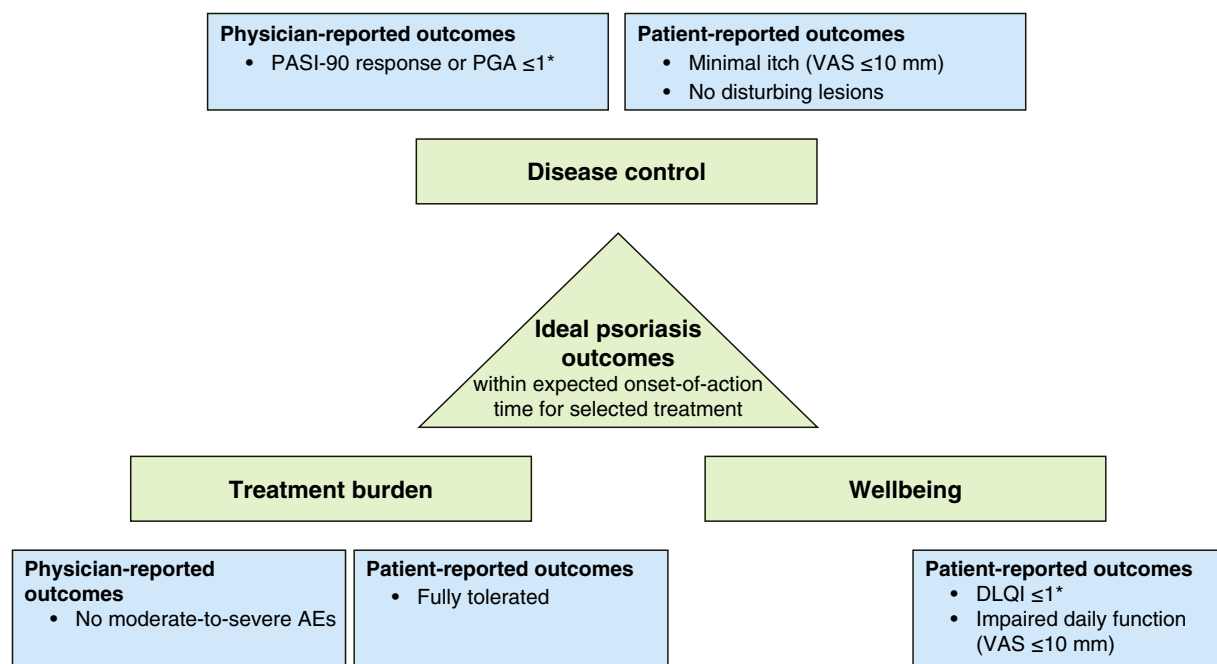
Healthcare costs are rising inexorably worldwide.<sup>24,25</sup> Reasons are manifold and include the needs of treating

**TABLE 3** Recommendations for treating-to-target and defining disease activity.

Statement + strength		Level of consensus
The aim of psoriasis treatment is to decrease the disease severity and disease burden to an acceptable level. A treat-to-target concept should be recommended for the management of psoriasis.	↑↑	100% consensus
These criteria could be considered as 'minimal disease activity' for psoriasis: PASI90 or PGA $\leq 1$ VAS for itch $\leq 10$ mm Absence of disturbing lesions No moderate-to-severe adverse events Full tolerability* DLQI $\leq 1$ Incapacity in daily functioning VAS score $\leq 10$ mm These targets should be reached within the expected onset-of-action timeframes for individual drugs. <i>*Full tolerability = when the patient replies yes to the question 'do you tolerate the treatment?'</i>	↑↑	Consensus
The following targets should be reached for an ideal treatment, and if these are not then a change in therapy should be considered: PASI90 or PGA $\leq 1$ VAS for itch $\leq 10$ mm Absence of disturbing lesions No moderate-to-severe adverse events Full tolerability* DLQI $\leq 1$ Incapacity in daily functioning VAS score $\leq 10$ mm These targets should be reached within the expected onset-of-action timeframes for individual drugs. <i>*Full tolerability = when the patient replies yes to the question 'do you tolerate the treatment?'</i>	↑↑	Consensus
In certain cases (e.g., pregnancy and history of cancer), not all systemic therapies can be prescribed. For these cases, the patient and physician can aim for 'acceptable' targets. These include the following: PASI75 or PGA $\leq 1$ VAS for itch $\leq 10$ mm Absence of disturbing lesions No moderate-to-severe adverse events Almost full tolerability* DLQI $\leq 3$ Incapacity in daily functioning VAS score $\leq 10$ mm These targets should be reached within the expected onset-of-action timeframes for individual drugs. <i>*Almost full tolerability = when the patient replies only with mild complaints to the question 'do you tolerate the treatment?'</i>	↑↑	Consensus

