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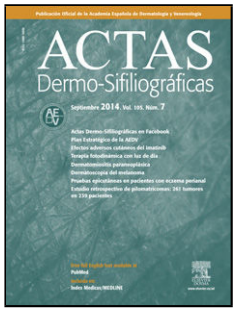

[[Translated article]]Updated Perspective from the Spanish Psoriasis Working Group (GPS) on Biosimilar Drug Use in Moderate-to-Severe Psoriasis

L. Salgado-Boquete L. Puig J.M. Carrascosa P de la Cueva A. López Ferrer

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Artículo de opinión

Actualización del documento de posicionamiento del Grupo Español de Psoriasis (GPS) sobre la utilización de fármacos biosimilares en el tratamiento de la psoriasis moderada y grave

[[Translated article]]Updated Perspective from the Spanish Psoriasis Working Group (GPS) on Biosimilar Drug Use in Moderate-to-Severe Psoriasis

Autores:

1. L. Salgado-Boquete. Servicio de Dermatología. Complejo Hospitalario Universitario de Pontevedra.
2. L. Puig. Departamento de Dermatología. Hospital de la Santa Creu i San Pau. Universidad Autónoma de Barcelona (Facultad de Medicina).
3. J. M. Carrascosa. Servicio de Dermatología. Hospital Germans Trias i Pujol. Barcelona.
4. P. de la Cueva. Servicio de Dermatología. Hospital Universitario Infanta Leonor. Madrid
5. A. López Ferrer. Departamento de Dermatología. Hospital de la Santa Creu i San Pau. Universidad Autónoma de Barcelona (Facultad de Medicina).

Autor de Correspondencia:

Laura Salgado-Boquete
laurasalgado.derma@gmail.com

Introduction and Context

In 2020, the Psoriasis Working Group of the Spanish Academy of Dermatology and Venereology (GPS) expressed its position, through an opinion article signed by several members[1], following the incorporation of biosimilar drugs into the therapeutic arsenal for moderate-to-severe plaque psoriasis. This document described the great opportunity that the incorporation of these drugs had represented by reducing acquisition costs and increasing therapeutic efficiency, but it also raised some concerns. One of them was the impact that the incorporation of biosimilars had had on some institutional decisions, such as the drafting of "therapeutic positioning reports" (TPRs) that refer to the reimbursement conditions of the drugs. Specifically, it was argued that, for newly approved drugs after the implementation of the use of anti-tumor necrosis factor (TNF) biosimilars, reimbursement restrictions related to the prior use of this therapeutic family had been included, prioritizing unjustified class criteria over the adequate assessment of efficiency.

It was also stated that this approach would complicate the therapeutic pathway of patients, generating situations of inequity, depending on the territorial interpretation carried out. The GPS stood for the importance of including clinicians in therapeutic decision-making, prioritizing medical criteria over issues subject to variable or changing financial scenarios, both locally and nationally.

In 2023, the GPS published an updated document on the positioning and use of biosimilar drugs in moderate-to-severe psoriasis[2]. The conclusions presented several relevant points. While the use of biosimilar drugs was considered appropriate as a first-line therapy in many patients, mainly due to efficiency criteria, this approach should coexist with the availability of other therapeutic alternatives with better efficacy and safety profiles in specific patients. The recommendation to standardize the different scenarios presented in the various autonomous communities regarding the guidelines for access and restrictions on the use of biological drugs was also mentioned, as well as the need to reinvest the benefits derived from the introduction of biosimilars in the healthcare system itself through shared benefit strategies.

The changing landscape regarding biosimilar drugs has motivated the GPS to again propose the need to update this positioning document in 2024.

