**Assessing the Value Contribution of Bimekizumab for the Treatment of Moderate-to-Severe Psoriasis Using a Multidisciplinary Reflective Multi-Criteria Decision Analysis**

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**Introduction**

There are multiple biological drugs, with different mechanisms of action, to treat moderate-to-severe psoriasis. For the realisation of this MCDA, in order to avoid excessive complexity of the exercise, we have selected the comparators of bimekizumab based on the inclusion of at least one treatment representative of each type of mechanism of action (prioritising those that have head-to-head trials with bimekizumab, except for the IL-17A, for which we will use two alternative comparators). Therefore, biological drugs such as guselkumab, brodalumab, tildrakizumab, certolizumab, infliximab and etanercept, as well as conventional systemic therapies, are excluded from this exercise.

**Table (S1).1: Drugs**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Bimekizumab  (BKZ) | Placebo  (PBO) | Adalimumab  (ADA) | Ustekinumab  (UST) | Secukinumab  (SEC) | Ixekizumab  (IXE) | Risankizumab  (RIS) |
| Drug type | IL-17A / IL-17F | - | TNFα | IL-12 / IL-23 | IL-17A | IL-17A | IL-23 |
| Marketing authorisation by EMA | Yes | - | Yes | Yes | Yes | Yes | Yes |
| Commercialisation in Spain | No | - | 2004, 2018 (biosimilars) | 2010 | 2015 | 2016 | 2020 |

The summary tables in this document summarise the evidence published on the 15 criteria validated in the first meeting of the committee: the first three criteria refer to the pathology (moderate-to-severe psoriasis) and the others refer to the evaluated drug, with some criteria being absolute and others relative to the different selected comparators. Where data are available, drug comparisons are based on head-to-head trials (direct comparisons). In the rest of the cases (for ixekizumab and risankizumab), the evidence is shown based on the data that is available, that is, each of these drugs versus placebo, compared to bimekizumab versus placebo, so the scientific rigor is lower, since results of different studies are compared without having individual data (“eyeball comparison”). Finally, for the criterion of consistency of de effect, part of the provided evidence is also based on comparisons of different studies without individual data.

# **1. Need for the intervention**

## **Disease severity**

**Table (S1).2: Main aspects related to the severity of moderate-to-severe psoriasis**

|  |  |
| --- | --- |
| Domain | Main elements |
| Description of the disease | * Immune-mediated and chronic inflammatory dermatosis1, with a clinical course of persistent relapses and remissions1. * Plaque psoriasis is the most common type of psoriasis, accounting for around 90% of cases2. It is characterized by the presence of erythematous plaques with clear margins, variable size (between 1 and several cm in diameter) and covered with fine and pearly scales of different thickness1. * Moderate-to-severe psoriasis affects 29% of psoriasis patients (19% moderate; 10% severe)3. |
| Diagnosis | * It is usually based on the history and the finding of characteristic skin lesions, morphology, and distribution of skin lesions.4. * Moderate-to-severe psoriasis can be defined according to several parameters: involvement >10% of the body surface; a Psoriasis Area Severity Index (PASI) ≥10, or deterioration in quality of life evaluated by a Dermatology Quality of Life Index (DLQI) >104. |
| Mortality | * Life expectancy: 3 to 6 years lower than that of the healthy population4–6. * Risk of death: 16% higher than in the healthy population (13% and 52% higher risk in moderate and severe psoriasis, respectively)7. * Risk of death from cardiovascular causes: 15% higher (38% higher for patients with severe psoriasis)7. * Risk of death from infections: 24% higher (41% higher in moderate psoriasis; 58% in severe psoriasis)7. * 2 times the risk of death from kidney and liver causes (up to 4 times higher in patients with severe psoriasis)7. |
| Morbidity | * Symptoms and signs: peeling of the skin, itching, redness (<65% of patients), pain, fatigue, swelling, burning, bleeding and cracking (20% of patients)8.9. * Comorbidities: psoriatic arthritis (25-35% of patients), overweight (53%), hypertension (18%), diabetes (8%), and increased risk of inflammatory bowel disease and liver disease10. * Psychological state: anxiety / depression (39% of patients), major anxiety / depression (19%)11. * Social activities: discrimination / humiliation (80-90% of patients), discomfort in appointments (72%) and intimate relationships (60%)12.13. * Daily activities: levels of affectation of 7/10 (severe) vs. 3/10 (mild)14; days without activities (32 vs 11, without / with treatment)15. |
| Quality of life | * Quality of life between 32-46% lower than that of the healthy Spanish population over 65 years (physical and mental SF-36: 49.7 and 46.2 vs. 73.3 and 84.8)10.16. |
| Economic burden | * Cost / patient / year with moderate-to-severe psoriasis: €11,000 (Spain)17. * Proportion of social costs (caregivers, loss of productivity) over the total cost per patient with moderate-to-severe psoriasis: 19-27% (Spain)17. * Cost of severe psoriasis vs. moderate: + 200% (Spain)17. * Consumption of resources / productivity: medical visits (40% more in psoriasis vs. healthy population)20, productivity loss: 29% (severe)21.22. |

## **Size of affected population**

* Incidence of between 0.06% and 1.50% of the world population (scarce and heterogeneous evidence)23.
* Global prevalence: between 0.09% and 5.1% (more than 60 million people affected)4.
* Prevalence in Spain: 2.3% of the total population2.
  + - Higher for men than for women (2.7% vs. 1.9%)2.
    - It follows an ascending curve until 60-69 years of age (3.4%), decreasing thereafter (prevalence of 2.6% for those older than 70 years)2.
* Based on these data, it is estimated that in Spain there may be 1,090,000 adult patients with psoriasis (2.3% of the total population2). Of these, 90% are patients with plaque psoriasis2 (980 thousand; 2.1%), of which 29% (280 thousand; 0.6%) have moderate-to-severe psoriasis3, and are therefore possible candidates to be treated with biologics. Of these, only a part (about 5-10%) receives treatment with biologics9.