ageing populations with multiple chronic conditions and the proliferation of targeted therapies which, although undoubtedly effective, are extremely expensive.<sup>24,26</sup>

While Belgian estimates are unavailable, a systematic review in five other European countries found the annual per-patient cost for treating psoriasis or psoriatic arthritis ranged from US \$2077 to \$13,132 (2015 purchasing power parity exchange rates), with more severe disease costing more. Biologics' introduction increased direct costs three to five-fold.<sup>27</sup> Thus, healthcare is under intense pressure, with calls for a dramatic shift from the current unsustainable system.<sup>28</sup>



**FIGURE 1** 'Ideal' psoriasis treatment outcomes, as defined in the Belgian treat-to-target guidelines. Adapted from Grine L, et al. 2020.<sup>3</sup> AE, adverse event. DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; VAS, visual analogue scale.

All countries use mixed regulatory mechanisms to contain pharmaceutical expenditure and maximize efficiency.<sup>25</sup> In Belgium, reimbursement criteria for psoriasis have drawbacks: biologics are reimbursed only after failure, intolerance or contraindication to phototherapy, methotrexate and cyclosporine. Further, reimbursement hinges on severity: only patients with PASI >10 or BSA >10% are eligible. Previous experts have suggested these reimbursement criteria are disconnected from the clinical criteria for biologic use.<sup>3</sup> For example, a patient may experience significant psychological, social or functional impairment because of severe itch despite conventional treatments or distressing disease localization, but may have an overall PASI <10. This is a clear biologics indication per Belgian and EuroGuiDerm guidelines,<sup>12,13</sup> yet only certain small molecules would be available under existing reimbursement criteria. Further, from our clinical experience we suggest these criteria sometimes delay biologics use, leading to preventable morbidity.

Most experts agreed the reimbursement criteria need updating to allow more patients to access biologics. However, several expressed concern about the budgetary impact of such changes. Others explained that a lack of objective adherence assessments makes applying existing reimbursement criteria difficult and that stricter adherence monitoring may help standardize reimbursement among patients. Others suggested that widespread adoption of the treat-to-target recommendations outlined by Grine et al.<sup>3</sup> may support the best use of biologics within existing or modified reimbursement frameworks. Overall, most agreed policymakers should consider amending the biologics reimbursement

criteria as shown in Table 5. We suggest removing the requirement to have tried multiple conventional therapies before considering biologics.

### Impact of changing psoriasis severity classification

Each existing tool for measuring psoriasis severity (e.g. BSA, PGA and PASI) has drawbacks.<sup>2</sup> BSA underestimates severity if the affected area is small but particularly itchy or involves special areas such as the face, genitals, soles or palms.<sup>2</sup> PASI depends on having an accurate baseline assessment.<sup>1</sup> None is well tuned to the fluctuating and unpredictable nature of this long-term condition<sup>29</sup> and each overlooks its quality-of-life impact, necessitating the use of questionnaires such as the DLQI.<sup>13</sup>

The 'Rule-of-Tens' aid to clinical decision-making is used in Belgium to identify severe disease and inform biologics access. This classifies severe psoriasis as BSA >10%, PASI >10 or DLQI >10, with patients fulfilling any of these criteria being considered as having severe psoriasis needing intervention.<sup>29</sup> While this formula has benefits, particularly its simplicity for busy clinical settings, some experts feel it sets the bar to treatment too low and may mean more patients receive systemic therapy than need it.

