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Highlights of the updated Dutch evidence- and consensus-based guideline on psoriasis 2017

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Conflicts of interest statements are listed in the Appendix.

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Introduction

This is a summary of the 2017 updated Dutch psoriasis guideline, based on the Dutch Society of Dermatology and Venereology guideline on the treatment of psoriasis (2011),[1,2] the European Dermatology Forum (EDF) guideline on the treatment of psoriasis (2015)[3] and newer literature. The focus is mainly on patients with moderate-to-severe psoriasis, which is the minority of the total patient population. Topical therapies and phototherapies are outside the scope of this update, but remain important treatment options.

We provide sections per drug and patient group, aiming for a useful manual for daily clinical practice, including recommendations for screening and monitoring. In the section on treatment decisions in psoriasis we address the most important aspects of therapeutic decision making. To support dermatologists in making treatment decisions, we provide a concise physician decision aid for the biologics and the small molecule inhibitor apremilast (Table S1; see Supporting Information).

The following sections have been updated: systemic therapy (methotrexate, fumarates, adalimumab, etanercept, infliximab, ustekinumab), treatment for paediatric patients, serum concentration and antibody formation in biologics, and quality of life. There are newly added sections on treatment decisions in psoriasis, secukinumab, apremilast, combination therapy, psoriatic arthritis, biosimilars, and pregnancy and biologics. The

section on paediatric patients provides guidance on topical therapy and phototherapy in addition to conventional systemic therapy and biologics. We have only included agents that were available in the Netherlands at the start of the update in 2015, meaning that ixekizumab, brodalumab, guselkumab, certolizumab and risankizumab are not included. The sections on retinoids and ciclosporin were not updated; only when strictly necessary minor changes were made, which are clearly indicated in the text. For more detailed information, we refer readers to the full guideline.[4]

Guideline development

The systematic literature search used for the EDF guideline on the treatment of psoriasis[5] was updated until July 2015. For topics that were not covered in the EDF guideline a separate systematic literature search was conducted in MEDLINE, Embase and CENTRAL in July 2015. Details of the search strategies are presented in the full guideline.[4] The guideline working group consisted of dermatologists and a rheumatologist, a dermatology nurse and a patient with psoriasis as representatives of their national societies. This working group formulated research questions and outcome measures for the updated and new sections. The outcomes are presented in Table 1. Induction or short-term therapy was defined as 16 weeks, long-term therapy as 24 weeks.

Articles were screened for inclusion and exclusion criteria based on the title and abstract by two researchers independently. The full texts were analysed by members of the working group. The risk of bias of the included studies was assessed using the Cochrane Risk of Bias Assessment Tool.[6] Data analysis was performed using Review Manager. We added data from the new literature to the EDF analysis, and shared this updated version with the EDF psoriasis guideline working group. The quality of evidence was evaluated using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system for grading evidence[7] using GRADEpro GDT online software[8] for most sections.

Recommendations

Recommendations were formulated by the working group based on the level of evidence according to GRADE. To indicate the strength of the recommendation the formulation in Table 2 was used.

Summary of the guideline

Treatment decisions in psoriasis (2017)

The majority of patients with psoriasis have mild disease in which topical therapy is sufficient to suppress the lesions. If necessary, different forms of phototherapy and/or conventional systemic therapy are considered with or without topical agents. With the arrival of biologics, treatment options have increased and the effects of treatments have improved drastically.

Table 1 Assessed outcomes and assigned rating of importance

Outcome	Importance
Efficacy	
Induction or short-term therapy (16 weeks)	
PASI 75 response	Crucial
PASI 90 response	Important
Reduction in mean PASI/final PASI score	Important
Clearance (i.e. PGA 0, PASI 100, 'clear')	Important
PGA 0/1 (e.g. 'clear/almost clear')	Crucial
Long-term therapy (24 weeks)	
PASI 75 response	Crucial
PASI 90 response	Important
Reduction in mean PASI/final PASI score	Important
Clearance (e.g. PGA 0, PASI 100, 'clear')	Important
PGA 0/1 (e.g. 'clear/almost clear')	Crucial
Safety	
Withdrawal due to adverse event	Crucial
Number of patients with at least one adverse event	Important
Number of patients with at least one serious adverse event (as listed in study)	Crucial
Patient reported	
Response in DLQI score ≤ 5	Important
Reduction in mean DLQI	Important
Others	
Time until onset of action: time until 25% of patients achieve a PASI 75 response	Important
Time until onset of action: time until a 25% reduction in the mean baseline PASI is achieved	Important
Time to relapse (after discontinuation of treatment)	Important
Relapse rate at a given point X in the publication	Important

PASI, Psoriasis Area and Severity Index; PASI 75, 75% improvement in PASI; PGA, Physician's Global Assessment; DQLI, Dermatology Quality of Life Index.