## **Unmet needs**

**Effectiveness**

* With the most recent (and effective: IL-17 and IL-23) drugs, between 8 and 9 patients out of 10 achieve PASI 75 during the induction therapy period, which is maintained over a year, while this proportion is reduced to between 7-8 / 10 for PASI 90, and 4-6 / 10 for PASI 100, demonstrating that, despite the advances, there are still between 35% and 60% of patients who do not achieve complete clearance after one year with the most effective therapies available24.
* In the best-case scenario with currently available treatments, for half of the patients who manage to obtain a total clearance (PASI 100 to 50% of patients), these results are only obtained 3 months (up to 8 months) from the start of the treatment. The drugs of the IL-17 class are the fastest in obtaining total clearance25.
* Half of the patients discontinue or change their treatment within 4 years from its start, and the main reason is the lack of persistence of efficacy. The 4-year persistence rate for current biologics is between 41% and 56%, which means that 44% to 59% of patients have to stop their treatment before the fourth year26.

**Safety and tolerability**

* One of the common concerns regarding the safety and tolerability of the use of biologicals is related to the possible reactivation of hepatitis B27–32. Different classes of drugs produce specific adverse events that must be taken into account when prescribing treatment27–29: (i) TNF: severe infections, tuberculosis, paradoxical reactions, lupus, infusion reaction, congestive heart failure, autoimmune diseases, abnormal liver function results, some neurological disorders and demyelinating diseases. (ii) IL-12 / IL-23: although some observational studies have raised some concern related to the production of cardiovascular and major cardiovascular events due to the use of IL-12 / IL-23, this causality has not been demonstrated. (iii) IL-17: candidiasis, neutropenia, inflammatory bowel disease, upper respiratory tract infections, nasopharyngitis, headaches, diarrhoea, and some psychiatric effects in brodalumab. IL-23: To date, no serious adverse events specific to IL-23 have been reported.
* Biological treatments are generally safe, with a low proportion of patients affected by serious adverse events. The proportion of patients with moderate-to-severe psoriasis treated with biological drugs who experience some type of adverse event in the two years after treatment ranges between 46% and 93%. This percentage drops to between 5.3% and 11.7% if we consider serious adverse events, and to less than 0.5% if we consider deaths caused by adverse events33.34.
* The proportion of patients who have to interrupt their treatment for safety reasons is less than that related to failure or loss of efficacy. In this sense, the IL-17, IL-23 and IL-12 / IL-23 have lower discontinuation rates (0% to 2.6%) than the TNFs (6.5% to 15.6% ) considering 1-2 years after the start of treatment35.36.

# **2. Outcomes of the intervention**



## **Level of clearance**

**Table (S1).3: Level of clearance, PASI, IGA, PGA, % of patients, weeks 12-24**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Sources | Gordon (2021)37 | | Warren (2021)38 | | Reich (2021)39 | | Reich (2021)40 | | Griffiths (2015)41 and Gordon (201642, 202137) | | Gordon (201843, 202137) | |
| Variable | **BKZ** | **PBO** | **BKZ** | **ADA** | **BKZ** | **UST** | **BKZ** | **SEC** | **BKZ** | **IXE** | **BKZ** | **RIS** |
| PASI 100 Week 12 | - | - | - | - | - | - | - | - | - | 35-41 | - | - |
| PASI 100 Week 16 | 68 | 1 | 61 | 24 | 59 | 21 | 62 | 49 | 68 | - | 68 | 36-51 |
| PASI 100 Week 24 | - | - | 67 | 30 | - | - | - | - | - | - | - | - |
| PGA 0 Week 12 | - | - | - | - | - | - | - | - | - | 40-42 | - | - |
| IGA 0 Week 16 | 70 | 1 | - | - | 59 | 22 | - | - | 70 | - | 70 | - |
| PGA 0 Week 16 | - | - | - | - | - | - | - | - | - | - | - | 37-51 |
| IGA 0 Week 24 | - | - | 87 | 58 | - | - | - | - | - | - | - | - |
| PASI 90 Week 12 | - | - | - | - | 85 | 44 | - | - | - | 68-71 | - | - |
| PASI 90 Week 16 | 91 | 1 | 86 | 47 | 85 | 50 | 86 | 74 | 91 | - | 91 | 75 |
| PASI 90 Week 24 | - | - | 86 | 52 | - | - | - | - | - | - | - | - |
| IGA 0/1 Week 12 | - | - | - | - | 82 | 52 | - | - | - | - | - | - |
| PGA 0/1 Week 12 | - | - | - | - | - | - | - | - | - | 81-83 | - | - |
| IGA 0/1 Week 16 | 93 | 1 | 85 | 57 | 84 | 53 | 86 | 79 | 93 | - | 93 | - |
| PGA 0/1 Week 16 | - | - | - | - | - | - | - | - | - | - | - | 84-88 |
| PASI 75 Week 12 | - | - | - | - | - | - | - | - | - | 87-90 | - | 87-89 |
| PASI 75 Week 16 | - | - | - | - | - | - | 93 | 91 | 95 | - | 95 | - |

Notes: (i) **All data refer to head-to-head comparisons, except for the comparison between bimekizumab and ixekizumab, and between bimekizumab and risankizumab, which uses trials of each comparator vs. placebo.** (ii) the data are ordered according to the level of clearance (from highest to lowest). (iii) Data of trials that reflect the posology applied in the technical product specification have been prioritized. PASI 75/90/100 = improvement in the level of clearance of ≥ 75/90/100% compared to the start of treatment. IGA: Investigators' Global Assessment, where 0 means complete clearance, and 1, almost complete clearance. PGA: Physician Global Assessment, where 0 means complete clearance and 1, almost complete clearance. BKZ: Bimekizumab. PBO: placebo. ADA: Adalimumab. UST: Ustekinumab. SEC: Secukinumab. IXE: Ixekizumab. RIS: Risankizumab.

