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For the chapters 1 (Notes on use/Disclaimer), 3 (Funding), 4 (Scope and purpose of this guideline), 5 (Population and health questions covered by the guideline) and 6 (Targeted users of this guideline) see the long version of the guideline.
Disease severity and treatment goals

Measuring disease activity

Although it has its drawbacks, the most established parameter to measure the severity of skin symptoms in psoriasis is the Psoriasis Area and Severity Index (PASI), which was first introduced in 1978 as an outcome measure in a retinoid trial [1]. A physician global assessment (PGA) score to evaluate disease severity can be beneficial for the everyday clinician in order to assess rapidly the severity of psoriasis. It is important to note that different PGAs exist and that they may differ in the way they are defined and scales that are used. An estimate of the percentage of the affected body surface (BSA) is also being used as a means to measure disease severity [2]. Health related quality of life (HRQoL) is an important aspect of psoriasis, not only in defining disease severity but also as an outcome measure in clinical trials. The Dermatology Life Quality Index (DLQI) is the most commonly used score for assessing the impact of psoriasis on HRQoL. It consists of a questionnaire with ten questions related to symptoms and feelings, daily activities, leisure, work and school, personal relationships, and bother with psoriasis treatment [3]. The construct validity of the DLQI has been challenged, as items answered as being “not relevant” to a specific patient may not be accompanied by an adequate adjustment in the final result of the patient’s DLQI [4]. In addition to the options described above, further parameters of measuring disease severity can be useful.

Defining disease severity

Defining disease severity in psoriasis is complex, and a multitude of clinical aspects and aspects related to HRQoL need to be taken into consideration. The existing scores have various limitations, and patients have pointed out repeatedly that none of the existing scores successfully comprise a patient’s full complexity.

“Severity has become defined technically and bureaucratically, in terms of scores derived from instruments like say, PASI, DLQI and Skindex-25. These simply fail to capture the seriousness of psoriasis as experienced by those who have the disease.” (Mara Maccarone, Ray Jobling, Patient perspective, patient representatives EDF Guidelines 2015.)

Currently, the disease definition most commonly used for psoriasis was strongly influenced by the definition used in clinical trials and was thoroughly discussed and formally agreed upon in a European consensus project in 2011.

Definition of psoriasis disease severity (based on Mrowietz et al.) [5]:

- **Mild psoriasis**: BSA ≤ 10 und PASI ≤ 10 and DLQI ≤ 10
- **Moderate to severe psoriasis**: (BSA > 10 or PASI > 10) und DLQI > 10

Criteria to further “upgrade” mild disease to moderate-to-severe: major involvement of visible areas, major involvement of the scalp, involvement of the genitals, palms of hands or feet, onycholysis or onychodystrophy of at least two fingernails, presence of itch leading to scratching and the presence of recalcitrant plaques.

Strong Consensus

Treatment goals

The fundamental goal of any therapy is to achieve complete clearance of symptoms – that is, the absence of cutaneous symptoms of psoriasis. This goal is not realistically achievable in all patients at this time, however.

The successful establishment of treatment goals requires that a minimum target be defined which must be achieved by therapy. If the “lowest hurdle” is not reached within a given amount of time, the therapy must be modified. Various forms of adjustment include increasing the dosage, initiation of combination therapy, or transitioning to another drug or procedure.

At the end of the induction period, a PASI 75 response is the minimal target, which should be controlled for at regular intervals during the further course of treatment.

In light of even higher achievable treatment goals for the majority of patients, such as a PASI 90 response when using the new antibody therapies, which allow a higher quality of life with higher response rates, there is an ongoing discussion about higher treatment goals or an absolute PASI ≤ 3 or DLQI ≤ 2.
In the presence of criteria such as distinct involvement of visible areas, involvement of major parts of the scalp, genitals, palms of hands or feet, onycholysis or onychodystrophy of at least two fingernails, pruritus leading to scratching, presence of recalcitrant plaques, we recommend to follow up treatment goals individually determined for this specific manifestation (using appropriate scores e.g., NAPSI) and to modify the therapy if necessary.

For treatments with a fast onset of action, treatment goals should be controlled for at the end of the induction therapy (10–12 weeks); for treatments with a slower onset of action, this should be done after 16 to 24 weeks. These time frames may not always include the time point of maximal therapeutic effect. During maintenance therapy, control of treatment goal should be done at the same intervals as the general monitoring, usually every eight to twelve weeks.

**Methods Section**

For more detailed information, see the Guideline Development Report (online supplement or www.awmf.org). This guideline is an update of the 2017 version of the “S3 Guideline for the treatment of psoriasis vulgaris” [12, 13]. The update took the form of an adaptation of the “EuroGuiDerm Guideline on the systemic treatment of Psoriasis vulgaris” by Nast A. et al., which has been published in its final form at https://doi.org/10.1111/jdv.16915 and https://doi.org/10.1111/jdv.16926 and is also available at the European Dermatology Forum website (https://www.edf.one/home/Guidelines/EuroGuiDerm-psoriasis-vulgaris.html), licensed under CC BY NC 4.0 (https://creativecommons.org/licenses/by-nc/4.0/).