New Scenario and Approaches of the Spanish Psoriasis Working Group of the Spanish Academy of Dermatology and Venereology

The main change experienced in this therapeutic context has been the recent incorporation of the ustekinumab biosimilar for the treatment of moderate-to-severe psoriasis. The European extension of the patent (Supplementary Protection Certificate) for ustekinumab, a fully human IgG1k monoclonal antibody that binds with high affinity and specificity to the p40 subunit of interleukins (IL-) 12 and 23, inhibiting their activity by preventing their binding to the receptor, expired in Europe on July 20th, 2024. Since then, ustekinumab biosimilar alternatives have become an additional option for the treatment of patients. The efficacy data for this drug, obtained from both clinical trials[3–5] and indirect comparisons through meta-analyses[6], are superior to those of etanercept and adalimumab, and its safety profile is more favorable than that of TNF inhibitors.

Several ustekinumab biosimilars are available for use in Spain for the indication of moderate-to-severe psoriasis, of which Uzpruvo® (Alvotech AVT04, marketed in Europe by STADA), Pyzchiva® (Samsung Bioepis SB17, marketed by Sandoz), Wezenla® (ABP654, marketed by Amgen), and SteQeyma® (CT-P43, Celltrion Healthcare) received marketing authorization from the European Medicines Agency (EMA) between January and August 2024, while Eksunbi® (SB17, Samsung Bioepis), Fymskina® (FYB202, Formycon AG), and Otulfi® (FYB202, Fresenius Kabi) received a positive opinion from the Committee for Medicinal Products for Human Use of EMA in July 2024.

As a consequence of the foregoing, the GPS proposes that:

1. The incorporation of ustekinumab biosimilar alternatives should be understood as an opportunity to increase the efficiency of systemic therapy for psoriasis and facilitate patient access to it[7]. The published price of ustekinumab biosimilars, according to the agreement of the Interministerial Commission on Drug Prices, is €2747.36 for the 45 mg unit dose and €3100 for the 90 mg dose. However, the

dynamic nature of prices, with a tendency to decrease as new references enter the market and the possibility of additional agreements at regional or local level, makes it difficult to specify the actual acquisition prices or provide concrete cost data. Tools such as the NNT (number needed to treat) can be useful in the individualized evaluation of the efficiency of each treatment.

2. Although ustekinumab represented a qualitative leap in the treatment of patients with moderate.to-severe psoriasis 15 years ago, its expectations in terms of efficacy have now been largely surpassed. In this regard, biological drugs that block IL-17 or IL-23 have demonstrated advantages in efficacy while maintaining or even improving the safety expectation or convenience for the patient. In fact, several clinical trials propose a direct comparison between these new molecules and ustekinumab, showing statistically significant benefits in efficacy that have also been confirmed in clinical practice[5],[6],[8–13].
3. Faced with the uncertainty posed by the possible prescription scenarios that may arise since July 2024, the GPS considers that biosimilars of this molecule should be on an equal footing with biosimilars of anti-TNF drugs in terms of first-line prescription for moderate-to-severe psoriasis. Furthermore, in Spain, the financing criteria for the drug (BIFIMED) do not require prior treatment with a TNF alpha inhibitor in psoriasis.
4. The GPS also considers it necessary to reaffirm that the prescription of biosimilar drugs should be based on individualized clinical criteria (probability of response, presence or absence of psoriatic arthritis, patient weight, possible contraindications to anti-TNFs, convenience of the regimen or route of administration, etc.). All these criteria refer to issues of efficacy, safety, convenience, and, of course, efficiency.
5. The therapeutic change, for any biological agent, should be made either due to insufficient response in any of the domains of psoriatic disease, or for safety reasons (for example, coexistence of inflammatory bowel disease, risk of infections or reactivation of latent tuberculosis infection, or possible contraindications to chemoprophylaxis). Although the biosimilars approved by the EMA are interchangeable from a scientific point of view, automatic substitution by the pharmacy is a decision that depends on each Member State of the European Union; in Spain, the substitution of Stelara® for any of its biosimilars or between them, when appropriate, is the prerogative of the prescriber, and automatic substitution by the pharmacist is not legal.
6. Another parallel issue, derived from the introduction of biosimilar drugs, on which the GPS wishes to comment again is the incongruity posed by some TPRs in the current prescription context, in addition to their lack of updating, which deepens the inconsistency when comparing drugs that have been approved at different times. The requirement of prior treatment with a TNF inhibitor for the financing and reimbursement of some innovative drugs[14],[15], not based on any scientific evidence but presumably on cost terms, complicates, hinders, and makes the therapeutic sequence irrational in some patients. In fact, the paradox of having to perform an inverted therapeutic sequence (from drugs with a higher expected response to others with lower efficacy such as anti-TNFs, or even lower efficiency if they are not biosimilars) may arise, ignoring clinical criteria and exclusively attending to the need to comply with regulatory requirements in case the patient requires innovative therapeutic alternatives. The GPS expresses its concern about this scenario, which is detrimental to the quality of care and contrary to current patient care standards. It is foreseeable that the incorporation of ustekinumab