## **Rapidity of clearance**

**Table (S1).4: Level of clearance, % of patients with PASI 75, week 4**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Sources | Gordon (2021)37 | | Warren (2021)38 | | Reich (2021)39 | | Reich (2021)40 | | Griffiths (2015)41 and Gordon (201642, 202137) | | Gordon (201843, 202137) | |
| Variable | **BKZ** | **PBO** | **BKZ** | **ADA** | **BKZ** | **UST** | **BKZ** | **SEC** | **BKZ** | **IXE** | **BKZ** | **RIS** |
| PASI 75 Week 4 | 76 | 1 | 77 | 31 | 77 | 15 | 71 | 47 | 76 | 49-54 | 76 | 25 |

Notes: (i) **All data refer to head-to-head comparisons, except for the comparison between bimekizumab and ixekizumab, and between bimekizumab and risankizumab, which uses trials vs. placebo**(ii) the data are ordered according to the level of clearance (from highest to lowest). (iii) Data of trials that reflect the posology applied in the technical product specification have been prioritized. PASI 75 = improvement in the level of clearance of ≥75% compared to the start of treatment. BKZ: Bimekizumab. PBO: placebo. ADA: Adalimumab. UST: Ustekinumab. SEC: Secukinumab. IXE: Ixekizumab. RIS: Risankizumab.

**Table (S1).5: Rapidity ​​of clearance, response time to achieve specified objectives, in weeks**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Sources | - | | Lebwohl (2021)44 | | Lebwohl (2021)44 | | - | | - | | - | |
| Variable | **BKZ** | **PBO** | **BKZ** | **ADA** | **BKZ** | **UST** | **BKZ** | **SEC** | **BKZ** | **IXE** | **BKZ** | **RIS** |
| PASI 100 | - | - | 12.1 | > 16 | 12.1 | > 16 | - | - | - | - | - | - |
| PASI 90 | - | - | 8.0 | 12.6 | 8.0 | 12.6 | - | - | - | - | - | - |
| IGA 0/1 | - | - | 4.3 | 12.1 | 4.3 | 12.1 | - | - | - | - | - | - |
| PASI 75 | - | - | 4.0 | 8.3 | 4.0 | 8.4 | - | - | - | - | - | - |
| DLQI 0/1 | - | - | 8.1 | 12.3 | 8.1 | > 16 | - | - | - | - | - | - |

Notes: (i) **All data refer to direct comparisons**(ii) the data are ordered according to the level of clearance (from highest to lowest). (iii) Data of trials that reflect the posology applied in the technical product specification have been prioritized. PASI 75/90/100 = improvement in the level of clearance of ≥ 75/90/100% compared to the start of treatment. IGA: Investigators' Global Assessment, where 0 means complete clearance, and 1, almost complete clearance. BKZ: Bimekizumab. PBO: placebo. ADA: Adalimumab. UST: Ustekinumab. SEC: Secukinumab. IXE: Ixekizumab. RIS: Risankizumab.

## **Persistence of clearance**

**Table (S1).6: Persistence of clearance, % of patients, weeks 48-60**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Sources | Gordon (2021)37 | | Warren (2021)38 | | Reich (2021)39 | | Reich (2021)40 | | Gordon (201642, 202137) | | Gordon (201843, 202137) | |
| Variable | **BKZ** | **PBO** | **BKZ** | **ADA** | **BKZ** | **UST** | **BKZ** | **SEC** | **BKZ** | **IXE** | **BKZ** | **RIS** |
| PASI 100 Week 48 | - | - | - | - | - | - | 66 | 48 | - | - | - | - |
| PASI 100 Week 52 | - | - | - | - | 65 | 38 | - | - | - | - | - | 55-57 |
| PASI 100 Week 56 | 83 | 11\* | 70 | 30 → 67 \*\* | - | - | - | - | 83 | - | 83 | - |
| PASI 100 Week 60 | - | - | - | - | - | - | - | - | - | 52 | - | - |
| IGA 0 Week 52 | - | - | - | - | - | - | - | - | - | - | - | - |
| IGA 0 Week 56 | - | - | - | - | - | - | - | - | - | - | - | - |
| PASI 90 Week 48 | - | - | - | - | - | - | 86 | 74 | - | - | - | - |
| PASI 90 Week 52 | - | - | - | - | 82 | 56 | - | - | - | - | - | 72-85 |
| PASI 90 Week 56 | 91 | 16 \* | 83 | 52 → 82 \*\* | - | - | - | - | 91 | - | 91 | - |
| PASI 90 Week 60 | - | - | - | - | - | - | - | - | - | 73 | - | - |
| IGA 0/1 Week 48 | - | - | - | - | - | - | 86 | 77 | - | - | - | - |
| IGA 0/1 Week 52 | - | - | - | - | 78 | 61 | - | - | - | - | - | - |
| PGA 0/1 Week 52 | - | - | - | - | - | - | - | - | - | - | - | 83-91 |
| IGA 0/1 Week 56 | 90 | 24 \* | 83 | 58 → 81 \*\* | - | - | - | - | 90 | - | 90 | - |
| IGA 0/1 Week 60 | - | - | - | - | - | - | - | - | - | 75 | - | - |
| PASI 75 Week 48 | - | - | - | - | - | - | 91 | 85 | - | - | - | - |

Notes: (i) **All data refer to head-to-head comparisons, except for the comparison between bimekizumab and ixekizumab, and between bimekizumab and risankizumab, which uses trials vs. placebo. (ii)** the data are ordered according to the level of clearance (from highest to lowest). (iii) Data of trials that reflect the posology applied in the technical product specification have been prioritized (in the case of bimekizumab, data from the maintenance schedule have been used every 8 weeks, according to the marketing authorisation by EMA. (\*) Patients who were treated with bimekizumab until week 16, and who were reassigned to the placebo group at week 16, to receive bimekizumab. (\*\*) The two data represent the % of patients who had achieved this goal at week 24 (adalimumab W0-24), and the% of patients who achieved it at week 56, after reassignment at week 24 (bimekizumab W24-56). W: week. PASI 75/90/100 = improvement in the level of clearance of ≥ 75/90/100% compared to the start of treatment. IGA: Investigators' Global Assessment, where 0 means complete clearance, and 1, almost complete clearance. PGA: Physicians' Global Assessment, where 0 means complete clearance and 1, almost complete clearance. BKZ: Bimekizumab. PBO: placebo. ADA: Adalimumab. UST: Ustekinumab. SEC: Secukinumab. IXE: Ixekizumab. RIS: Risankizumab.