Table 2 Wording for recommendations

Strength	Wording
Strong recommendation for the use of an intervention	Intervention X is recommended
Weak recommendation for the use of an intervention	Intervention X is suggested
No recommendation	No recommendation can be made
Weak recommendation against the use of an intervention	Intervention X is not suggested
Strong recommendation against the use of an intervention	Intervention X is not recommended

It can be challenging to choose a suitable therapy for an individual patient. However, we expect that if the treatment is in line with patients' expectations, preferences and lifestyle, adherence to the treatment and increased treatment satisfaction are more likely.[9] We recommend that treatment decisions should therefore be made by patients and physicians together

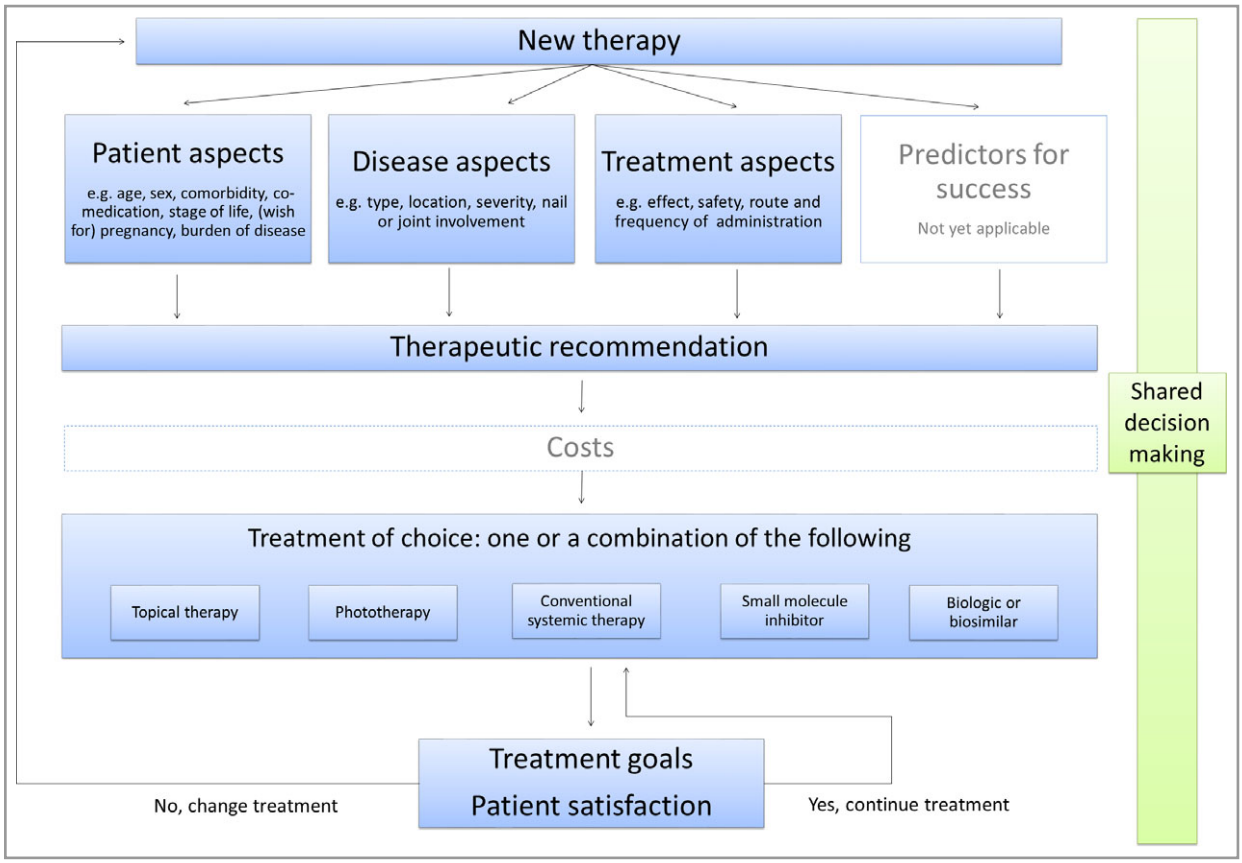

Fig 1. Flowchart for treatment decisions in psoriasis.

('shared decision making'). In our opinion it is important that all agents remain equally accessible and available. A preferred policy for rigid application of one drug is undesirable.