biosimilars will further complicate this situation, making the participation of clinicians and scientific societies in the updating and drafting of TPRs advisable. The temptation to condition a forced step of psoriatic patients through different classes of available biosimilars could lead to their treatment corresponding to therapeutic standards that have been obsolete for more than a decade, with the corresponding detriment to the management of psoriatic disease vs the current therapeutic standards and objectives. In any case, we consider that the TPR should never be a limitation for prescription, especially if it is not supported by scientific evidence that justifies it.

Summary and Conclusions

- The recent addition of ustekinumab biosimilars in July 2024 to the therapeutic armamentarium of moderate-to-severe psoriasis requires updating the GPS positioning document on the use of biosimilar drugs.
- The addition of ustekinumab biosimilars is an opportunity in the context of greater efficiency, allowing patients access to better treatment alternatives for moderate-to-severe psoriasis.
- The GPS considers that ustekinumab biosimilars should be on an equal footing with biosimilars of the anti-TNF family in terms of first-line prescription of biologics in moderate-to-severe psoriasis.
- The prescription of biosimilar drugs should always be based on individualized clinical and efficiency criteria and should not be justified exclusively on pure cost criteria.
- The drafting of TPRs for drugs approved after the incorporation of biosimilars poses inconsistencies in prescription and limits current standards of care. Their review and updating would be advisable and necessary.

Conflicts of interest

1. L. Salgado-Boquete received speaker's fees and/or consultant's fees and/or researcher's fees from Abbvie, Almirall, Amgen, Biogen, Boheringer, BMS, Celgene, Janssen-Cilag, Leo Pharma, Novartis, Pfizer, Sandoz, MSD-Schering-Plough, Lilly and UCB.
2. L. Puig received speaker's fees or consultant's fees and/or has been involved in clinical trials sponsored by Abbvie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Fresenius-Kabi, Horizon (DSMB), J&J Innovative Medicine, Leo-Pharma, Lilly, Novartis, Pfizer, STADA, Sun-Pharma, and UCB.
3. JM Carrascosa has been involved as PI/SI and/or advisor and/or invited speaker for Sandoz, UCB, Amgen, Lilly, Almirall, Janssen, Novartis, BMS, Abbvie, Leo Pharma.
4. P. de la Cueva received speaker's fees and/or consultant's fees and/or researcher's fees from Abbvie, Almirall, Amgen, Astellas, Beiersdorf, Biogen, BMS, Boehringer, Celgene, Gebro, Johnson&Johnson, LEO Pharma, Lilly, MSD, Novartis, Pfizer, Roche, Sandoz, Sanofi, SVR, Takeda, UCB.
5. López received fees for educational events, support to attend meetings, and participated in advisory boards from Abbvie, Almirall, Amgen, Janssen, Eli Lilly, Leo Pharma, Novartis, UCB. Has received support to attend congresses from: Abbvie, Almirall, Eli Lilly, Janssen, Novartis and UCB. Has received payments

for talks or consultancies from: Abbvie, Almirall, Amgen, Bristol Myers Squibb, Janssen, Eli Lilly, Leo Pharma, Novartis, UCB.

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