## **Safety / tolerability**

**Table (S1).7: Safety / tolerability, % of patients, short term\***

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Sources | Gordon (2021)37 | | Warren (2021)38 | | Reich (2021)39 | | Reich (2021)40 | | Gordon (201642, 202137) | | Gordon (201843, 202137) | |
| Period (in weeks) | **(0-16)** | | **(0-24)** | | **(0-16)** | | **-** | | **(0-16 / 0-12)** | | **(0-16)** | |
| Variable | **BKZ** | **PBO** | **BKZ** | **ADA** | **BKZ** | **UST** | **BKZ** | **SEC** | **BKZ** | **IXE** | **BKZ** | **RIS** |
| Serious AE ϮϮ | 2 | 2 | <1 | 3 | 2 | 3 | - | - | 2 | 2 | 2 | 2 |
| Severe AE Ϯ | 1 | 1 | 1 | 3 | 2 | 2 | - | - | 1 | - | 1 | 2 |
| Discontinuations | 1 | 0 | 4 | 3 | 2 | 2 | - | - | 1 | 2 | 1 | <1 |
| Deaths | 0 | 0 | 0 | <1 | <1 | 1 | - | - | 0 | 0 | 0 | <1 |
| AE caused by the drug | - | - | 29 | 24 | - | - | - | - | - | - | - | - |
| Any AE | 61 | 41 | 72 | 70 | 56 | 51 | - | - | 61 | 59 | 61 | 46-50 |
| Most common AE |  |  |  |  |  |  |  |  |  |  |  |  |
| Nasopharyngitis | 7 | 5 | - | - | 9 | 9 | - | - | 7 | 9 | 7 | - |
| Oral candidiasis | 6 | 0 | 12 | 0 | 9 | 0 | - | - | 6 | 1 | 6 | - |
| URT infection | 4 | 8 | 28 | 35 | 3 | 3 | - | - | 4 | 4 | 4 | - |
| AE of special interest |  |  |  |  |  |  |  |  |  |  |  |  |
| Serious infections | 1 | 0 | <1 | <1 | 0 | 1 | - | - | 1 | <1 | 1 | <1 |
| IBD | 0 | 0 | 0 | 0 | <1 | 0 | - | - | 0 | - | 0 | - |
| Neoplasms | <1 | 0 | 3 | <1 | 0 | 0 | - | - | <1 | - | <1 | <1 |
| Skin cancer\*\* | <1 | 0 | 2 | 0 | 0 | 0 | - | - | <1 | <1 | <1 | 0 |
| MACE | 0 | 0 | 0 | 0 | <1 | 0 | - | - | 0 | 0 | 0 | 0 |
| LE elevation | 3 | 1 | 3 | 7 | 1 | 0 | - | - | 3 | - | 3 | - |

Notes: \* ordered according to severity of AE (i) **All data refer to direct comparisons, except the comparison with IXE and RIS, which uses trials vs. placebo.** (ii) Data of trials that reflect the posology applied in the technical product specification have been prioritized. (iii) We have not included, in common AE, the episodes of hypertension and diarrhoea, since they were only reported in the comparison of bimekizumab vs. adalimumab (6 vs. 8 and 3 vs. 2, respectively. (iv) there were no episodes of active tuberculosis, latent tuberculosis, suicidal ideation and behaviour, and hypersensitivity reactions, which is why they are not included in this table. (v) The data period is indicated in the line top line of the table. In the BKZ vs. IXE comparison, the number of weeks for BKZ is 0-16, and for IXE, 0-12. (Vi) No data has been reported short-term in the BKZ vs. SEC comparison. **ϮϮ** serious adverse events: threat to the life or functioning of the patient45. Ϯ severe adverse event: describes the intensity (severity) of a specific event45. AE: Adverse events. URT: upper respiratory tract. IBD: inflammatory bowel disease. (\*\*) non melanoma. MACE: Major adverse cardiac events. LE: liver enzymes. BKZ: Bimekizumab. PBO: placebo. ADA: Adalimumab. UST: Ustekinumab. SEC: Secukinumab. IXE: Ixekizumab. RIS: Risankizumab.

**Table (S1).8: Safety / tolerability, % of patients, long term\***

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Sources | Gordon (2021)37 | | Warren (2021)38 | | Reich (2021)39 | | Reich (2021)40 | | Gordon (201642, 202137) | | Gordon (201843, 202137) | |
| Period (in weeks) | **(16-56)** | | **(24-56)** | | **(0-52)** | | **(0-48)** | | **(16-56 / 0-60)** | | **(16-56 / 16-52)** | |
| Variable | **BKZ** | **PBO** | **BKZ** | **ADA** | **BKZ** | **UST** | **BKZ** | **SEC** | **BKZ** | **IXE** | **BKZ** | **RIS** |
| Serious AE ϮϮ | 3 | 4 | 5 | 6 | 6 | 8 | 6 | 6 | 3 | 7 | 3 | 4-5 |
| Severe AE Ϯ | 1 | 4 | 5 | 5 | 5 | 6 | 7 | 4 | 1 | - | 1 | 2-4 |
| Discontinuations | 2 | 3 | 1 | 3 | 5 | 4 | 3 | 3 | 2 | 4 | 2 | <1 |
| Deaths | 0 | 0 | 0 | 0 | 1 | 1 | <1 | <1 | 0 | <1 | 0 | <1 |
| AE caused by the drug | - | - | 24 | 30 | - | - | 43 | 32 | - | - | - | - |
| Any AE | 77 | 69 | 70 | 75 | 82 | 80 | 86 | 81 | 77 | 81 | 77 | 56-61 |
| Most common AE |  |  |  |  |  |  |  |  |  |  |  |  |
| Nasopharyngitis | 23 | 19 | - | - | 22 | 22 | - | - | 23 | 20 | 23 | - |
| Oral candidiasis | 9 | 6 | 9 | 17 | 15 | 1 | 19 | 3 | 9 | 2 | 9 | - |
| URT infection | 8 | 5 | 24 | 28 | 9 | 11 | 39 | 41 | 8 | 10 | 8 | - |
| AE of special interest |  |  |  |  |  |  |  |  |  |  |  |  |
| Serious infections | 0 | 0 | 1 | 3 | 1 | 3 | 2 | 2 | 0 | 1 | 0 | <1 |
| IBD | 0 | 0 | 0 | 0 | <1 | 0 | <1 | <1 | 0 | - | 0 | - |
| Suicidal ideation\* | - | - | - | - | <1 | 1 | <1 | 0 | 0 | - | 0 | - |
| Neoplasms | 0 | 1 | 1 | <1 | <1 | 1 | 1 | <1 | 0 | - | 0 | <1 |
| Skin cancer\*\* | 0 | 0 | 0 | <1 | 0 | 1 | <1 | <1 | 0 | <1 | 0 | 0 |
| Latent tuberculosis | - | - | 2 | <1 | 0 | 0 | 1 | 1 | 0 | - | 0 | <1 |
| MACE | 1 | 0 | 0 | 0 | 1 | 0 | 0 | <1 | 1 | <1 | 1 | <1 |
| LE elevation | 3 | 0 | 1 | 4 | 3 | 3 | 6 | 5 | 0 | - | 0 | - |