We suggest that the following aspects should be addressed in order to choose the best-suiting therapy. These aspects are also summarized in Figure 1.

- *Patient aspects*. Patient-related factors that should be considered in treatment decisions are (but not limited to) age, sex, comedication, comorbidity, previous agents, stage of life, (wish for) pregnancy, profession, hobbies and (psychosocial) burden of disease.
- *Disease aspects*. The type of psoriasis, severity and localization of the lesions, joint and/or nail involvement should be taken into consideration.
- *Treatment aspects*. This includes short-term and long-term treatment effects and safety, route of administration, frequency of administration, burden of treatment, adverse events and antibody formation.
- *Predictors for treatment success*. Ideally, we should include predictors for treatment success or failure in the therapeutic decision. Research is ongoing but an applicable set of such predictors is not yet defined.
- *Therapeutic recommendations*. Considering the high costs of biological therapy, cost-efficient prescription is necessary. Topical therapy, phototherapy and conventional systemic therapy remain important in the treatment of psoriasis and are effective in a substantial proportion of patients. Even though some biologics can be prescribed as a first-line systemic treatment (according to the label text) when a patient is eligible for systemic therapy, we have formulated the following recommendation: we recommend only prescribing biologics and/or apremilast in cases of inadequate response to, or intolerance/contraindications for phototherapy and one or more conventional systemic agents as mentioned in this guideline. In the case of high disease activity, contraindications and/or adverse prognostic factors then deviation from this advice is possible.
- *Costs*. There are ways to help keep the costs of biological therapy manageable. Studies on the effects of dose reduction, interval extension and treatment optimization (by combining biologics with other conventional systemic agents) are important and currently ongoing. Physicians should take the extra costs into account when considering increasing a dose or interval shortening of biologics. Also, prescription of biosimilars might lower the costs, and this is discussed further in the section on biosimilars. Although important, costs should never be the only leading factor in the treatment decision.

Treatment goals

After carefully choosing a therapy, it remains important to check regularly if the treatment still meets the requirements and/or goals. To prevent undertreatment of psoriasis, it is recommended to adapt and follow the treatment goals as described by Mrowietz *et al.*[10] in daily practice (see their Fig. 2):

- ≥ 75% improvement in the Psoriasis Area and Severity Index (PASI 75) after induction therapy: continue treatment.
- < PASI 50 improvement after induction therapy: modify therapy.
- ≥ PASI 50 and < PASI 75 improvement after induction therapy: continue treatment if Dermatology Life Quality Index (DLQI) ≤ 5 and modify treatment if DLQI > 5.

In addition, patients' satisfaction with treatment should be taken into consideration.

To support physicians in the choice of therapy we have developed a physician decision aid (Table S1; see Supporting Information) combining the aspects discussed above.

Systemic therapy (2017)

See Table S2 (Supporting Information) for advice on screening and monitoring in systemic therapy.

Methotrexate (2017)

Recommendations Methotrexate is recommended for both induction and long-term therapy in patients with moderate-to-severe plaque-type psoriasis (Table S3; see Supporting Information). In case of inadequate response (according to the treatment goals), it is recommended to increase the dose from 15 to 30 mg per week.

Table S4 details blood tests and their timing. Routine measurement of procollagen III N-terminal peptide is no longer recommended, because of the limited added value in the detection of liver fibrosis compared with alanine transaminase and low specificity of increased procollagen III N-terminal peptide.[11] Physicians should be alerted to other risk factors for liver fibrosis (e.g. hepatic steatosis, metabolic syndrome) aside from methotrexate therapy. Monitoring according to Figure 2 is recommended.

Ciclosporin (2011)

Recommendations Ciclosporin is recommended as induction therapy in moderate-to-severe plaque-type psoriasis (Table S5; see Supporting Information). Because of its fast-acting effect, ciclosporin is particularly useful for short-term therapy and crisis intervention. Ciclosporin may be prescribed for longer terms (maximum of 2 years) in individual cases, but close monitoring for signs of toxicity such as renal impairment and hypertension is important. Table S6 (see Supporting Information) details blood tests and their timing.