In 2020, the International Psoriasis Council proposed criteria for defining severe psoriasis as *Psoriasis patients should be classified as candidates for topical therapy or candidates for systemic therapy. The latter are patients who meet at least one of the following criteria: (1) BSA >10%; (2) disease involving special areas; and (3) failure of topical therapy.*<sup>2</sup> Our views



**TABLE 4** Recommendations on clinical decision-making for systemic treatments, adopted from EuroGuiDerm.

Published statement + strength		Level of consensus on adopting statement to BETA-PSO
We recommend initiating a systemic treatment in patients with moderate to severe psoriasis.	↑↑	100% consensus
We recommend taking account of efficacy and safety, time until onset of treatment response, comorbidities, and individual patient factors when choosing a systemic treatment for moderate to severe psoriasis.	↑↑	Consensus
For most patients who require systemic treatment, we recommend the initiation of 'conventional' systemic agents as first line treatment.	↑↑	Consensus
We recommend initiating a biologic if 'conventional' systemic agents were inadequate in response or if contraindicated or not tolerated.	↑↑	Consensus
In case of severe disease, where a sufficient treatment success cannot be expected with the use of a 'conventional treatment*', the initiation of a biologic with a first-line label** is suggested as a first-line treatment.	↑	Consensus
We suggest using apremilast if an oral treatment is desired and 'conventional' systemic agents led to an inadequate response or are contraindicated or not tolerated.	↑	Consensus
If a patient fails to respond to 2 biologics targeting either IL-17 or IL-23, a reconsideration of the diagnosis of psoriasis should be done with recommendation to take a (new) skin biopsy.	↑↑	100% Consensus

\*e.g. particularly severe disease (e.g. PASI $\geq$ 20) or rapid worsening of disease; severe involvement of the nails, the genitals or the scalp; or a particularly strong impact on QoL (e.g. DLQI $\geq$ 15).

\*\*'First line label' refers to the therapeutic indication as approved by the EMA.

were mixed, but overall we do not adopt this definition into BETA-PSO in its current form.

Those uncertain suggested this definition sets the bar to systemic treatment too low, could have unsustainable budgetary impacts and could expose patients to systemic therapy unnecessarily. One concern was the proposal's lack of specificity in some areas. For example, 'special areas' needs clearer definition, and that alone these should not prompt systemic therapy; other considerations, such as the feasibility of topical treatment, should be appraised. Moreover, the classification should clarify that failure of one topical therapy does not necessarily mean failure of all: alternative topicals and phototherapy should be considered before escalating to systemics. Another concern with the proposal is its suggestion that treatment is binary—topical versus systemic—when, in fact, treatment may combine both, sometimes alongside phototherapy and may fluctuate over a patient's life.

## Rationalizing biologics for financial sustainability

Targeted agents are available against tumour necrosis factor (TNF) $\alpha$ , interleukin (IL)-12, IL-23 and IL-17A, with more in development against other targets.<sup>30</sup> Correspondingly, treatment expectations have increased: in 2011, the European Consensus on Treatment Goals defined success as  $\geq$ 75% PASI improvement.<sup>17</sup> Now, more stringent goals—PASI-90 or even -100—are sought.<sup>3,13</sup>

Despite their benefits, biologics are not accessible to every patient who needs them.<sup>31</sup> In 2010, direct costs for treating high-need psoriasis were ~77% higher in the biologics than pre-biologics era.<sup>32</sup> Recent research confirms similar

'First-line label' conventional treatments (alphabetical order)		'First-line label' targeted treatments (alphabetical order)				
		Anti-TNF $\alpha$	Anti-IL12/23	Anti-IL-17	Anti-IL-23	Anti-PDE4
In case of severe disease, where sufficient treatment success cannot be expected with the use of a conventional treatment, initiate a biologic with a first-line label as a first-line treatment.		Adalimumab	✓			
		Bimekizumab		✓		
		Brodalumab		✓		
		Certolizumab	✓			
		Guselkumab			✓	
		Ixekizumab		✓		
		Risankizumab			✓	
		Secukinumab		✓		
		Tildrakizumab			✓	
		'Second-line label' targeted treatments (alphabetical order)				
		Anti-TNF $\alpha$	Anti-IL12/23	Anti-IL-17	Anti-IL-23	Anti-PDE4
Acitretin						
Cyclosporine	If response to conventional treatments is inadequate, contra-indicated or not tolerated, use targeted therapies.					✓
Fumarates		✓				
Methotrexate		✓				
			✓			

**FIGURE 2** Recommendations for first- and second-line systemic treatments, adopted from EuroGuiDerm. Adapted from Nast A, et al. 2020.<sup>13</sup> IL, interleukin; PDE-4, phosphodiesterase-4; TNF $\alpha$ , tumour necrosis factor- $\alpha$ .