Notes: \*ordered according to severity of AE (i) **All data refer to direct comparisons, except the comparison with IXE and RIS (vs. placebo).** (ii) Data of trials that reflect the posology applied in the technical product specification have been prioritized. (iii) We have not included, in common AE, the episodes of hypertension and diarrhoea, only reported in BKZ vs. ADA (2 vs. 2 and 2 vs. 1, respectively). Nor have we included urinary tract infections, as they are only reported in BKZ vs. SEC (7 vs 6) (iv) There were no active tuberculosis episodes and hypersensitivity reactions, which is why they are not included in this table. (v) The period of the data is indicated in the top line of the table. In the BKZ vs. IXE, the number of weeks for BKZ is 16-56, and for IXE, 0-60. In the comparison of BKZ vs. RIS, the number of weeks of RIS is 16-52 (vi) The PBO data include patients who came from the BKZ group of weeks 0-16.**ϮϮ** serious adverse events: threat to the life or functioning of the patient45. Ϯ severe adverse event: describes the intensity (severity) of a specific event45. AE: Adverse events. URT: upper respiratory tract. IBD: inflammatory bowel disease. (\*) suicidal ideation and behaviour (\*\*) non melanoma. MACE: Major cardiac adverse events. LE: liver enzymes. BKZ: Bimekizumab. PBO: placebo. ADA: Adalimumab. UST: Ustekinumab. SEC: Secukinumab. IXE: Ixekizumab. RIS: Risankizumab.

## **Patient reported outcomes**

**Table (S1).9: Patient reported outcomes, % of patients, weeks 12-56**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Sources | Gordon (2021)37 | | Warren (2021)38 | | Reich (2021)39 | | Reich (2021)40 | | Griffiths (2015)41 | | Gordon (201843, 202137) | |
| Variable | **BKZ** | **PBO** | **BKZ** | **ADA** | **BKZ** | **UST** | **BKZ** | **SEC** | **BKZ** | **IXE** | **BKZ** | **RIS** |
| DLQI 0/1 Week 12 | - | - | - | - | - | - | - | - | - | 64 | - | - |
| DLQI 0/1 Week 16 | 76 | 6 | - | - | 67 | 42 | - | - | 76 | - | 76 | 66-67 |
| DLQI 0/1 Week 24 | - | - | 67 | 48 | - | - | - | - | - | - | - | - |
| DLQI 0/1 Week 48 | - | - | - | - | - | - | 78 | 70 | - | - | - | - |
| DLQI 0/1 Week 52 | - | - | - | - | - | - | - | - | - | - | - | - |
| DLQI 0/1 Week 56 | 86 | 19 \* | 79 | 48 → 73 \*\* | 75 | 63 | - | - | 86 | - | 86 | - |
| P-SIM itch Week 12 | - | - | - | - | - | - | - | - | - | 85 | - | - |
| P-SIM itch Week 16 | 76 | 6 | - | - | 68 | 55 | - | - | 76 | - | 76 | - |
| P-SIM itch Week 24 | - | - | 67 | 46 | - | - | - | - | - | - | - | - |
| P-SIM pain Week 16 | 79 | 9 | - | - | 74 | 60 | - | - | 79 | - | 79 | - |
| P-SIM pain Week 24 | - | - | 70 | 47 | - | - | - | - | - | - | - | - |
| P-SIM scaling Week 16 | 78 | 6 | - | - | 76 | 57 | - | - | 78 | - | 78 | - |
| P-SIM scaling Week 24 | - | - | 70 | 48 | - | - | - | - | - | - | - | - |
| PSS 0 Week 16 | - | - | - | - | - | - | - | - | - | - | - | 29-31 |
| PSS, Week 16 variation | - | - | - | - | - | - | - | - | - | - | - | 54-81 \*\*\* |

Notes: (i) **All data refer to direct comparisons, except the comparison between BKZ / IXE, and BKZ / RIS, which uses trials vs. placebo. (ii)** Data of trials that reflect the posology applied in the technical product specification have been prioritized. P-SIM: Questionnaire to measure the Impact and Symptoms of Psoriasis. Each item is evaluated based on an 11-point scale, where 0 means absence of symptoms, signs or impact. Responses were defined as the proportion of patients who achieved a 4-point reduction in one item of the P-SIM (clinically significant improvement). PSS: Psoriasis Symptom Scale. It is an eight-item questionnaire, which aims to assess the severity of the main symptoms, signs and impact of psoriasis. Each item is evaluated based on an 11-point scale, where 0 means absence of symptoms, signs or impact. The results range from 0 to 40 (Symptoms), and 0 to 30 (Signs), where higher scores indicate greater severity. DLQI: Dermatology Quality of Life Index. The result of the questionnaire can range from 0 to 30, where a score of 0-1 represents no involvement of the disease in the patient's Health-Related Quality of Life (HRQoL) and a score of 21-30 represents a very high impact of the disease on HRQoL. A 4-point change in this indicator represents a minimal clinically significant difference. (\*) data from patients who were in the bimekizumab group in the induction period and switched to placebo in the maintenance period. (\*\*) patients with ADA W0-24 and BKZ W24-56. (\*\*\*) % improvement compared to the start of treatment. BKZ: Bimekizumab. PBO: placebo. ADA: Adalimumab. UST: Ustekinumab. SEC: Secukinumab. IXE: Ixekizumab. RIS: Risankizumab.