Some sections of the guideline have been adopted from the previous versions without changes. The sections on climate therapy, psychosocial therapy, topical therapy (one change in the background text), phototherapy, interfaces between different providers and sectors of care from the 2015 version of the guideline were reviewed with regard to relevant changes, and their period of validity was prolonged. These sections are included in the online supplement as an appendix.

Standardised wording as suggested by the GRADE Working Group was used for all recommendations in the newly developed sections, as shown in the overview below [14].

**Wording of recommendations, adapted from [15–18]**

| Strength | Wording | Symbols | Implications |
|----------|---------|---------|--------------|
| **Strong recommendation for the use of an intervention** | “We recommend...” | ↑↑ | We believe that all or almost all informed people would make a choice in favour of using this intervention. Clinicians will not have to spend as much time on the process of decision-making with the patient and may devote that time instead to overcoming barriers to implementation and adherence. In most clinical situations, the recommendation can be adopted as a policy. |
| **Weak recommendation for the use of an intervention** | “We suggest...” | ↑ | We believe that most informed people would make a choice in favour of using this intervention, but a substantial number would not. Clinicians and other health care providers will need to devote more time to the process of shared decision-making. Policy makers will have to involve many stakeholders and policy making will require substantial debate. |
Each formally agreed upon recommendation is presented in the guideline in a box as displayed below: the leftmost column shows the content of the recommendation using standardised wording; the middle column shows arrows and colours indicating the direction and the strength of the recommendation; and the right-most column indicates the strength of consensus among the author group and the evidence base (consensus-based vs. evidence-based).

Example of a recommendation from the long version of the guideline with standardised wording and symbols

**Open recommendation/no recommendation**

“We cannot make a recommendation for or against…”

Currently, a recommendation in favour of or against using this intervention cannot be made due to certain circumstances (for example, unclear or balanced benefit-risk ratio, no data available)

**Weak recommendation against the use of an intervention**

“We suggest against…”

We believe that most informed people would make a choice against using this intervention, but a substantial number would not.

**Strong recommendation against the use of an intervention**

“We recommend against…”

We believe that all or almost all informed people would make a choice against using this intervention. This recommendation can be adopted as a policy in most clinical situations.

How to read and understand a network meta-analysis

By Emilie Sbidian, MD PhD & Laurence Le Cleach, MD PhD

A network meta-analysis (NMA) provides estimates of effect size for all pairwise comparisons of interventions that are connected within a network, including those that have never been directly compared in randomised controlled trials (RCTs). The latter being referred to as indirect comparisons.

Prerequisites for a methodologically sound network meta-analysis

See long version of the guideline.

How to interpret the results of an NMA

First, network plots (Figure 1) provide useful information: Each circle is a different intervention and its size is proportional to the number of included participants; each line represents a direct comparison and its size is proportional to the number of trials assessing this comparison.

Then, forest plots (Figure 2) show all the relative effects from the network meta-analyses against placebo with their 95% confidence intervals.

For each outcome, a so-called cumulative ranking curve can be plotted for each intervention. This curve indicates, for each possible rank, the cumulative probability of the intervention occupying that rank. The surface under the cumulative ranking (SUCRA) curve is a numeric presentation of the overall ranking for each intervention with regard to the outcome, and is expressed as a percentage between 0% (when it is certain that an intervention is the worst with year. The contact person regarding updates is Prof. Dr. med. Alexander Nast (debm01@charite.de).
regard to this outcome) and 100 % (when it is certain an intervention is the best with regard to this outcome). However, the ranking does not consider the magnitude of differences in effects between treatments, among other factors. For example, intervention 1 could be ranked higher than intervention 2 (i.e. have a better probability of being classified as the best intervention) without there being a significant difference between the two interventions in terms of the relevant efficacy outcome(s).

A square matrix called a league table (Figure 3) can help address this problem by presenting the summary estimates, generated in the NMA, of the relative effect and their uncertainty for all possible pairs of interventions. The interventions are reported in rank order of the relative effect for the primary benefit outcome. In the lower triangle, a relative effect larger than 1 favours the intervention to the left.

When reading results from an NMA, keep in mind that the level of certainty of evidence is not equal between outcomes and interventions.

Network meta-analysis results should be interpreted with caution depending on the level of certainty per outcome, intervention and dosages pooled, keeping in mind gaps in research.

Summary of network meta-analysis (taken from Sbidian et al. 2020)

“[… ] Network meta-analysis at class level showed that all of the interventions (conventional systemic agents, small molecules, and biological treatments) were significantly more effective than placebo in terms of reaching PASI 90.

At class level, in terms of reaching PASI 90, the biologic treatments anti-IL17, anti-IL12/23, anti-IL23, and anti-TNF alpha were significantly more effective than the small molecules and the conventional systemic agents.

At drug level, in terms of reaching PASI 90, infliximab, all of the anti-IL17 drugs (ixekizumab, secukinumab, bimekizumab and brodalumab) and the anti-IL23 drugs (risankizumab and guselkumab, but not tildrakizumab) were significantly more effective in reaching PASI 90 than ustekinumab and three anti-TNF alpha agents: adalimumab, certolizumab and etanercept. Adalimumab and ustekinumab were significantly more effective in reaching PASI 90 than certolizumab and etanercept. There was no significant difference between tofacitinib or apremilast and between two conventional drugs: ciclosporin and methotrexate.