**TABLE 5** Recommended amendments to biologic reimbursement criteria.

Statement + strength	Level of consensus
<p>We do not agree with the current reimbursement criteria* and recommend changing them as follows:</p> <p>In Belgium, biologics should be reimbursed after the following therapies have failed or in case of intolerance or contraindication: (1) adequate phototherapy + (2) methotrexate for at least 3 months, or acitretin for at least 3 months or cyclosporine for at least 2 months.</p> <p><i>*In Belgium, biologics are reimbursed after the following therapies have failed, or in case of intolerance or contraindication: adequate phototherapy, methotrexate for at least 3 months, and cyclosporine for at least 2 months.</i></p>	11 Agreement of majority

trends.<sup>33,34</sup> Given their rising, unsustainable costs, a strategy is needed to rationalize the use of these important drugs.

## New versus old biologics classes

Newer biologics can be more costly than established drugs; however, whether these represent value for money is unclear. Various studies have attempted to identify the most cost-effective biologics, considering price, efficacy, quality-of-life, onset of action, tolerability and avoidance of long-term sequelae.<sup>35–39</sup> Most have evaluated first-generation biologics (e.g. etanercept, infliximab and adalimumab), while head-to-head studies, health economics analyses and post-marketing surveillance for newer agents are lacking, complicating cost-effectiveness assessments in the context of all therapies now available.<sup>40</sup>

Most experts felt that while using older drugs may save money in the short term, newer biologics are often more effective and better tolerated,<sup>38</sup> meaning they could offer ongoing cost-effectiveness benefits over older agents.<sup>41</sup> Nevertheless, some experts felt that using older biologics as a cost-saving strategy deserves more research.

Predicting who will respond favourably to a given drug is difficult: some patients need several switches before finding one that works.<sup>38</sup> Indeed, estimates suggest 11%–35% of patients respond poorly to their first biologic during the first year of treatment, either due to poor efficacy or adverse events.<sup>38</sup> Given this high first-line failure rate, the question of whether cheaper drugs should be exhausted before escalating to expensive, newer drugs deserves serious research.

## Biosimilars

Biosimilars are generally 15%–45% less costly than the originator medicines. These savings are attributable to their abbreviated clinical trial programmes, lower development costs and possibly more efficient production processes.<sup>13,41</sup> Together, these factors improve biosimilars' cost-effectiveness, possibly allowing reimbursement to be

extended to additional patient groups or to those at earlier disease stages.<sup>41</sup>

Various healthcare bodies recommend biosimilars and there are many incentives to their uptake. However, as biosimilars increasingly enter the treatment landscape, questions surrounding their true interchangeability and traceability and the ability to collect accurate pharmacovigilance data within existing frameworks, will warrant closer attention.<sup>42</sup>

Numerous biosimilars to first-generation anti-TNFα biologics are approved for psoriasis—most approvals are based on data extrapolated from studies in rheumatic disease<sup>43</sup>—and recommended in European guidelines. For example, EuroGuiDerm states their recommendations apply equally to originator biologics and their biosimilars.<sup>13</sup> In its position paper on biosimilars, the International Federation of Psoriasis Associations welcomes safe and effective biosimilars to improve treatment access, but emphasizes the importance of the patient–provider relationship when switching from an originator to a biosimilar.<sup>44</sup> Other groups suggest that switching decisions should proceed on an evidence-based, case-by-case basis.<sup>42,43,45</sup> Indeed, the International Psoriasis Council has published a consensus on biosimilars use in patients with psoriasis, providing global guidance to clinicians, patients and other stakeholders.<sup>42</sup>

Previously BETA-PSO<sup>12</sup> advised that, from an efficacy and safety perspective, it is possible to switch from anti-TNFα reference drugs to their respective biosimilars and we continue recommending this approach. We do not, however, recommend biosimilars as the default first-line biologics choice for all patients, as such decisions must be individualized. Deciding first-line treatment should consider the entire treatment landscape, including both reference biologics and their biosimilars.