Acitretin (2011)

Recommendations Acitretin is recommended for induction therapy in moderate-to-severe plaque-type psoriasis, although it is not recommended as a first-choice monotherapy (Table S7; see Supporting Information). In patients with a good clinical

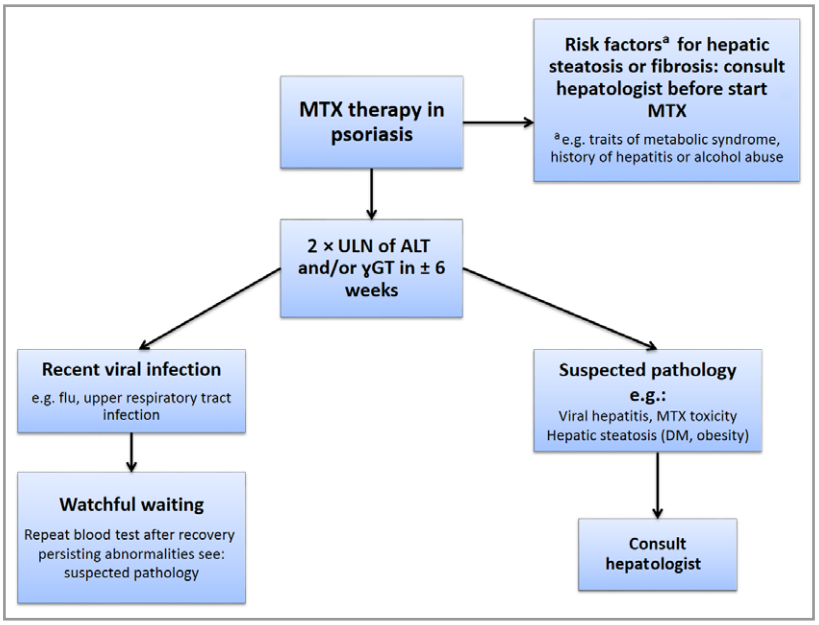

Fig 2. Flowchart for methotrexate (MTX) therapy. ULN, upper limit of normal; ALT, alanine transaminase; γGT, gamma-glutamyl transferase; DM, diabetes mellitus.

effect at the end of induction therapy (16 weeks), maintenance therapy is suggested with the lowest effective dose. Table S8 (see Supporting Information) details blood tests and their timing.

Women of childbearing age should not be treated with acitretin because of the teratogenic characteristics of the drug. Contraception is recommended during and up to 3 years after treatment discontinuation (modified in 2017).

Fumarates (2017)

Recommendations Fumarates are recommended as induction and long-term therapy for moderate-to-severe plaque-type psoriasis (Table S9; see Supporting Information). In general, the long-term safety profile of fumarates is favourable, but the evidence is relatively limited.[12–14] Acetylsalicylic acid (e.g. 80 mg) is suggested to treat flushing as an undesired side-effect of therapy.[15]

The incidence of progressive multifocal leucoencephalopathy during treatment with fumarates is unknown, but seems related to prolonged periods of lymphocytopenia. In addition to monitoring for lymphocytopenia (Table S10; see Supporting Information), we recommend being alert for neurological symptoms during fumarate therapy and referring a patient to a neurologist if needed. Table S11 (see Supporting Information) details recommended dosing.

Apremilast (2017)

Recommendations Apremilast is suggested as induction therapy and long-term therapy in moderate-to-severe plaque-type psoriasis (Table S12; see Supporting Information). Long-term safety data are relatively scarce.

In patients with severe renal impairment (creatinine clearance < 30 mL min^{-1}) 30 mg once daily is recommended. Table S13 and Table S14 (see Supporting Information) detail blood tests and dosing for apremilast, respectively.

Adalimumab (2017)

Recommendations Adalimumab is recommended as induction therapy and long-term therapy in moderate-to-severe plaque-type psoriasis (Table S15; see Supporting Information). Increasing the dose of adalimumab from 40 mg per 2 weeks to 40 mg per week is suggested for patients with an insufficient response to adalimumab 40 mg per 2 weeks. This dosage increase is according to the label change (November 2015). Table S16 (see Supporting Information) details blood tests for all biologics.

Etanercept (2017)

Recommendations Etanercept is recommended as induction therapy and long-term therapy in moderate-to-severe plaque-type psoriasis (Table S17; see Supporting Information). A starting dose of 50 mg twice weekly is suggested, over a dose of 50 mg once weekly. Undesired effects of long-term treatment are similar to induction therapy. A maintenance dose of 50 mg twice weekly is suggested over a dose of 50 mg once weekly.

Infliximab (2017)

Recommendations Infliximab is recommended as induction therapy for chronic plaque-type psoriasis in week 0, 2 and 6 (Table S18; see Supporting Information). Infliximab is recommended as maintenance therapy every 8 weeks (with at least 4 weeks between two administrations).

Secukinumab (2017)

Recommendations Secukinumab is recommended as induction therapy in chronic plaque-type psoriasis (Table S19; see Supporting Information). A dose of 300 mg is recommended over a dose of 150 mg in induction therapy. Secukinumab is suggested for maintenance therapy. Long-term safety data are limited.