Network meta-analysis also showed that infliximab, ixekizumab, risankizumab, bimekizumab, guselkumab, secukinumab and brodalumab outperformed other drugs when compared to placebo in reaching PASI 90. The clinical effectiveness for these seven drugs was similar: infliximab (versus placebo): risk ratio (RR) 29.52, 95 % confidence interval (CI) 19.94 to 43.70, Surface Under the Cumulative Ranking (SUCRA) = 88.5; moderate-certainty evidence; ixekizumab (versus placebo): RR 28.12, 95 % CI 23.17 to 34.12, SUCRA = 88.3, moderate-certainty evidence; risankizumab (versus placebo): RR 27.67, 95 % CI 22.86 to 33.49, SUCRA = 87.5, high-certainty evidence; bimekizumab (versus placebo): RR 58.64, 95 % CI 3.72 to 923.86, SUCRA = 83.5, low-certainty evidence; guselkumab (versus placebo): RR 25.84, 95 % CI
We recommend taking account of efficacy and safety (see respective figure / Cochrane Review and drug chapters), time until onset of treatment response, comorbidities (see decision grid and respective chapters in Part 2), and individual patient factors when choosing a systemic treatment for moderate to severe psoriasis.

**General recommendations**

Initiating and selecting a systemic treatment (see recommendations box and Figure 4).

Figure 3  League table relative effect (PASI 90 – lower triangle and SAE – upper triangle) [Copyright © 2020 The Cochrane Collaboration].

| CAS | CAS | CAS | CAS | CAS | CAS | CAS | CAS | CAS | CAS | CAS | CAS | CAS | CAS |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 20.90 to 31.95; SUCRA = 81; moderate-certainty evidence; secukinumab (versus placebo): RR 23.97, 95 % CI 20.03 to 28.70, SUCRA = 74.9; high-certainty evidence; and brodalumab (versus placebo): RR 21.96, 95 % CI 18.17 to 26.53, SUCRA = 68.7; moderate-certainty evidence. Conservative interpretation is warranted for the results for bimekizumab (as well as tyrosine kinase 2 inhibitor, acitretin, ciclosporin, fumaric acid esters, and methotrexate), as these drugs, in the NMA, have been evaluated in few trials.

We found no significant difference between any of the interventions and the placebo for the risk of SAEs. Nevertheless, the SAE analyses were based on a very low number of events with low to very low certainty for just under half of the treatment estimates in total, and moderate for the others. Thus, the results have to be viewed with caution and we cannot be sure of the ranking.

For other efficacy outcomes (PASI 75 and Physician Global Assessment [PGA] 0/1) the results were very similar to the results for PASI 90. [...] page 2, Sibidán et al. 2020 [19].

20.90 to 31.95; SUCRA = 81; moderate-certainty evidence; secukinumab (versus placebo): RR 23.97, 95 % CI 20.03 to 28.70, SUCRA = 74.9; high-certainty evidence; and brodalumab (versus placebo): RR 21.96, 95 % CI 18.17 to 26.53, SUCRA = 68.7; moderate-certainty evidence. Conservative interpretation is warranted for the results for bimekizumab (as well as tyrosine kinase 2 inhibitor, acitretin, ciclosporin, fumaric acid esters, and methotrexate), as these drugs, in the NMA, have been evaluated in few trials.

We found no significant difference between any of the interventions and the placebo for the risk of SAEs. Nevertheless, the SAE analyses were based on a very low number of events with low to very low certainty for just under half of the treatment estimates in total, and moderate for the others. Thus, the results have to be viewed with caution and we cannot be sure of the ranking.
For patients who require systemic treatment, we generally recommend initiating a “conventional” systemic agent in line with the efficiency principle set out in Book V of the German Code of Social Law (the “Wirtschaftlichkeitsgebot”).

We recommend initiating a biologic if conventional systemic agents were inadequate in response or if they are contraindicated or not tolerated.

In cases of psoriasis where conventional treatments are not expected to lead to a sufficient response*, we suggest initiating a biologic agent that has a “first-line label”.**

* e.g., particularly severe disease (e.g., PASI ≥ 20) or rapid worsening of disease; severe involvement of the nails, the genital area or the scalp; or a particularly strong impact on quality of life (e.g., DLQI ≥ 15)

** “First line label” refers to the therapeutic indication as approved by the EMA (European Medicines Agency).

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.

Specific recommendations

All boxes in the chapters Conventional systemic therapy and Biological therapy and small molecules containing “Instructions for use” achieved a strong consensus. Abstentions due to moderate or severe conflicts of interest have been taken into account.