**Table (S1).10: Convenience, number of times the drug is administered per year (in parentheses, number of injections per year), n**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Variable | BKZ | PBO | ADA | UST | SEC | IXE | RIS |
| Year 1 | 9 (18) | 0 | 27 (28) | 6 (6) | 17 (34) | 17 (18) | 6 (12) |
| Year 2 and following | 6.5 (13) | 0 | 26 (26) | 4.3 (4.3) | 12 (24) | 12 (12) | 4.3 (8.6) |

Notes: i) Many of these treatments require the dose to be administered in 2 separate injections, therefore the number of injections per year is often twice the number of times the drug is administered to the patient per year. (ii) have considered data related to the technical product sheet. iii) For bimekizumab, doses were considered every 4 weeks in the induction period (16 weeks), and every 8 weeks in the maintenance period (from week 16). It should be noted that, foreseeably, in 1 or 2 years a presentation of 360 mg of bimekizumab in a single injection might be approved, which will allow the number of injections to be reduced by half.

Source: AEMPS (2021)46

# **3. Type of benefit of the intervention**



## **Type of therapeutic benefit**

This is an absolute criterion; therefore, it only refers to the therapeutic benefit of bimekizumab. Bimekizumab has no curative effect. However, the therapeutic benefits of the drug translate into a high degree of clearance, rapidity of action and persistence of the clearance achieved. In addition, they are associated with improvements in the quality of life of patients and in the alleviation of their main symptoms, such as pain, itching and scaling, effects that are maintained over time.

## **Consistency of the effect**

*How effective is bimekizumab compared to the other drugs, taking into account the development of psoriatic arthritis (as it is the most prevalent comorbidity) and psoriasis in special locations (such as the scalp, hands and feet [palmoplantar]?*

**Table (S1).11: Consistency of the effect in patients with psoriasis and psoriatic arthritis, % of patients, weeks 12-24**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Sources | Ritchlin (2020)47 | | Ritchlin (2020)47 and Mease (2005)48 | | Ritchlin (2020)47 and McInnes (2013)49 | | Ritchlin (2020)47, Mease (2018)50 And Kivitz (2019)51 | | Ritchlin (2020)47 and Mease (2017)52 | | Ritchlin (2020)47 and UCB (2021)53 | |
| Variable | **BKZ** | **PBO** | **BKZ** | **ADA** | **BKZ** | **UST** | **BKZ** | **SEC** | **BKZ** | **IXE** | **BKZ** | **RIS** |
| ACR 50 Week 12 | 46 | 7 | 46 | 36 | 46 | - | 46 | - | 46 | 40 | 46 | 26-33 |
| ACR 50 Week 16 | - | - | - | - | - | - | - | 40 | - | - | - | - |
| ACR 50 Week 24 | - | - | - | - | - | 25-28 | - | - | - | - | - | - |
| PASI 100 Week 12 | 50 | 7 | 50 | - | 50 | - | 50 | - | 50 | 41 | 50 | - |
| PASI 90 Week 12 | 54 | 7 | 54 | 30 | 54 | - | 54 | - | 54 | 58 | 54 | 52-55 |
| PASI 90 Week 16 | - | - | - | - | - |  | - | 54 | - | - | - | - |
| PASI 75 Week 12 | 77 | - | 77 | - | 77 | - | 77 | - | 77 | 69 | 77 | - |
| PASI 75 Week 16 | - | - | - | - | - |  | - | 70 | - | - | - | - |
| PASI 75 Week 24 | - | - | - | - | - | 57-62 | - | - | - | - | - | - |
| SF-36, Week12 variation | 7.5 (20%) | 2.7 (7%) | 7.5 (20%) | 9.6 (28%) | 7.5 (20%) | - | 7.5 (20%) | - | 7.5 (20%) | 7.6 (22%) | 7.5 (20%) | - |
| SF-36 variation Week 16 | - | - | - | - | - |  | - | 3.4 (n.a) | - | - | - | - |
| SF-36, Week 24 variation | - | - | - | - | - | 4-6 (11-16%) | - | - | - | - | - | - |
| PsAID Week 12 | 73 | 29 | 73 | - | 73 | - | 73 |  | 73 | - | 73 | - |

Notes: (i) **The data presented refer to comparisons of each drug versus placebo (i.e. there is no direct comparison between them).** (ii) Data of trials that reflect the posology applied in the technical product specification have been prioritized. For BKZ, the EMA marketing authorisation recommendation was used. ACR50: proportion of patients with at least 50% improvement according to the response criteria of the American College of Rheumatology. PASI: Psoriasis Area and Severity Index. SF-36: questionnaire that measures quality of life, and is reported through two indicators, the physical component and the mental component. Both indicators have a score that ranges from 0 to 100, where 100 is the best possible health status. A change of between 2.5 and 5.0 points in these indicators represents a minimal clinically significant difference, although this value has not been specified for patients with psoriasis.54. PsAID-9: Psoriatic Arthritis Impact of Disease questionnaire for clinical trials55. PsAID results range from 0 to 10, where 0 represents a greater impact of psoriatic arthritis in patients. The variable used was the proportion of patients with results ≤3, which signify acceptable health states for patients with psoriatic arthritis47. BKZ: Bimekizumab. PBO: placebo. ADA: Adalimumab. UST: Ustekinumab. SEC: Secukinumab. IXE: Ixekizumab. RIS: Risankizumab.

