JDDG
Journal of the German Society of Dermatology

Guideline

DOI: 10.1111/ddg.13538

S3 Guideline for the treatment of psoriasis vulgaris, update – Short version part 2 – Special patient populations and treatment situations

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Summary

The German guideline for the treatment of psoriasis vulgaris was updated using GRADE methodology. The guideline is based on a systematic literature review completed on December 1, 2016, and on a formal consensus and approval process. The second part of this short version of the guideline covers the following special patient populations and treatment situations: tuberculosis screening before and during psoriasis treatment, choice of psoriasis treatment for individuals wishing to have children, as well as during pregnancy and breast-feeding, and patients with joint involvement and vaccinations. In addition, recommendations on the choice of treatment are presented for patients with the following comorbidities: hepatitis and other hepatic impairment, HIV, malignancies, neurological and psychiatric disorders, ischemic heart disease and congestive heart failure, diabetes mellitus, renal impairment and inflammatory bowel disease.

Introduction

This is a short version of the German evidence- and consensus-based (S3) guideline for the treatment of psoriasis vulgaris. The long version is available at www.awmf.org. Please refer to the long version for the following sections: introduction, aims of the guideline, indicators of quality of care, instructions on using the guideline, detailed description of methodology, definition of the severity of psoriasis vulgaris, quality of life, treatment aims, treatment costs, benefit-risk assessment and basic therapy, as well as systemic, topical and UV therapy. The sections on biosimilars, climate therapy, psychosocial therapy, topical therapy, phototherapy, interfaces between different providers and sectors of care, and references can also be found in the long version.

Methodology

This guideline is an update. At their initial meeting, the authors of the guideline agreed on the main points that required updating. It was decided to include new sections on "Special patient populations and treatment situations". A complete literature search was not performed for these sections; the authors of the different chapters carried out an indicative search that included systematic reviews and guidelines. Formal procedures were used to reach consensus for the recommendations. A detailed description of the methodology used to develop the guideline and declarations of interest can be found in the methods report (www.psoriasis-leitlinie.de).

Passages requiring consensus
The authors of the guideline have defined certain particularly relevant sections as requiring consensus. These passages were agreed on at consensus conferences and are highlighted in gray boxes.

Treatment recommendation

At present, there is no clear step-by-step procedure or strict clinical algorithm for the treatment of psoriasis vulgaris. The criteria for selecting an appropriate therapy are complex.

Key recommendations formulated in the text are augmented by symbols representing the strength of the treatment recommendation. Symbols have been used to help standardize the treatment recommendations:

↑↑	is recommended	(strongly recommended)
↑	may be recommended	(recommended)
→	may be considered	(neutral recommendation)
↓	cannot be recommended	(recommendation against its use)

Update/validity

The current version is valid until December 31, 2020.

Special patient populations and treatment situations

Tuberculosis screening before and during therapy

The number of cases of TB during immunosuppressant psoriasis therapy has been reduced significantly since the introduction of TB screening recommendations; not infrequently, TB reactivation is due to failure to follow the screening recommendations and would thus be preventable.

Table 1 shows the procedure used in everyday clinical practice. Besides obtaining the patient's history and performing a physical examination, IGRA and a chest X-ray are recommended as mandatory tests. An X-ray taken within the previous six months is acceptable if the past medical history is unremarkable.

Treatment recommendations		Consensus strength	Comment
Ruling out tuberculosis (TB) using IGRA (interferon-gamma release assays) and chest X-ray is recommended before initiating treatment with immunosuppressants (methotrexate [MTX], TNF-alpha antagonists, ustekinumab, secukinumab).	↑↑	Strong consensus	Clinical consensus point
If latent tuberculosis is suspected or the screening result is unclear, TB prophylaxis with isoniazid (INH) for 6–9 months is recommended. It is recommended to initiate treatment with a biologic at the earliest one month after starting TB prophylaxis.	↑↑	Strong consensus	Clinical consensus point
If there is justified suspicion of TB reactivation or new infection during biologic therapy, repeating the IGRA and chest X-ray is recommended.	↑↑	Strong consensus	Clinical consensus point

This section will address both screening and the procedure to follow if the TB status is unclear and/or latent tuberculosis (LTB) is suspected, based on the available literature and, in particular, the European S3 psoriasis vulgaris guideline.

According to WHO statistics, tuberculosis has for years been the leading fatal infectious disease worldwide. The most common pathogen in Germany is *Mycobacterium tuberculosis*, which infects predominantly the respiratory tract by droplet infection; other sites affected by TB are the urinary tract (kidneys), the nervous system and the skin.