Conventional systemic therapy

Acitretin

Instructions for use [20, 21]

Pre-treatment:
- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- History and clinical examination should focus on musculoskeletal problems. If patient reports complaints, further imaging investigations may be performed.
- Exclude pregnancy/breastfeeding: patient must be informed explicitly and extensively about the teratogenic risk of the medication, the necessity of effective long-term contraception (for three years after cessation of treatment), and the possible consequences of becoming pregnant while taking retinoids; written documentation of this informational interview should be obtained.
- Inform patient that during treatment and for three years after cessation of treatment, blood donation is not permitted.
- Laboratory parameters including pregnancy test (see long version of the guideline).
- Check need for vaccinations (see chapter “Vaccinations” in long version of the guideline)

During treatment:
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- The capsules should be taken with a meal containing some fat or with whole milk to improve absorption.
- In order to prevent elevation of serum lipids and liver enzymes, alcohol abstinence and a low-fat and low-carbohydrate diet are advised.
- Preventing pregnancy is mandatory. After satisfactory contraception for at least one month prior to treatment, start treatment on second or third day of the menstrual cycle. Double contraception is recommended (e.g., condom + pill; IUD/Nuva Ring + pill; Cave: no low-dosed progesterone preparations/mini-pills) during and up to three years after end of therapy; effectiveness of oral contraceptives is reduced by acitretin.
Guideline  S3-Guideline Psoriasis vulgaris Part 1

Post-treatment:

› Reliable contraception and monthly pregnancy test in women of child-bearing age for three years after cessation of therapy. Double contraception, as described above, is recommended.
› Remind patients that blood donation is not permitted for three years after cessation of therapy.

Ask patient about spine and joint complaints at follow-up visits. If patient reports complaints, further imaging investigation may be performed.

Laboratory parameters including monthly pregnancy test (see long version of the guideline).

Figure 4  Overview of therapeutic options.

CHRONIC PSORIASIS VULGARIS

MILD
(as defined in chapter “Disease severity and treatment goals”)

MODERATE / SEVERE
(as defined in chapter “Disease severity and treatment goals”)

TOPICAL THERAPY*

Anthralin / dithranol
Calcineurin inhibitors**
Coal tar
Corticosteroids
Laser therapy
Tazarotene
Vitamin D3

PHOTOTHERAPY / SYSTEMIC THERAPY

“first line label”
If treatment success cannot be expected with conventional drugs***

Addilimumab (anti TNF alpha)
Brodalumab (anti IL 17)
Cetuxizumab (anti TNF alpha)
Guselkumab (anti IL 23)
Ixekizumab (anti IL 17)
Risankizumab (anti IL 23)
Secukinumab (anti IL 17)
Tildrakizumab (anti IL 23)

“second line label”
Apremilast (if oral preferred) (PDE 4)
Etanercept (anti TNF alpha)
Infliximab (anti TNF alpha)
Ustekinumab (anti IL 12/23)

*** e.g. particularly severe disease (e.g. PASI ≥20) or rapid worsening of the disease; or severe nail disease or severe psoriasis manifestation involvement of the nails, the genital area or, the scalp; or a particularly high strong impact on the quality of life (e.g. DLIQ ≥15)

+ TOPICAL THERAPY if applicable

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For the subchapters “Recommendations for lab controls”, “Adverse drug reactions”, “Special considerations during treatment”, “Important contraindications” and “Drug interactions” see the long version of the guideline.

**Ciclosporin (CsA)**

*Instructions for use* [20, 21]

**Pre-treatment:**
- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- History and clinical examination should focus on past and concomitant diseases (e.g., arterial hypertension; severe infections; malignancies, including cutaneous malignancies; renal and liver diseases) and concomitant medication (see drug interactions in long version of the guideline).
- Measure blood pressure on two separate occasions.
- Laboratory parameters (see long version of the guideline).
- Reliable contraception (caution: reduced efficacy of progesterone-containing contraceptives).
- Regular gynaecologic screening according to current German guidelines.
- Consultation on vaccination (see chapter “Vaccinations” in long version of the guideline); susceptibility to infections (take infections seriously, seek medical attention promptly if necessary); drug interactions (inform other treating physicians about therapy); avoidance of excessive sun exposure; use of sun protection measures.

**During treatment:**
- During therapy with low dose ciclosporin (CsA; 2.5 to 3 mg/kg body weight daily), follow-up intervals may be extended to two months or more. Shorter intervals may be needed in patients with risk factors, after dose increases, or those who must take concomitant medications that are likely to contribute to adverse drug reactions.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Clinical examination should focus on status of skin and mucous membranes (hypertrichosis, gingival changes, malignancies), signs of infections, gastrointestinal or neurological symptoms (tremor, dysesthesia), musculoskeletal/joint pain.
- Repeat recommendation for need for sun avoidance and sun protection.

**Post-treatment:**
- After discontinuation of CsA, patients should be followed up for skin cancer, especially in case of high cumulative doses of prior UV therapy or natural UV exposure.

**Dimethyl fumarate/fumaric acid esters**

*Instructions for use*

Dimethyl fumarate (DMF) is a pro-drug for oral administration; the active in vivo moiety is monomethylfumarate [22]. For the treatment of psoriasis, a drug containing DMF is registered in Europe (Skilarence®) and a mixture of DMF and three salts of ethyl hydrogen fumarates (Fumaderm®) is registered in Germany only.

**Pre-treatment:**
- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- History and clinical examination.
- Reliable contraception.
- Laboratory parameters (see long version of the guideline).
- Check need for vaccinations (see chapter “Vaccinations” in long version of the guideline).

**During treatment:**
- Objective assessment of the severity of disease (such as PASI/BSA/PGA).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Clinical examination.
- Reliable contraception.
- Laboratory parameters (see long version of the guideline).

**Post-treatment:**
- None.
For subchapters “Recommendations for lab controls”, “Adverse drug reactions”, “Special considerations during treatment”, “Important contraindications” and “Drug interactions” see long version of the guideline.