## Personalized dosing

Biologics are particularly expensive in the first year of treatment, as the induction phase sometimes involves higher doses and frequency than ongoing maintenance. Furthermore, response typically declines over time, sometimes necessitating switching to maintain disease control.<sup>46</sup> A common alternative in practice is to escalate treatment by increasing the dose or reducing the dosing interval,<sup>47</sup> yet the economic drive to control costs must be balanced against the ethical imperative to ensure patients receive the minimum effective dose.<sup>48</sup>

While some evidence exists, more understanding is needed about different treatment sequences, and escalation and dose-tapering strategies. A randomized study (BeNeBio) began in Belgium and the Netherlands in 2020 to establish whether dose reduction of IL-17 and IL-23 agents is non-inferior to the usual fixed dosing for patients with stable psoriasis.<sup>49</sup>

The cost of escalation depends on its intensity and duration, while switching includes the higher cost of induction

therapy and possibly more clinic visits and diagnostics.<sup>47</sup> These were compared in a 2014 modelling study, which considered treatment with ustekinumab, etanercept and infliximab in patients with psoriasis for whom maintenance therapy had failed. In all cases, the costs of escalating first-line treatment quickly exceeded the annual costs of switching to a new drug, suggesting that switching is more cost-effective than dose escalating.<sup>47</sup> However, the study did not consider patients' likelihood to respond to the second biologic and the costs associated with its possible failure, and many more biologics have since become available.

A 2023 study analysed the cost-effectiveness of different sequences of anti-IL-17 treatments secukinumab, brodalumab, ixekizumab and bimekizumab in the Italian and German healthcare systems, considering drug survival, induction costs, maintenance costs and expected response rates. The costs of all combinations used first to fourth line were estimated and in all cases costs decreased with each successive line. Interestingly, beginning treatment with brodalumab then bimekizumab was consistently cheapest per responder. This study underscores how accounting for drug survival and the added costs of switching is vital to evaluate the cost-effectiveness of any treatment strategy.<sup>46</sup>

Whether and when to discontinue biologics after achieving remission is an important unanswered question in psoriasis care, but one beginning to receive research attention. A 2022 systematic review found that patients who received then discontinued biologics, particularly anti-IL-23 agents, had longer remission durations (12–34 weeks) than those who received traditional systemics (~4 weeks).<sup>50</sup> Further, a review of clinical trials identified several predictors for longer relapse-free durations, including early biologics intervention (<2 years of diagnosis), achieving PASI-90 and biologics naivety.<sup>51</sup> Identifying patients most likely to firstly achieve remission, then maintain it after biologics discontinuation, may help target biologics to those for whom they will be most effective, both clinically and economically.

We agreed detailed criteria are needed to help clinicians deliver personalized care efficiently and appropriately. These should include when to stop, taper or use intermittent dosing, but have yet to be developed for the entire biologics landscape. Our specific recommendations on intermittent biologics treatment are largely unchanged from the previous BETA-PSO, although these include bimekizumab, now approved in Europe (Table 6).

Teleconsultations

Telemedicine has expanded rapidly in dermatology, in which visual assessments are uniquely informative for triage, diagnosis and monitoring.<sup>52</sup> In May 2020, a survey of over 3500 members of the Professional Association of German Dermatologists (BvDD) found that nearly 40% offered teledermatological services—almost four times as many as before the COVID pandemic.<sup>53</sup>

TABLE 6 Recommendations on personalized dosing and intermittent treatment.

Statement + strength	Level of consensus
<p><b>Intermittent treatment.</b> Regarding biologics, we recommend continuous systemic treatment for patients with psoriasis when the patient is still receiving benefit. Should a psoriasis patient wish to stop and then restart systemic treatment, we advise that it is possible to do so, particularly with etanercept and ustekinumab. Conventional drugs and synthetic drug apremilast seem well suited for intermittent treatment. There is robust evidence that demonstrates these drugs can be stopped and then restarted with equivalent efficacy and without increased risk of flare of disease. For adalimumab, certolizumab pegol, guselkumab, risankizumab and tildrakizumab, ixekizumab, secukinumab and brodalumab, the evidence is less clear. Fumarates can also be used intermittently although they exhibit a slow onset of action.</p> <p>There is currently insufficient evidence to support stopping and then restarting treatment with other biological drugs, including adalimumab, certolizumab pegol, tildrakizumab and <b>bimekizumab</b>.</p> <p>We advise caution with this approach until these data are available.</p> <p>For guselkumab, risankizumab, ixekizumab and secukinumab, promising results when retreating after drug withdrawal were obtained in clinical trial settings indicating that intermittent treatment might be an option with the newer IL23/p19 inhibitors and IL17 blockers.</p> <p>However, we recommend against stopping and restarting infliximab due to reduced efficacy on restarting treatment as a result of the development of antidrug antibodies. From a safety perspective, there is also an increased risk of serious infusion reactions with intermittent infliximab dosing.</p>	<div>11</div> <div>Consensus</div>