Only 5–10 % of those infected become symptomatic during their lifetime; predisposing factors include chronic inflammation and immunosuppression.

The psoriasis patient in general and patients on immunosuppression or immunomodulation (those treated with TNF inhibitors in particular) are therefore at risk of developing tuberculosis, primarily by activation of latent tuberculosis infection. Due to the marked increase in recent years in the number of patients on (anti-TNF) biologics, the number of patients who can potentially develop tuberculosis or experience reactivation has grown. The majority of cases involve reactivation of latent infection. The interval between starting biologic therapy and the onset of initial clinical signs of TB or the diagnosis of TB can vary greatly, between three months and about a year.

If the TB status is unclear, immunosuppressant (biologic) therapy should never be initiated without prior isoniazid (INH) prophylaxis.

The interferon-gamma release assay (IGRA) is based on detection of IFN-γ, which is secreted by T lymphocytes that have been sensitized by current or prior infection with *Mycobacterium tuberculosis* (MTB).

The two IGRA tests commercially available in Germany are based on direct measurement of IFN-γ levels in whole blood (QuantiFERON-TB® Gold In-Tube, Cellestis, Australia; QFT) or measurement of the number of IFN-γ-secreting T lymphocytes from isolated peripheral mononuclear cells (PBMC; T-SPOT.TB®, Oxford-Immunotec, UK) [1].

Routine laboratories usually offer both or at least one of the tests; otherwise, the samples are forwarded by the laboratory. Three antigen-coated special tubes, which can be obtained from the respective laboratory, are needed for the QuantiFERON-TB® Gold In-Tube (QFT) test.

The T-Spot.TB test requires 8 mL (at least 2–4 mL in children) of fresh heparinized whole blood, which can be drawn using either Vacutainer cell preparation tubes or standard lithium heparin tubes. Subsequently, the blood samples must be shaken vigorously; they can then be transported at room temperature (QuantiFERON-TB® within 16 hours, T-Spot.TB test within 8 hours).

Table 1 Measures for ruling out tuberculosis (scheme), modified from Diel et al. [1].

1. History	– Immunosuppression – Other risk factors for TB – Previous LTBI/TB – (Occupational) TB contacts – Country of origin – BCG vaccination status – THT/IGRA status – Chest X-rays for comparison
2. Clinical examination	
3. Chest X-ray in two planes, thorax CT if necessary	If there are radiological signs of previous yet untreated or inadequately treated TB without evidence of activity, irrespective of the result of the IGRA test: – chemopreventive therapy with isoniazid (INH) for 9 months (see also S2k guideline: Tuberculosis in adulthood [2])
4. IGRA test	IGRA negative: – usually no chemoprevention IGRA positive: – after ruling out TB requiring treatment: chemopreventive therapy with isoniazid (INH) for 9 months
5. Supplementary TST	If, despite a negative IGRA test, a history of previous close exposure to a patient with infectious pulmonary TB is plausible and if BCG vaccination is unlikely considering the vaccination policy of the patient's country of origin. Or if the IGRA test is indeterminate even when repeated. – positive TST determines further course of action
Bacteriological tests if necessary	

Abbr.: LTBI, latent tuberculosis infection; TB, tuberculosis; TST, tuberculin skin test; IGRA, interferon-gamma release assay.

For billing options in the outpatient setting in Germany, see the resolution of the physicians/health insurance working group in lieu of the 255th session (written resolution) on September 24, 2010, on the inclusion of fee schedule code 32670 in section 32.3.7 of chapter 32 of the E-GO (standardized fee schedule used for patients insured by statutory health insurance funds) (resolution no. 930) effective January 1, 2011, Dtsch Arztebl 2010; 107(42): A-2069 / B-1801 / C-1773. For inpatient billing, see OPS Code 1–930.0.