**Methotrexate (MTX)**

*Instructions for use*

Methotrexate is a prodrug that is polyglutaminated into its active in vivo moiety. Methotrexate should be preferentially given subcutaneously once weekly for improved bioavailability, as well as increased patient safety (because oral intake has higher risk for overdosing as patients are more likely to take tablets daily instead of once weekly). The recommended initial and maintenance dose is usually 15 mg MTX once weekly. In case of insufficient response, the dose can be increased up to 20 mg MTX once weekly. A further increase up to 25 mg MTX is only beneficial for a small subgroup of patients. Subcutaneous dosing is recommended in patients with suboptimal response to oral treatment and may be considered as the starting route of administration in high need patients.

**Pre-treatment:**
- Consider enrolling the patient in a psoriasis registry.
- History and clinical examination.
- Objective assessment of the severity of the disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Laboratory parameters (see long version of the guideline).
- Exclude tuberculosis (see chapter “Tuberculosis” in Part 2).
- Chest X-ray.
- Reliable contraception in women of child-bearing age (starting after menstruation).
- If abnormalities in liver screening are found, the patient should be referred to a specialist for further evaluation.
- Check need for vaccinations (see chapter “Vaccinations” in long version of the guideline).

**During treatment:**
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Check concomitant medication.
- Clinical examination.
- Laboratory parameters (see long version of the guideline).
- Reliable contraception in women of child-bearing age.
- 5 mg folic acid once weekly 24 hours after MTX.
- Advise alcohol abstinence.

**Post-treatment:**
- Women should be advised not to become pregnant and men should be advised not to conceive for at least three months after cessation of therapy with MTX*.

*EMA recommends six months as a means of precaution; the practice of the guideline group differs from this.*

For subchapters “Recommendations for lab controls”, “Adverse drug reactions”, “Special considerations during treatment”, “Important contraindications” and “Drug interactions” see long version of the guideline.

**Biological therapy and small molecules**

**Adalimumab**

*Instructions for use*

**Pre-treatment:**
- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- History and clinical examination should focus on prior exposure to other treatments, malignancies, infections, congestive heart failure (CHF) and neurological disease or symptoms.
- Other recommended measures include:
  - Check for skin cancer
  - Check for lymphadenopathy
  - Laboratory parameters (see long version of the guideline)
  - Exclude tuberculosis (see chapter “Tuberculosis” in Part 2)
  - Check for evidence of active infection
  - Check need for vaccinations (see chapter “Vaccinations” in long version of the guideline)
- Reliable contraception

**During treatment:**
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Clinical examination should focus on malignancies, risk factors for serious infections, congestive heart failure, and neurological symptoms.
- Other recommended measures include:
  - Check for skin cancer
  - Check for lymphadenopathy
  - Laboratory parameters (see long version of the guideline)
- Reliable contraception

**Post-treatment:**
- After cessation of adalimumab therapy, patients should be followed up with medical history and physical examination.
- For information regarding the need for ongoing contraception immediately following biologic treatment cessation, see chapter “Wish for child/pregnancy” in part 2.
For subchapters “Recommendations for lab controls”, “Adverse drug reactions”, “Special considerations during treatment”, “Important contraindications” and “Drug interactions” see long version of the guideline.

**Apremilast**

*Instructions for use*

**Pre-treatment:**
- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Medical history and physical examination including:
  - Check for skin cancer
  - Check for evidence of active and chronic infection
  - Check for contraception and breastfeeding
  - Check for need for vaccinations (see chapter “Vaccinations” in long version of the guideline)
  - Check for hypersensitivity, metabolic, gastrointestinal and renal disorders/dysfunction and underweight
  - Check for depression, anxiety
  - Check for co-medication: CYP3A4 enzyme inducers
  - Laboratory parameters including pregnancy test (see long version of the guideline)

**During treatment:**
- Objective assessment of the severity of the disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Medical history and physical examination focusing on malignancies, infections, contraception, depression and anxiety.
- Laboratory parameters only when indicated on medical history or physical examination.
- Reliable Contraception.

**Post-treatment:**
- For information regarding the need for ongoing contraception immediately following treatment cessation, see chapter “Wish for child/pregnancy” in Part 2.

For subchapters “Recommendations for lab controls”, “Adverse drug reactions”, “Special considerations during treatment”, “Important contraindications” and “Drug interactions” see long version of the guideline.

**Brodalumab**

*Instructions for use*

**Pre-treatment:**
- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Medical history and clinical examination including prior exposure to treatments, malignancies, infections (e.g. candidiasis), inflammatory bowel disease, depression and/or suicidal ideation or behaviour.
- Other recommended measures include:
  - Check for skin cancer
  - Check for lymphadenopathy
  - Laboratory parameters (see long version of the guideline)
  - Exclusion of tuberculosis (see chapter “Tuberculosis” in Part 2)
  - Check for evidence of active infection
  - Check need for vaccinations (see chapter “Vaccinations” in long version of the guideline)
- Reliable contraception.

**During treatment:**
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17).
- Laboratory parameters (see long version of the guideline).
- Medical history and physical examination focusing on infections (in particular upper respiratory tract infections, candida, tuberculosis), contraception, symptoms of depression and/or suicidal behaviour and signs or symptoms of inflammatory bowel disease.