Ustekinumab (2017)

Recommendations Ustekinumab is recommended as induction therapy in chronic plaque-type psoriasis (Table S20; see Supporting Information). Ustekinumab 45 mg is suggested in patients ≤ 100 kg. Ustekinumab 90 mg is suggested in patients > 100 kg. Ustekinumab is recommended as a maintenance therapy for at least 5 years. The long-term safety profile of ustekinumab over a period of 5 years appears not to be evidently different from that for 1 year in additional literature.

Combination therapy (2017)

Prescription of systemic combination therapy is currently off-label. Patients should be informed about this off-label use and possible side-effects. Therapy should be started only after careful weighing of benefits and risks tailored to the individual patient.[16]

Recommendations Etanercept in combination with methotrexate is suggested as induction and maintenance therapy of chronic plaque-type psoriasis. Etanercept in combination with acitretin is suggested as induction and maintenance treatment of chronic plaque-type psoriasis (based on one maintenance study).[16]

Biologics or methotrexate in combination with ultraviolet B is not recommended as a maintenance treatment in patients with chronic plaque-type psoriasis because of a lack of data on safety.[16]

Treatment with adalimumab, infliximab, ustekinumab or secukinumab in combination with methotrexate is suggested in treatment-resistant psoriasis.

Serum trough level and detection of antidrug antibodies (2017)

The serum trough level of a biologic depends on many factors, among which are dose and dose frequency, treatment adherence, disease activity, antibody formation and

comedication with immunosuppressants. The extent to which the presence or absence of antibodies and the drug serum concentrations correlate to the clinical response depends on the type of biologic and needs further exploration.

At the moment a correlation between trough level concentration and clinical effect has only been demonstrated for adalimumab.[17] A therapeutic algorithm based on serum trough levels has potential to improve adalimumab therapy, but no prospective studies have been performed yet.

Recommendations It may be useful to determine adalimumab serum trough levels before altering the frequency of administration or stop/switch therapy. A low serum trough level concentration can be caused by antidrug antibodies. The optimal serum trough concentration has been established for adalimumab (3·51–7·00 mg L^{-1}).[18] Measurement of only antidrug antibodies provides limited information.

Biosimilars (2017)

Currently approved biosimilars are available for infliximab (Remsima™, Celltrion Healthcare, Budapest, Hungary; Inflectra™, Hospira, Maidenhead, U.K.; and Flixabi®, Biogen Idec, Cambridge, MA, U.S.A.) and for etanercept (Benepali,® Biogen, Cambridge, MA, U.S.A.; and Erelzi, Novartis Pharma AG, Stein, Switzerland).

Recommendations There are no major objections to starting a registered biosimilar for patients eligible for biological therapy. It is recommended that patients be included in a registry to monitor efficacy and safety. Substitution of a biologic with a biosimilar in patients who are responding well is not recommended, but the decision to switch to a biosimilar in these patients is reserved for the physician and patient. Physicians should take into consideration that long-term safety data for biosimilars are limited.

It is possible for patients who discontinue a biological therapy (for example for more than 6 months) to restart with a biosimilar. In the case of switching to a biosimilar, it is recommended to administer the first dose of the biosimilar when the old reference product was supposed to be re-administered and not before, as the old drug may still be partially present in the body, which makes it impossible to attribute side-effects to either of the two drugs. These recommendations are in line with the Dutch national guideline on biosimilars.[19]

Psoriatic arthritis (2017)

The following paragraph is based on the Dutch guideline for axial spondyloarthritis (2014)[20] and international European League Against Rheumatism (2015)[21] and Group for Research and Assessment of Psoriasis and Psoriatic Arthritis guidelines (2016).[22]

Recommendations As a result of the increased risk in patients with psoriasis, it is recommended that physicians be alert for signs of psoriatic arthritis (PsA): spontaneous persistent pain, swelling or stiffness of one or more joints and nearby ligaments and tendons, or chronic back pain present for at least 3 months before the age of 45 years. It is recommended that patients with psoriasis be referred to a rheumatologist if there is a suspicion of peripheral arthritis, dactylitis, enthesitis or if they have experienced daily chronic back pain for at least 3 months before the age of 45 years. Cooperation with and consultation with a rheumatologist is strongly recommended not just for diagnostics but also for treatment of PsA. Routine additional testing before referral to a rheumatologist is not recommended. Nonsteroidal anti-inflammatory drugs are recommended as the first step in the treatment of PsA.