Hepatitis and hepatic impairment

Treatment recommendations		Consensus strength	Comment
Hepatitis B serology is recommended before initiation of treatment with MTX, adalimumab, etanercept, infliximab, secukinumab or ustekinumab.	↑↑	Strong consensus	Clinical consensus point
Hepatitis B serology may be recommended before initiation of treatment with cyclosporine.	↑	Strong consensus	Clinical consensus point
Hepatitis C serology is recommended before initiation of treatment with MTX, adalimumab, etanercept, infliximab, secukinumab or ustekinumab if there is a corresponding past medical history or clinical or laboratory evidence.	↑↑	Strong consensus	Clinical consensus point
Notification of all reactivations/exacerbations of hepatitis during therapy is recommended.	↑↑	Strong consensus	Clinical consensus point

HIV

Treatment recommendations		Consensus strength	Comment
The combination of antiretroviral therapy and topical agents (corticosteroids, vitamin D analogues or a combination thereof) is recommended as first-line treatment for mild to moderate psoriasis in HIV-infected patients.	↑↑	Strong consensus	Clinical consensus point
Highly active antiretroviral therapy (HAART) in combination with topical and/or phototherapy (narrowband UVB) is recommended as first-line therapy for moderate to severe psoriasis.	↑↑	Strong consensus	Clinical consensus point
Acitretin may be recommended as second-line treatment in addition to HAART.	↑	Strong consensus	Clinical consensus point
Methotrexate or cyclosporine or biologics may be recommended in patients with severe recalcitrant psoriasis only if their HIV infection is well controlled by HAART, and in consultation with an HIV specialist.	↑	Strong consensus	Clinical consensus point
Etanercept may be recommended as biologic of first choice in patients with severe recalcitrant psoriasis if their HIV infection is well controlled by HAART.	↑	Strong consensus	Clinical consensus point

Malignancy including lymphoma and skin cancer

Treatment recommendations		Consensus strength	Comment
Topical therapy, phototherapy (UVB 311 nm, UVB 308 nm) and/or therapy with acitretin is recommended in patients with recently diagnosed malignant tumors (except nonmelanocytic and melanocytic skin cancer).	↑↑	Consensus	Clinical consensus point
It is recommended to take into account the type and extent of the tumor, the risk of recurrence and the patient's psychological distress caused by psoriasis when deciding on initiation of immunosuppressant/immunomodulatory therapy.	↑↑	Strong consensus	Clinical consensus point
Depending on the severity of the psoriasis and the individual impairment of quality of life due to the skin disease, it is recommended to initiate immunosuppressant/immunomodulatory therapy on a case-by-case basis even in the first five years after the cancer diagnosis, in consultation with the patient and the patient's oncologist.	↑↑	Strong consensus	Clinical consensus point
In the case of an inadequate response to topical therapies, phototherapy or acitretin, treatment with MTX or fumaric acid esters may be considered.	→	Strong consensus	Clinical consensus point
Biologics may be considered as treatment of second choice.	→	Strong consensus	Clinical consensus point
A recommendation for a certain biologic cannot be made at present.			

Neurological and psychiatric disorders

No consensus recommendations; see long version for background information.

Coronary heart disease and heart failure

Treatment recommendations		Consensus strength	Comment
Cyclosporine A cannot be recommended as antipsoriatic drug of first choice in patients with arterial hypertension.	↓	Strong consensus	Clinical consensus point
The use of TNF-alpha antagonists cannot be recommended in patients with NYHA class III or IV heart failure.	↓	Strong consensus	Clinical consensus point

Diabetes mellitus

Treatment recommendations		Consensus strength	Comment
Cyclosporine cannot be recommended as antipsoriatic drug of first choice in patients with diabetes mellitus.	↓	Strong consensus	Clinical consensus point
It is recommended to consider antipsoriatic treatment with methotrexate particularly carefully in patients with diabetes and metabolic syndrome.	↑↑	Strong consensus	Clinical consensus point
It is recommended to discuss with the patient the beneficial effects of improved diet, exercise and weight reduction on the treatment of moderate-to-severe psoriasis.	↑↑	Strong consensus	Clinical consensus point

Renal failure

Treatment recommendations		Consensus strength	Comment
Before initiating any systemic therapy, careful investigation of renal function is recommended in patients with known or suspected kidney disease.	↑↑	Strong consensus	Clinical consensus point
Collaboration with a nephrologist is recommended before initiating systemic therapy in patients with stage 3 (and higher) chronic kidney disease.	↑↑	Strong consensus	Clinical consensus point
In patients with stage 2 and 3 chronic kidney disease, use of MTX (at a reduced dose in stage 3 patients), acitretin, apremilast and biologics are recommended.	↑↑	Strong consensus	Clinical consensus point
Use of cyclosporine cannot be recommended in patients with stage 2 (and higher) chronic kidney disease; fumaric acid esters cannot be recommended from stage 3.	↓	Strong consensus	Clinical consensus point
In patients with stage 4 and 5 chronic kidney disease, use of biologics and apremilast (at a reduced dose), yet not of conventional systemic agents, may be recommended.	↑	Strong consensus	Clinical consensus point