**Table (S1).12: Consistency of the effect in patients with psoriasis in different locations, % of patients, weeks 12-24**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Sources | Gordon (2021)37, Daddy (2021)56 | | Reich (2021)57 , Papp (2021)56 | | Reich (2021)39 , Daddy (2021)56 | | Daddy (2021)56, Mrovietz (2019)58, Reich (2021)59 | | Gordon (2021)37 , Reich (2017)60, Daddy (2021)56, van de Kerkhof (2017)61, Guenther (2020)62 | | Daddy (2021)56 | |
| Variable | **BKZ** | **PBO** | **BKZ** | **ADA** | **BKZ** | **UST** | **BKZ** | **SEC** | **BKZ** | **IXE** | **BKZ** | **RIS** |
| Scalp |  |  |  |  |  |  |  |  |  |  |  |  |
| PASI 100 Week 12 | - | - | - | - | - | - | - | - | - | 74 | - | - |
| PASI 90 Week 12 | - | - | - | - | - | - | - | - | - | 82 | - | - |
| IGA 0/1 Week 12 | - | - | - | - | - | - | - | 57 | - | - | - | - |
| IGA 0/1 Week 16 | 92 | 7 | - | - | 84 | 71 | 92 | - | 92 | - | 92 | - |
| IGA 0/1 Week 24 | - | - | 78 | 58 | - | - | - | - | - | - | - | - |
| Palmoplantar |  |  |  |  |  |  |  |  |  |  |  |  |
| IGA 0 Week 16 | 87 | 29 | 87 | - | 87 | 75 | 87 | - | 87 | - | 87 | - |
| PPPASI75 Week 16 | - | - | - | - | - | - | - | 75 | - | - | - | - |
| PASI 100 Week 12 | - | - | - | - | - | - | - | - | - | 50 | - | - |
| Nails |  |  |  |  |  |  |  |  |  |  |  |  |
| mNAPSI 0 Week 16 | 19 | 3 | 19 | - | 19 | 11 | 19 | - | 19 | - | 19 | - |
| mNAPSI 0 Week 12 | - | - | - | - | - | - | - | - | - | 20 | - | - |
| PASI 90 Week 16 | - | - | - | - | - | - | - | 73 | - | - | - | - |
| Genitals |  |  |  |  |  |  |  |  |  |  |  |  |
| PGA 0 Week 12 | - | - | - | - | - | - | - | - | - | 56 | - | - |

Notes: (i) **The data presented refer to comparisons of each drug versus placebo (there are no direct comparisons)**, and reflect results of the technical product sheet. For BKZ, the one recommended by the EMA marketing authorisation was used. (ii) The target variables and the periodicity are indicated in the "variables" row. PASI: Psoriasis Area and Severity Index. IGA: Investigators' Global Assessment. PPPASI: PASI Palmoplantar. mNAPSI: Nail Psoriasis Severity Index. PGA: Physicians' Global Assessment. BKZ: Bimekizumab. PBO: placebo. ADA: Adalimumab. UST: Ustekinumab. SEC: Secukinumab. IXE: Ixekizumab. RIS: Risankizumab.

# **4. Economic consequences of the intervention**



## **Cost of intervention**

**Table (S1).13: Annual cost of intervention (drug acquisition cost per patient, PVL)**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Variable | BKZ | PBO | ADA | UST | SEC | IXE | RIS |
| Year 1 | € 19,433 | € 0 | € 12,237 - € 14,396 | € 16,484 - € 18,600 | € 19,433 | € 18,180 | € 23,001 |
| Year 2 and following | € 14,860 | € 0 | € 11,362 - € 13,368 | € 10,989 - € 12,400 | € 14,860 | € 13,130 | € 15,334 |

Notes: (i) PVL: laboratory sales price (“notified price”). (ii) The prices considered are PVL, without considering the discount related to the Royal Decree RDL 8/2010, and without VAT. (iii) The costs related to the administration of the drug are not considered, since they are self-administered. (iv)**Bimekizumab is not yet marketed in Spain, so its acquisition price is unknown. For this MCDA, we assume the same annual costper patient as secukinumab**, being a drug that inhibits interleukin IL17A. (v) The costs of adalimumab consider the prices of the biosimilars, in addition to the cost of the original biological. (vi) The costs of ustekinumab consider the guidelines and prices according to the weight of the patient. (vii) It should be taken into account that the costs shown in the table refer to notified prices, but that biological drugs actually have a price financed by the SNS (confidential) that is lower than the official notified price. BKZ: Bimekizumab. PBO: placebo. ADA: Adalimumab. UST: Ustekinumab. SEC: Secukinumab. IXE: Ixekizumab. RIS: Risankizumab.

Sources: BOTPLUS (2021)63 and AEMPS (2021)46

## **Impact on other direct costs**

* No specific evidence is available for this criterion.
* It must therefore be scored trying to determine to what extent the improvement in health produced by bimekizumab could translate into a lower consumption of other direct health resources compared to the different comparators, in terms of medical visits, tests, hospitalizations or visits to the emergency room.
* What is documented is that, in Spain, the cost of a patient with severe psoriasis is 1.7 times higher than that of a patient with moderate psoriasis and that, of the total direct healthcare costs, 15% - 43% are non-pharmacological costs, the most important being medical visits3.17.67.
* On the other hand, in a North American study, it has been shown that patients who require treatment changes (switch) have average non-pharmacological direct healthcare costs between 12% and 33% higher than those of patients who do not require changes in treatment65.
* In a study in Italy, the introduction of biological drugs (TNF) resulted in savings of 69% in other non-pharmacological direct healthcare costs66.
* **Adalimumab, secukinumab, ustekinumab**: The use of adalimumab and secukinumab seems to be associated with a similar consumption of direct healthcare costs (non-pharmacological) to that of other biologics already marketed, while the use of ustekinumab seems to be associated with a greater consumption of these resources. For reference only, a study based on data from routine clinical practice with 7,800 patients in the United States compared direct healthcare and non-drug costs between adalimumab, secukinumab, ustekinumab, etanercept, and apremilast. The total costs, over a 2-year horizon, of medical visits and hospitalizations for patients treated with adalimumab amounted to $ 18,500, compared to $ 17,650 for etanercept, $ 18,800 for apremilast and secukinumab, and $ 24,750 for ustekinumab67.