**Post-treatment:**
- After cessation of brodalumab therapy, patients should be followed up with medical history and physical examination.
- For information regarding the need for ongoing contraception immediately following biologic treatment cessation, see chapter “Wish for child/pregnancy” in Part 2.

For subchapters “Recommendations for lab controls”, “Adverse drug reactions”, “Special considerations during treatment”, “Important contraindications” and “Drug interactions” see long version of the guideline.
Certolizumab pegol

Instructions for use

Pre-treatment:
- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- History and clinical examination should focus on prior exposure to treatments, malignancies, infection, congestive heart failure, and neurological disease or symptoms.
- Other recommended measures include:
  - Check for skin cancer
  - Check for lymphadenopathy
  - Laboratory parameters (see long version of the guideline)
  - Exclusion of tuberculosis (see chapter “Tuberculosis” in Part 2)
  - Check for evidence of active infections
  - Check need for vaccinations (see chapter “Vaccinations” in long version of the guideline)
- Discuss contraception (see chapter “Wish for child/pregnancy” in Part 2).

During treatment:
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Clinical examination should focus on lymphadenopathy, malignancies, especially skin cancer, premalignant lesions, risk factors for serious infections, congestive heart failure, and neurological symptoms.
- Other recommended measures include:
  - Check for skin cancer
  - Check for lymphadenopathy
  - Laboratory parameters (see long version of the guideline)
- Discuss contraception (see chapter “Wish for child/pregnancy” in Part 2).

Post-treatment:
- After cessation of certolizumab pegol therapy, patients should be followed up with medical history and physical examination.
- For information regarding the need for ongoing contraception immediately following biologic treatment cessation, see chapter “Wish for child/pregnancy” in Part 2.

Etanercept

Instructions for use

Pre-treatment:
- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- History and clinical examination should focus on prior exposure to treatments, malignancies, infection, congestive heart failure, and neurological symptoms.
- Other recommended measures include:
  - Check for malignancy, mainly skin cancer, and premalignant lesions
  - Check for lymphadenopathy
  - Laboratory parameters (see long version of the guideline)
  - Exclusion of tuberculosis (see chapter “Tuberculosis” in Part 2)
  - Check for evidence of active infection
  - Check need for vaccinations (see chapter “Vaccinations” in long version of the guideline)
- Reliable contraception

During treatment:
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Clinical examination should focus on lymphadenopathy, malignancies, especially skin cancer, premalignant lesions, risk factors for serious infections, congestive heart failure, and neurological symptoms.
- Other recommended measures include:
  - Laboratory parameters (see long version of the guideline)
- Reliable contraception.

Post-treatment:
- After cessation of etanercept therapy, patients should be followed up with medical history and physical examination.
- For information regarding the need for ongoing contraception immediately following biologic treatment cessation, see chapter “Wish for child/pregnancy” in Part 2.
Guselkumab

Instructions for use

Pre-treatment:
- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17).
- Medical history and physical examination including prior exposure to treatments, malignancies, infections.
- Other recommended measures include:
  - Check for skin cancer
  - Check for lymphadenopathy
  - Laboratory parameters (see long version of the guideline)
  - Exclusion of tuberculosis (see chapter “Tuberculosis” in Part 2)
  - Check for evidence of active infection
  - Check need for vaccinations (see chapter “Vaccinations” in long version of the guideline)
- Reliable contraception.

During treatment:
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17).
- Medical history and physical examination including infections, including monitoring signs and symptoms of tuberculosis.
- Reliable contraception.

Post-treatment:
- After cessation of guselkumab therapy, patients should be followed up with medical history and physical examination.
- For information regarding the need for ongoing contraception immediately following biologic treatment cessation, see chapter “Wish for child/pregnancy” in Part 2.

Infliximab

Instructions for use

Pre-treatment:
- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- History focusing on prior exposure to treatments. History and clinical examination should focus on malignancies, infection, congestive heart failure, and neurological symptoms.
- Other recommended measures include:
  - Check for skin cancer
  - Check for lymphadenopathy
  - Laboratory parameters (see long version of the guideline)
  - Exclusion of tuberculosis (see chapter “Tuberculosis” in Part 2)
  - Check for evidence of active infection
  - Check need for vaccinations (see chapter “Vaccinations” in long version of the guideline)
- Reliable contraception.

During treatment:
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Clinical examination should focus on malignancies, risk factors for serious infections, congestive heart failure, and neurological symptoms.
- Other recommended measures include:
  - Check for skin cancer
  - Check for lymphadenopathy
  - Laboratory parameters (see long version of the guideline)
- Reliable contraception.

Post-treatment:
- After cessation of infliximab therapy, patients should be followed up with medical history and physical examination.
- For information regarding the need for ongoing contraception immediately following biologic treatment cessation, see chapter “Wish for child/pregnancy” in Part 2.

For subchapters “Recommendations for lab controls”, “Adverse drug reactions”, “Special considerations during treatment”, “Important contraindications” and “Drug interactions” see long version of the guideline.
Ixekizumab

Instructions for use

Pre-treatment:
- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or -17).
- Medical history and physical examination including prior exposure to treatments, malignancies, infection (e.g. candidiasis), inflammatory bowel disease.
- Other recommended measures include:
  - Check for skin cancer
  - Check for lymphadenopathy
  - Laboratory parameters (see long version of the guideline)
  - Exclusion of tuberculosis (see chapter “Tuberculosis” in Part 2)
  - Check for evidence of active infection
  - Check need for vaccinations (see chapter “Vaccinations” in long version of the guideline)
- Reliable contraception.