Tuberculosis screening (2017)

Recommendations A Dutch multidisciplinary guideline is currently being developed on screening for tuberculosis before the start of immunosuppressive therapy. For now, we recommend screening all patients before starting biological therapy. In line with the EDF guideline and the current national statement on screening for latent tuberculosis infection we recommend undertaking the following:[3,23]

- Medical history including tuberculosis history.
- Physical examination.
- Chest X-ray.
- Tuberculin skin test (Mantoux) and interferon gamma release assay.

Vaccination (2017)

The use of live vaccines is discouraged during immunosuppressive therapy (Table 3).[24] Exceptions can be made in

Table 3 Advice on duration between stopping immunosuppressant and administration of live vaccine in adult patients

Advice on duration	Time
Between stopping immunosuppressant and administration of live vaccine	
Methotrexate	3 months (based on half-life 1 month may be sufficient; nevertheless wait 3 months if possible)[24,26]
Ciclosporin	3 months[24,26,59,60]
Fumarates	No known contraindication (no data)
Apremilast	No data, 3 months is advised
Etanercept	3 months (no data, based on expert opinion and half-life of the drug)
Adalimumab	3 months[24,26,59,60]
Infliximab	3 months, for yellow fever vaccine minimum of 6 months[24,26,59,60]
Ustekinumab	3 months[24,26,59,60]
Secukinumab	No data, 3 months is advised
Ixekizumab	No data, 3 months is advised
Between live vaccine and (re)starting immunosuppressive therapy	
All systemic agents	Minimum of 4 weeks[3,24–26]

specific circumstances (e.g. for mumps, measles, rubella and varicella in specific cases), in consultation with a vaccine specialist. In patients with immunosuppressive therapy, it is recommended that (live) vaccines, except for the yearly influenza vaccine, be given in consultation with a specialist in the field of vaccinations/immunology/travel diseases; additional measures may be necessary (e.g. titre control in common vaccines, live vaccine measures). Vaccines should preferably be administered before starting immunosuppressants.

It is advised to wait for at least 4 weeks after a live vaccine to (re)start immunosuppressive medication.[3,24–26] Beware of live vaccinations in newborns of mothers treated with immunosuppressive therapy, as it might be necessary to postpone live vaccines.

Pregnancy (2017)

The time a woman should wait to conceive after stopping biological therapy depends on the half-life of the drug.

Recommendations Our recommendations are summarized in Table 4. We suggest starting or continuing biological therapy in pregnant women and women planning a pregnancy only if the benefits outweigh the risks of treatment. In such cases there is a slight preference for etanercept given the short half-life and the relatively low transplacental transfer to the fetus. It is recommended that biologics be stopped, especially the IgG immunoglobulins such as infliximab and adalimumab, before the end of the second trimester to minimize the risk of neonatal immunosuppression.

Pregnancy in a woman treated with a biologic requires a multidisciplinary approach, therefore counselling by a gynaecologist is recommended. It might be necessary to postpone administration of live vaccinations and bacillus Calmette–Guérin vaccinations in neonates exposed to biologics *in utero*, especially in the third trimester. Pregnant patients treated with biologics should preferably be treated in an academic hospital. Data on pregnancy should preferably be kept in a registry.

Table 4 Advice on contraception[a]

Drug	
Methotrexate	Women: during therapy and at least 3–6 months after stop (no consensus in literature)
	Men: during therapy and at least 3–6 months after stop (no consensus in literature)
Acitretin	Women: during therapy and at least 3 years after stop[b]
	Double contraceptive measures are advised because of very teratogenic character
	Men: no specific preventive measures
Ciclosporin	Women: during therapy
	Men: no specific preventive measures
Fumarates	Women: during therapy and at least 2 weeks after stop
	Men: no specific preventive measures
Apremilast	Women: during therapy and at least 28 days after stop
	Men: during therapy and at least 28 days after stop (lack of data)
Adalimumab	Women: during therapy and at least 5 months after stop
	Men: no specific preventive measures (limited data)
Etanercept	Women: during therapy and at least 3 weeks after stop. When treatment is unavoidable and benefits outweigh the risks, treatment with etanercept during pregnancy can be considered
	Men: no specific preventive measures (limited data)
Infliximab	Women: during therapy and at least 6 months after stop
	Men: no specific preventive measures (limited data)
Secukinumab	Women: during therapy and at least 20 weeks after stop
	Men: during therapy (lack of data)
Ustekinumab	Women: during therapy and at least 15 weeks after stop
	Men: during therapy (lack of data)

[a]Based on drug-specific summary of product characteristics and Nast, Garritsen, Yiu, and Grunewald.[3,61–63] [b]Modified in 2017 based on changed recommendations in summary of product characteristics.