Patients wishing to become pregnant/pregnancy/breast-feeding

Treatment recommendations		Consensus strength	Comment
Use of topical skin care products and low- to moderate-potency topical corticosteroids is recommended for patients currently planning to become pregnant or those who are pregnant.	↑↑	Strong consensus	Clinical consensus point
UVB therapy is recommended for patients currently planning to become pregnant or those who are pregnant who do not adequately respond to skin care products and topical corticosteroids.	↑↑	Consensus	Clinical consensus point

Cyclosporine may be considered for pregnant women or women planning to become pregnant who do not adequately respond to skin care products, topical corticosteroids and UV therapy.	→	Strong consensus	Clinical consensus point
TNF inhibitors such as adalimumab, etanercept and infliximab may be recommended for pregnant women or women planning to become pregnant who require systemic therapy; as far as possible, such treatment should be limited to the first and second trimesters.	↑	Consensus	Clinical consensus point
Given their teratogenicity, acitretin and methotrexate cannot be recommended for women planning to become pregnant or those who are pregnant.	↓	Strong consensus	Clinical consensus point

Psoriatic arthritis (PsA)

Treatment recommendations		Consensus strength	Comment
NSAIDs/coxibs are recommended for symptomatic therapy of arthralgia, i.e., without objective clinical evidence of joint swelling or dactylitis.	↑↑	Consensus	Clinical consensus point
Referral to a rheumatologist is recommended if there are persistent inflammatory musculoskeletal symptoms.	↑↑	Consensus	Clinical consensus point
In order to reduce the likelihood of a destructive disease course, initiation of disease-modifying therapy is recommended if there is clinical evidence of peripheral arthritis/dactylitis, or objective evidence thereof on ultrasound, conventional X-ray or MRI.	↑↑	Strong consensus	Clinical consensus point
In the initial therapy of psoriatic arthritis/dactylitis associated with cutaneous psoriasis, conventional DMARDs (disease-modifying anti-rheumatic drugs), which simultaneously have a positive effect on psoriasis of the skin, are recommended.	↑↑	Consensus	Clinical consensus point
In patients with peripheral arthritis/dactylitis who have not adequately responded to at least one conventional synthetic DMARD, initiation of a biologic DMARD as monotherapy or in combination with a synthetic DMARD is recommended.	↑↑	Strong consensus	Clinical consensus point
Due to lack of efficacy, monotherapy with a synthetic DMARD cannot be recommended for axial involvement or enthesitis.	↓	Strong consensus	Clinical consensus point
Adalimumab, certolizumab, etanercept, golimumab, infliximab, secukinumab and ustekinumab are recommended as biologic DMARDs for the treatment of patients with predominant psoriatic arthritis associated with psoriasis of the skin.	↑↑	Strong consensus	Clinical consensus point
Apremilast may be recommended as an alternative to biologic DMARDs (bDMARDs) for the treatment of patients with predominant psoriatic arthritis associated with psoriasis of the skin.	↑	Consensus	Clinical consensus point

Screening for psoriatic arthritis

Recommendation		Consensus strength	Comment
It is recommended to assess every patient for evidence of PsA (at initial presentation and during follow-up) and to inform patients about the possibility of developing PsA. Use of a validated questionnaire may be recommended.	↑↑	Consensus	Clinical consensus point

Vaccination

No consensus recommendations; see long version for background information.

Systemic therapy of psoriasis in patients with chronic inflammatory bowel disease (IBD)

Treatment recommendations		Consensus strength	Comment
For patients with active IBD, it is recommended to select systemic antipsoriatic therapy in consultation with the treating gastroenterologist.	↑↑	Strong consensus	Clinical consensus point
Adalimumab, infliximab and ustekinumab are recommended for systemic antipsoriatic therapy in patients with a previous history of IBD or active IBD (Crohn's disease or ulcerative colitis).	↑↑	Strong consensus	Clinical consensus point
Methotrexate may be recommended for systemic antipsoriatic therapy in patients with a previous history of Crohn's disease or with active Crohn's disease.	↑	Strong consensus	Clinical consensus point
Etanercept or cyclosporine may be considered for systemic antipsoriatic therapy in patients with a previous history of IBD or with active IBD.	→	Majority agreement	Clinical consensus point
Fumaric acid esters or secukinumab may be considered for systemic antipsoriatic therapy in patients with a previous history of IBD or with active IBD only after thorough review and with close monitoring.	→	Strong consensus	Clinical consensus point

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