During treatment:
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17).
- Laboratory parameters (see long version of the guideline).
- Medical history and physical examination focusing on infections (in particular upper respiratory tract infections, candida, tuberculosis), contraception, signs or symptoms of inflammatory bowel disease.

Post-treatment:
- After cessation of ixekizumab therapy, patients should be followed up with medical history and physical examination.
- For information regarding the need for ongoing contraception immediately following biologic treatment cessation, see chapter “Wish for child/pregnancy” in Part 2.

For subchapters “Recommendations for lab controls”, “Adverse drug reactions”, “Special considerations during treatment”, “Important contraindications” and “Drug interactions” see long version of the guideline.

Risankizumab

Instructions for use

Pre-treatment:
- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (such as DLQI, Skindex-29 or 17)
- Medical history and physical examination including prior or exposure to treatments, malignancies, infections
- Other recommended measures include:
  - Check for skin cancer
  - Check for lymphadenopathy
  - Laboratory parameters (see long version of the guideline)
  - Exclusion of tuberculosis (see chapter “Tuberculosis” in Part 2)
  - Check for evidence of active infection
  - Check need for vaccinations (see chapter “Vaccinations” in long version of the guideline)
- Reliable contraception.

During treatment:
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17).
- Laboratory parameters (see long version of the guideline).
- Medical history and physical examination including infections, including monitoring signs and symptoms of tuberculosis.
- Reliable contraception.

Post-treatment:
- After cessation of risankizumab therapy, patients should be followed up with medical history and physical examination.
- For information regarding the need for ongoing contraception immediately following biologic treatment cessation, see chapter “Wish for child/pregnancy” in Part 2.

For subchapters “Recommendations for lab controls”, “Adverse drug reactions”, “Special considerations during treatment”, “Important contraindications” and “Drug interactions” see long version of the guideline.
Secukinumab

Instructions for use

Pre-treatment:
- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI/Skindex-29 or 17).
- Medical history and physical examination including prior exposure to treatments, malignancies, infections (e.g. candidiasis), inflammatory bowel disease.
- Other recommended measures include:
  - Check for skin cancer
  - Check for lymphadenopathy
  - Laboratory parameters (see long version of the guideline)
  - Exclusion of tuberculosis (see chapter “Tuberculosis” in Part 2)
  - Check for evidence of active infection
  - Check need for vaccinations (see chapter “Vaccinations” in long version of the guideline)
- Reliable contraception.

During treatment:
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17).
- Laboratory parameters (see long version of the guideline).
- Medical history and physical examination focusing on infections (in particular upper respiratory tract infections, candida, tuberculosis), contraception, signs or symptoms of inflammatory bowel disease.

Post-treatment:
- After cessation of secukinumab therapy, patients should be followed up with medical history and physical examination.
- For information regarding the need for ongoing contraception immediately following biologic treatment cessation, see chapter “Wish for child/pregnancy” in Part 2).

For subchapters “Recommendations for lab controls”, “Adverse drug reactions”, “Special considerations during treatment”, “Important contraindications” and “Drug interactions” see long version of the guideline.

Tildrakizumab

Instructions for use

Pre-treatment:
- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17).
- Medical history and physical examination including prior exposure to treatments, malignancies, infections.
- Other recommended measures include:
  - Check for skin cancer
  - Check for lymphadenopathy
  - Laboratory parameters (see long version of the guideline)
  - Exclusion of tuberculosis (see chapter “Tuberculosis” in Part 2)
  - Check for evidence of active infection
  - Check need for vaccinations (see chapter “Vaccinations” in long version of the guideline)
- Reliable contraception.

During treatment:
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17).
- Laboratory parameters (see long version of the guideline).
- Medical history and physical examination including infections, including monitoring signs and symptoms of tuberculosis.
- Reliable contraception.

Post-treatment:
- After cessation of tildrakizumab therapy, patients should be followed up with medical history and physical examination.
- For information regarding the need for ongoing contraception immediately following biologic treatment cessation, see chapter “Wish for child/pregnancy” in Part 2).

For subchapters “Recommendations for lab controls”, “Adverse drug reactions”, “Special considerations during treatment”, “Important contraindications” and “Drug interactions” see long version of the guideline.
Ustekinumab

Instructions for use

Pre-treatment:
- Consider enrolling the patient in a psoriasis registry.
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17).
- Medical history and physical examination including prior exposure to treatments, malignancies, infections.
- Other recommended measures include:
  - Check for skin cancer
  - Check for lymphadenopathy
  - Laboratory parameters (see long version of the guideline)
  - Exclusion of tuberculosis (see chapter “Tuberculosis” in Part 2)
  - Check for evidence of active infection
  - Check need for vaccinations (see chapter “Vaccinations” in long version of the guideline)
- Reliable contraception.

During treatment:
- Objective assessment of the severity of disease (such as PASI/BSA/PGA; arthritis).
- Measure HRQoL (e.g., using DLQI, Skindex-29 or 17).
- Laboratory parameters (see long version of the guideline).
- Medical history and physical examination including infections, including monitoring signs and symptoms of tuberculosis.
- Reliable contraception.