Paediatric psoriasis (2017)

This section is based on van Geel *et al.* (2015),[27] supplemented with more recent literature.

Topical therapy

Recommendations Topical corticosteroids are useful in the treatment of paediatric psoriasis, with class II–III potency recommended. Dependent on the disease severity, a combination with vitamin D3 analogues is recommended. Since the combination calcipotriol/betamethasone dipropionate contains a class III corticosteroid, it is recommended that this treatment be prescribed only for short-term therapy (a maximum of 4 weeks) if possible.

For maintenance therapy vitamin D3 analogues (especially calcipotriol) are first choice, given the effect and favourable side-effects. If necessary a class II corticosteroid can be added.

If, in recalcitrant psoriasis, a combination with class III steroid is necessary, intermittent use is strongly recommended.

Tacrolimus (0·03% or 0·1%) ointment is suggested to treat resistant psoriasis of the face and intertriginous folds. If treatment with (a combination of) topical corticosteroids or vitamin D3 analogues fails in paediatric psoriasis (and adherence is ensured), dithranol in a day care setting should be seriously considered before phototherapy or systemic therapy is started.

Phototherapy

Recommendations It is recommended that narrowband-ultraviolet B phototherapy is only used to a limited extent in paediatric

psoriasis. It should be used cautiously, particularly in young (age < 12 years) and in fair-skinned children. It is the opinion of the guideline working group, that children should not be treated with home ultraviolet B. Given the proven carcinogenic effect, psoralen–ultraviolet A therapy is contraindicated in paediatric psoriasis.

Systemic therapy

Recommendations The effect of antibiotics in children with guttate psoriasis remains controversial. In the case of a suspect medical history of tonsillitis and positive throat culture, treatment with antibiotics can be considered.

Acitretin is suggested for paediatric psoriasis (including pustular or erythrodermic forms). Treatment in adolescent women is advised against because of the teratogenic potential of acitretin. Ciclosporin is recommended in exceptional situations and for short-term treatment only, given the potential nephrotoxicity. Methotrexate is recommended in a dose range between 0·2 and 0·4 mg kg^{-1} weekly. Folic acid 5–10 mg 24 h after ingestion of methotrexate is recommended. If fumarates are used for paediatric psoriasis, one should be aware of prolonged leucocytopenia/lymphocytopenia and follow the recommendations described in the section on fumarates in this guideline.

Biologics

Recommendations Biologics should be administered with caution in children with moderate-to-severe psoriasis given the uncertainty about long-term safety. The working group suggests considering the conventional systemics first.

In order to evaluate long-term safety, it is recommended including children treated with a biologic in a (national) registry. Treatment of paediatric patients with psoriasis with biologics should be the preserve of dermatologists with experience in biological therapy, especially in children.

For instructions for use/screening/frequency of laboratory checks of biological therapy in children please refer to the instructions described for adults in the various sections. It is recommended to check the vaccination status of children (according to the national vaccination programme) before starting biological therapy.

Etanercept is recommended as an induction and maintenance therapy in children and adolescents with plaque-type psoriasis from the age of 6 years who are inadequately controlled with use of, or are intolerant to, other systemic agents or phototherapy. Dosage is 0·8 mg kg^{-1} (up to 50 mg per dose) once a week.

Adalimumab is recommended as an induction therapy in children and adolescents aged 4 years and older with plaque-type psoriasis who have had an inadequate response to or are inappropriate candidates for topical therapy and phototherapy. Long-term safety data in children are not available. Dosage is 0·8 mg kg^{-1} (up to 40 mg per dose) week 0, 1 and thereafter every other week.

Ustekinumab is recommended in adolescent patients with chronic plaque-type psoriasis from the age of 12 years whose condition is inadequately controlled with use of, or who are intolerant to, other systemic agents or phototherapy. Long-term safety data in children are not available. The recommended dose for adolescents < 60 kg is 0·75 mg kg^{-1}, for those with a weight ≥ 60 to ≤ 100 kg the dose is 45 mg and for patients > 100 kg the dose is 90 mg. Administration is at week 0 and 4, and every 12 weeks thereafter.

Quality of life and treatment satisfaction in psoriasis (2017)

Quality of life

Many patients with psoriasis experience an impairment in their quality of life, and anxiety and depression occur more frequently compared with healthy individuals.[28–33] Patients with psoriasis experience limitations in physical functioning because of itching, reduced sleep quality, fatigue and pain, and experience limitations in social functioning, including stigmatization.[34–42] Biologics, systemic agents, phototherapy and topical therapy have a beneficial effect on patient's quality of life.[43–50]

Recommendations It is recommended that attention be explicitly paid to the impact of psoriasis on quality of life in dermatological practice. Physicians are encouraged, where possible and relevant, to determine patient's quality of life by asking, or with the use of standardized questionnaires such as the DLQI or Skindex-29. Optionally, measurements of itch, pain and loss of sleep can be performed.