## **Impact on indirect costs**

* There are no studies on the impact of bimekizumab on the work productivity or personal care of patients.
* The score should therefore be based on your experience and / or intuition, trying to assess to what extent the improvement produced by bimekizumab in the patient's health could be reflected in lower indirect costs.
* The total cost of a patient with moderate-to-severe psoriasis in Spain could reach € 11,000 per year (based on data from studies published up to 2009), of which 20% would be indirect costs17.
* A UK study found a positive correlation between PASI and labour productivity. Patients with PASI <50 had a loss of productivity of 22.8%, compared to 13.3% of patients with PASI 50-74 (p = 0.001); 6.4% of patients with PASI 75-89 (p <0.001) and 4.9% of patients with PASI ≥90 (p <0.001). The number of annual hours lost by these patients was 429 (PASI <50), 251 (PASI 50-74), 121 (PASI 75-89) and 93 (PASI ≥90) 68.
* Another study concluded that the implementation of an IL-23 generated savings of 50% in indirect costs for patients with psoriasis. At week 16, 65.6% of patients treated with an IL-23 (guselkumab) reported being able to return to work, compared to 22.2% of patients on placebo. This difference represented a saving of $ 7,578 in indirect costs ($ 6,225 with IL-23 vs. $ 13,803 in the placebo group)69. This same study found that the use of an IL-23 (guselkumab) versus adalimumab generated productivity gains. At week 48, the indirect costs of patients with IL-23 amounted to $ 5,452, and were therefore 34% lower than the indirect costs of patients treated with adalimumab ($ 8,337)69.
* Another study found that the use of secukinumab versus ustekinumab created productivity gains. At week 48, indirect costs for patients on secukinumab amounted to 1,611£, and were 20% lower than the indirect costs of patients treated with ustekinumab (1,996£)68.
* In the UNCOVER trials, ixekizumab patients reported improvements in work productivity versus placebo. This was measured through the average changes compared to the start of treatment observed in the data collected by the Work Productivity and Activity Impairment Questionnaire: Psoriasis (WPAI-PSO). At the beginning of treatment, the productivity index was between 22 and 25. After 60 months, these indexes were reduced to between 5 and 18 (improvements of between 28% and 77%)70.
* In a recent North American study based on machine learning algorithm, the authors estimated that the use of risankizumab could generate 17% improvements in the patient's labour productivity compared to the use of placebo, with indirect cost savings of $ 11,301 per patient / year71.

# **5. Knowledge of the intervention**



## **Quality of the evidence**

* All clinical trials included in this study were randomized, double-blind, multinational, and multicentre trials, which were conducted in accordance with the Good Clinical Practices (GCP) guidelines of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), the principles of the Declaration of Helsinki and the local laws of the countries involved. All data refer to head-to-head comparisons, except for the comparison between bimekizumab and ixekizumab, and between bimekizumab and risankizumab, which uses trials vs. placebo.
* For the comparison of these drugs (bimekizumab versus ixekizumab, and bimekizumab versus risankizumab), an indirect comparison study was also used (Sbidian, 2021)72, which includes 158 randomized clinical trials, published until September 2020, with 57,831 adult patients with moderate-to-severe psoriasis, and 20 drugs (systemic non-biological agents, small molecules and biological agents). 58% of the included trials were placebo controlled, while 30% were head-to-head comparisons, and 12% were active comparator and placebo studies. The main variables analysed are PASI 90 and serious adverse events in the induction period (weeks 8 to 24). The secondary variables included in the analysis are PASI 75, the Physician's Global Assessment (PGA 0/1) and quality of life data (different instruments). The authors emphasize that one of the main limitations of any meta-analysis is that indirect comparisons are made. They add other limitations, especially in relation to the measures adopted by the researchers to perform double blindness in the included studies (30% of the studies were considered as having a high risk of implementation bias - "performance bias", and 22% with high risk related to double blindness - “blinding bias”). In addition, they comment on limitations in relation to how the missing data have been treated, and to a selective reporting of the results. The authors claim to have rigorously considered all the assumptions related to the validity of the comparisons, ensuring that the evidence presented is sufficiently consistent. Finally, it should be noted that this NMA only collects information from the phase 2 trial of bimekizumab (BE ABLE)73, versus information from all phase 3 trials of ixekizumab72.
* The NMA published by Armstrong (2021)74 includes 85 studies and 23 comparators (systemic non-biologics, small molecules and biologics), published up to July 2020. The results of the phase 3/3b studies of bimekizumab, which had not yet been published, are included. The primary endpoint analysed was PASI at weeks 10-16. This is a communication to the ISPOR congress, therefore, there are not enough details in the abstract related to the limitations of the study.

## **Expert consensus / clinical practice guidelines**

* Bimekizumab does not appear in current clinical practice guidelines (CPG), as it has only recently received the marketing authorisation by the EMA75,76.
* Therefore, the inclusion of bimekizumab in the clinical practice guidelines may take a few years, so this section should be scored based, on the one hand, on your opinion on the possible incorporation of bimekizumab in future guidelines (given the current evidence) and, on the other, in recommendations or consensus of experts already available.
* Currently, in the American, European and Spanish clinical practice guidelines for moderate-to-severe psoriasis, adalimumab, ustekinumab and secukinumab are listed as first-line biologics, after the failure of conventional or topical systemic therapies77–81.
* Ixekizumab and risankizumab are listed in the American clinical practice guidelines as first-line drugs within biologics, for the treatment of moderate-to-severe psoriasis in adult patients (recommendation levels: A for ixekizumab and B for risankizumab)77.
* Beyond the CPGs, the consensus of experts may also be of interest. In this sense, articles based on expert opinions regarding the use of bimekizumab are still scarce. In one of them, Huang and Feldman (2021)82, physicians from the department of dermatology at the Wake Forest School of Medicine, in North Carolina (USA), comment that bimekizumab is possibly the most effective drug currently available for the treatment of moderate-to-severe psoriasis and that it seems to be especially effective in patients with severe psoriasis whose previous treatments have failed, or in patients who opt for the fastest available treatment. The authors believe that the use of bimekizumab as a first-line treatment for patients with severe psoriasis would be conditioned by the way in which patients and clinicians perceive the adverse events produced by them (especially in relation to candidiasis). Furthermore, Gotesman and Vender (2021)83, from the Department of Dermatology at the University of Ottawa (Canada), are of the opinion that, due to the high efficacy of bimekizumab, at the time that long-term safety data are available, this drug is a good candidate to become a first-line treatment within biologics for moderate-to-severe psoriasis.

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