Post-treatment:
- After cessation of ustekinumab therapy, patients should be followed up with medical history and physical examination.
- For information regarding the need for ongoing contraception immediately following biologic treatment cessation, see chapter “Wish for child/pregnancy” in Part 2.

For subchapters “Recommendations for lab controls”, “Adverse drug reactions”, “Special considerations during treatment”, “Important contraindications” and “Drug interactions” see long version of the guideline.

For chapters “Biosimilars” and “Newly approved medicines and treatments in the pipeline” see long version of the guideline.

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References

1 Fredriksson T, Pettersson U. Severe psoriasis – oral therapy with a new retinoid. Dermatologica 1978; 157: 238–44.
2 Puzenat E, Bronsard V, Prey S et al. What are the best outcome measures for assessing plaque psoriasis severity? A systematic review of the literature. J Eur Acad Dermatol Venereol 2010; 24 (Suppl 2): 10–6.
3 Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI) – a simple practical measure for routine clinical use. Clin Exp Dermatol 1994; 19: 210–6.
4 Rencz F, Brodzszy V, Gulácsi L et al. Time to revise the Dermatology Life Quality Index scoring in psoriasis treatment guidelines. J Eur Acad Dermatol Venereol 2019; 33: e267–e69.
5 Mrowietz U, Kragballe K, Reich K et al. Definition of treatment goals for moderate to severe psoriasis: a European consensus. Arch Dermatol Res 2011; 303: 1–10.
6 Seston EM, Ashcroft DM, Griffiths CEM. Balancing the benefits and risks of drug treatment: a stated-preference, discrete choice experiment with patients with psoriasis. Arch Dermatol 2007; 143: 1175–9.
7 Egeberg A, Andersen VMF, Halling-Overgaard AS et al. Systematic review on rapidity of onset of action for interleukin-17 and interleukin-23 inhibitors for psoriasis. J Eur Acad Dermatol Venereol 2020; 34: 39–46.
8 Nast A, Sporbeck B, Rosumeck S et al. Which antipsoriatic drug has the fastest onset of action? Systematic review on the rapidity of the onset of action. J Invest Dermatol 2013; 133: 1963–70.
9 Pham PA, Dressler C, Eisert L et al. Time until onset of action when treating psoriatic arthritis: meta-analysis and novel approach of generating confidence intervals. Rheumatol Int 2019; 39: 605–18.
10 Nast A, Dilleen M, Liyanage W et al. Time, Psoriasis Area and Severity Index and Dermatology Life Quality Index of patients with psoriasis who drop out of clinical trials on etanercept because of lack of efficacy: a pooled analysis from 10 clinical trials. Br J Dermatol 2018; 178: 400–5.
11 Zidane M, Dressler C, Gaskins M, Nast A. Decision-analytic modeling for time-effectiveness of the sequence of induction treatments for moderate to severe plaque psoriasis. JAMA Dermatol 2019.
12 Nast A, Amelunxen L, Augustin M et al. S3 Guideline for the treatment of psoriasis vulgaris, update – Special patient populations and treatment situations. J Dtsch Dermatol Ges 2018; 16: 806–13.
13 Nast A, Amelunxen L, Augustin M et al. S3 Guideline for the treatment of psoriasis vulgaris, update – Systemic treatment. J Dtsch Dermatol Ges 2018; 16: 645–69.
14 Guyatt G, Oxman AD, Akl EA et al. GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. J Clin Epidemiol 2011; 64: 383–94.
15 Guyatt GH, Oxman AD, Schunemann HJ et al. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. J Clin Epidemiol 2011; 64: 380–2.
16 The GRADE Working Group. GRADE recommendations. Available on: http://www.gradeworkinggroup.org/ [Last accessed November 10, 2020].
17 Werner RN, Niikels AF, Marinovic B et al. European consensus-based (S2k) Guideline on the Management of Herpes Zoster – guided by the European Dermatology Forum (EDF) in cooperation with the European Academy of Dermatology and Venereology (EADV), Part 1: Diagnosis. J Eur Acad Dermatol Venereol 2017; 31: 9–19.
18 Werner RN, Niikels AF, Marinovic B et al. European consensus-based (S2k) Guideline on the Management of Herpes Zoster – guided by the European Dermatology Forum (EDF) in cooperation with the European Academy of Dermatology and Venereology (EADV), Part 2: Treatment. J Eur Acad Dermatol Venereol 2017; 31: 20–9.
19 Sbidian E, Chaimani A, Afach S et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database Syst Rev 2020; 1: Cd011535.
20 Nast A, Spuls PI, van derKraaij G et al. European S3-Guideline on the systemic treatment of psoriasis vulgaris – Update Apremilast and Secukinumab – EDF in cooperation with EADV and IPC. Journal of the European Academy of Dermatology and Venereology: JEADV 2017; 31: 1951–63.
21 Pathirana D, Ormerod AD, Siaag P et al. European S3-guidelines on the systemic treatment of psoriasis vulgaris. J Eur Acad Dermatol Venereol 2009; 23 (2): 1–70.
22 Mrowietz U, Morrison PJ, Suhrkamp I et al. The pharmacokinetics of fumaric acid esters reveal their in vivo effects. Trends Pharmacol Sci 2018; 39: 1–12.