As patients with psoriasis are often stigmatized, it is recommended this topic be discussed.

In the case of suspicion of (serious) psychological problems, it is suggested the patient be referred to a psychologist or psychosocial worker who can investigate this with validated questionnaires.

Treatment satisfaction

Only about half of patients with psoriasis are satisfied with their current treatment.[51,52] Treatment satisfaction is highest in patients treated with biologics compared with systemic therapy, phototherapy and topical therapy.[1,53–58]

Recommendations It is recommended attention be paid, where possible and relevant, to treatment satisfaction by asking patients about their satisfaction with treatment and care. The generic Treatment Satisfaction Questionnaire for Medication (TSQM) can be used for this purpose. If necessary, treatment adjustments should be made.

Discussion

This summary highlights the most important aspects of systemic therapy in patients with psoriasis. The decision aid for

systemic therapies (Table S1) can serve as a useful tool for clinical practice, and it also clearly highlights the gaps in current evidence. Clinical signs are described most extensively, with the PASI and the Physician's Global Assessment as frequently reported efficacy outcome measures. However, comparison between studies remains challenging because of the extensive variation in study outcomes, such as PASI 75, PASI 90, PASI 100 and change in mean PASI and also the different time points of evaluations (e.g. 12, 16, 24, 52 weeks after start of treatment). In addition, in other domains, such as quality of life, different instruments are used, such as the DLQI, Skindex-29, TSQM and visual analogue scale scores, making comparison between studies very difficult. The development of a core outcome set for psoriasis is recommended by the working group, as this will increase the comparability between studies and therefore improve the quality of the aggregated evidence. We encourage the involvement of patients in treatment decisions. To improve shared decision making we are currently developing a nationwide, online patient decision aid for psoriasis.

A limitation of the guideline is that it focuses on chronic plaque-type psoriasis and therefore not all types of psoriasis are discussed. Strengths are that we have included a section on PsA, with recommendations for screening, referral indications and treatment in collaboration with the Dutch Society of Rheumatology and in which we strongly encourage a multidisciplinary treatment approach for patients with psoriatic skin lesions and PsA. Psoriasis in children is discussed in a separate section.

In this guideline we recommend following the European consensus treatment goals described by Mrowietz *et al.*[10] in 2011, but given the increased effectiveness of the newest classes of targeted biologics, we should reconsider if these goals are still sufficient. Is it time to raise the standards? The present gold standard of PASI 75 may be abandoned in favour of PASI 90 or PASI 100. Beside treatment goals, we also recommend including patient satisfaction in the decision to adjust, stop or continue treatment. Importantly, treatment goals for mild psoriasis are lacking, but are needed to standardize the step towards systemic therapy.

New therapies are developed and approved rapidly, and as a consequence regular updates of guidelines are required. The process of writing a guideline is precise, time consuming and as a result also expensive. To improve the efficiency in guideline development and to lower the burden of data analysis, we worked together with the EDF guideline working group, and shared our literature searches and GRADE analysis back and forth. Although treatment recommendations can differ between countries because of local regulations, availability of medicines, cooperation with other medical specialists and healthcare costs, the quality assessment of the literature should be uniform. We propose that further collaboration between guideline developers on quality assessment could limit the workload and that sharing of knowledge and expertise might also increase the overall quality of the guidelines.

Currently, we are discussing a collaboration between the Cochrane Skin Group, network systematic review groups, the EDF and national guideline development groups. We expect that in this way we will be able to create living guidelines, which will be updated frequently and therefore will remain up to date.

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Appendix

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an interest in psoriasis: Pfizer, Lilly, Novartis, Dermira. S.R. was part of the methodologist group of the European psoriasis guideline 2015. P.I.S. has acted as a consultant for AbbVie, LEO Pharma and Novartis and has received independent research grants from LEO Pharma and Schering-Plough. P.I.S. has participated in studies sponsored by companies that manufacture drugs used for the treatment of psoriasis and atopic dermatitis. All funding is not personal but goes to the research fund of the department of dermatology of Amsterdam Medical Centre, Amsterdam, the Netherlands. All other authors have no interests to declare.

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

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Table S8 Blood tests: acitretin.
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File S1 Additional references.