Teledermatology benefits include the possibility to ease healthcare pressures as populations age and to expand access to care.<sup>6,52</sup> Patients report high satisfaction with reduced waiting times, need for travel and associated costs. A high concordance (usually >90%) between the diagnoses made in teledermatology consultations and face-to-face appointments has been reported, and dermatologists working remotely can examine and treat patients more quickly than with face-to-face visits.<sup>10</sup> Moreover, growing evidence shows teledermatology can be both directly and indirectly cost-effective.<sup>6–9</sup>

In 2019, a 3- to 6-month pilot study explored the benefits and barriers to teledermatology in Belgium.<sup>6</sup> The study, involving 12 general practitioners (GPs) and 3 academic dermatologists, showed teledermatology is feasible and acceptable for clinicians and patients and especially valuable for reducing unnecessary referrals. These findings are supported by other studies.<sup>54,55</sup> After the pilot ended, all clinicians wanted to continue using teledermatology, believing it safe for dermatological evaluations if safeguards were incorporated for uncertain cases. GPs were satisfied with dermatologists' response times and both valued the improved collaboration. Difficulties were reported in taking

good pictures and in evaluating them and some clinicians worried whether teledermatology may increase their workload. Others were concerned about the inability to palpate lesions and the lack of feedback on outcomes, although conceded that good management may overcome some of these difficulties.<sup>6</sup>

The first teledermatology guidelines were issued in 2007 by the American Telemedicine Association, and updated in 2016.<sup>56</sup> However, discussion of teledermatology for psoriasis is missing from European guidelines, so we considered the topic in detail.

## Benefits and hurdles

Our experts strongly agreed teleconsultations are valuable for patients with psoriasis and almost all recognized the need for such services in Belgium. We recommend them in specific situations: (1) following-up known patients; (2) triaging referred patients for urgency or the need to visit specialist centres; (3) providing on-demand consultations for known patients experiencing flares or needing advice; and (4) triaging non-referred patients. Mirroring the pilot study described above, we agreed teledermatology for these uses could improve communication between dermatologists and patients, save patients time and reduce waiting times. We feel it unlikely that teledermatology will save dermatologists time. While it may reduce some areas of workload, others may increase due to lacking good software, impracticalities of integrating video consultations into existing care and concerns about misdiagnosis based on the inability to examine clinically.

Teleconsultations are recommended for following-up patients with well-controlled psoriasis receiving systemics (both conventional and biologic), although patients must be evaluated in person at least annually. In this context, half our experts felt that on-demand follow-up is more useful than fixed-date consultations. Some felt that follow-up appointments scheduled following a patient's proactive request would avoid unnecessary consultations; conversely, others worried that patients may be unaware of other clinical issues or that treatment changes are needed, or that possibly better treatments are available.

We do not recommend teleconsultations for a patient's first consultation: face-to-face is important to holistically understand the patient and their condition. Nor do we recommend them for following-up patients with psoriasis well controlled with topical treatments, because good skin inspection is impossible and comorbidities cannot be screened. For patients whose disease is poorly controlled, we suggest teleconsultations may be inappropriate as these may need intensive monitoring (Table 7).

## Optimum modalities and financial implications of current tariffs

Teledermatology has three modalities: store-and-forward, real-time video conferencing and a hybrid of both.<sup>10,53</sup>

**TABLE 7** Recommendations for using teleconsultations for patients with psoriasis.

Statement + Strength		Level of consensus
The use of teleconsultations is useful (i.e., has an added value) in the management of psoriasis patients.	↑↑	Consensus
Teleconsultations cannot be recommended for the follow-up of well-controlled psoriasis patients receiving only topical treatments as good skin inspection is not possible and comorbidities cannot be screened. Moreover, these patients usually come only once a year.	↑↑	100% consensus
Teleconsultations can be recommended for the follow-up of well-controlled psoriasis patients receiving systemic treatments (both conventional immunosuppressants and biologics), although the patient has to be evaluated in person (not teleconsultation) at least once a year.	↑↑	Consensus
Teleconsultations are less ideal in patients with limited disease control despite active treatment.	↑↑	Consensus

Store-and-forward involves sending pictures and information to a dermatologist for review later, while video conferencing enables real-time assessment. Sometimes a hybrid is used, in which patients can be reviewed instantaneously but with images captured for reassessment later.<sup>53</sup>

In Europe, store-and-forward is most usual because of its flexibility and lower costs compared with video conferencing.<sup>6,57</sup> We recommend either approach, as well as telephone consultations. We reached no consensus on which is best, deferring to physicians' preferences and systems' availability.

All experts agreed existing tariffs for teledermatology services are too low and that this blocks their implementation in Belgium. We suggest tariffs should be higher since the responsibility in making a correct diagnosis and clinical expertise needed to do so, is as high for teleconsultations as for face-to-face consultations. Particularly, store-and-forward methods are not reimbursed, disincentivising their use.

## CONCLUSIONS

These updated BETA-PSO recommendations aim to guide physicians to make clinically optimal, yet sustainable treatment decisions for patients with psoriasis in the era of biologics. Our guidelines build on those published in 2020 and incorporate additional advice from the EuroGuiDerm and German guidelines. The new guidelines are intended to reflect emerging evidence, new drug approvals and updated best practices. We discuss how to balance the rising costs of biologic drugs against their ability to improve patient outcomes and consider how treat-to-target guidelines, personalized dosing, biosimilars and teledermatology could fit into the Belgian healthcare landscape.

Key strengths of these guidelines include the meticulous approach to consensus and focus on contentious areas in this evolving treatment landscape. Key limitations include their



consideration of the viewpoints of dermatologists only, and not other specialists involved in caring for patients with psoriasis, or indeed patients themselves and the inherent participation bias common to all Delphi projects. We acknowledge that not all settings where these guidelines will be used, nor all stakeholders who may use them, were consulted (e.g. primary care and community dermatology), which may necessitate their adaptation to be applicable for these settings. Nevertheless, we stress throughout the need for multidisciplinary working and wish to reiterate that the wishes of patients form a vital part of treatment decision-making. These limitations notwithstanding, since these recommendations present 'best practice' suggestions, we hope that these stakeholders will find them useful in their practice. Note our recommendations were developed before the approval of deucravacitinib, a small molecule indicated for moderate-to-severe psoriasis in adult candidates for systemic therapy. In developing these guidelines, it has become clear to us that health economic considerations will become ever more important as the price of optimal psoriasis care continues expanding. Therefore, in future we hope to seek the viewpoints of health economists and policymakers on reimbursement considerations in the Belgian healthcare setting.

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## CONFLICT OF INTEREST STATEMENT

RS is a speaker for AbbVie, Ammirall, Incyte, Janssen, Leo Pharma and UCB and has received funding for meeting attendance/travel from AbbVie, Ammirall and Janssen. AFN, FB and VR have none to declare. JL has received consulting fees, honoraria and/or speaker fees from AbbVie, Ammirall, Galderma, Eli Lilly & Co, J&J, Leo Pharma, La Roche Posay, Novartis, Pfizer and UCB. He has received funding for meeting attendance/travel from AbbVie and UCB. He has also received grants for his institution from Leo Pharma and Pfizer. PDG has received consulting fees, honoraria and/or speaker fees from AbbVie, Ammirall, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Janssen, Eli Lilly & Co, Novartis, Sandoz, UCB and Viartis. He has participated in data safety monitoring boards or advisory boards for AbbVie, Ammirall, Amgen, Bristol-Myers Squibb, Eli Lilly & Co, Leo Pharma, Novartis and UCB. TH has received honoraria and/or speaker fees from AbbVie, Ammirall, Amgen,

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## DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available in its supplementary material.

## ETHICS STATEMENT

This work involved no experimentation on humans; therefore, ethics permission was not necessary or sought.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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