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Immunizations in immunocompromised patients: a guide for dermatologists

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Summary

The increasingly frequent use of immunomodulatory agents in dermatology requires the observance of specific recommendations for immunization. These recommendations are developed and regularly updated by the German Standing Committee on Vaccination (STIKO), an independent advisory group at the Robert Koch Institute. Dermatological patients on immunosuppressive treatment should ideally receive all vaccinations included in the standard immunization schedule. Additionally, it is recommended that they also undergo vaccination against the seasonal flu, pneumococci, and herpes zoster (inactivated herpes zoster subunit vaccine for patients ≥ 50 years). Additional immunizations against *Haemophilus influenzae* type B, hepatitis B and meningococci may be indicated depending on individual comorbidities and exposure risk. Limitations of use, specific contraindications and intervals to be observed between vaccination and immunosuppression depend on the immunosuppressive agent used and its dosing. Only under certain conditions may live-attenuated vaccines be administered in patients on immunosuppressive therapy. Given its strong suppressive effect on the humoral immune response, no vaccines – except for flu shots – should be given within six months after rituximab therapy.

This CME article presents current recommendations on immunization in immunocompromised individuals, with a special focus on dermatological patients. Its goal is to enable readers to provide competent counseling and to initiate necessary immunizations in this vulnerable patient group.

Introduction

The German STIKO (*Ständige Impfkommission; Standing committee on Vaccination)* is an independent advisory group associated with the Robert Koch Institute (RKI). The group is tasked with developing and updating immunization recommendations in Germany; they are published once a year in the *Epidemiological Bulletin* issued by RKI [1]. On the one hand, these recommendations include *standard vaccinations* that apply to the general population and that are therefore part of the basic medical services provided by general practitioners and pediatricians. On the other hand, STIKO issues recommendations for *non-routine vaccinations* that may be indicated in certain groups, either because they may have an increased risk of infection or complications, or because they may be exposed to a significant degree, or because they may easily spread the disease if infected. For instance, the latter group also includes medical personnel, which is why it is recommended that

STIKO recommendations for standard and non-routine vaccinations are updated on a regular basis.

they receive annual flu shots [1]. Individuals with innate or disease-related immunodeficiency as well as those with treatment-related immunosuppression have an increased risk of infection. Given the complexity of their underlying conditions, these patients are usually cared for by various specialists including dermatologists. In recent years, there has been a steady increase in the number and spectrum of immunomodulatory and immunosuppressive drugs used in dermatology, not least due to the approval of novel biological agents for the treatment of psoriasis [2, 3]. It is safe to assume that this trend will continue in the future. The prescription of these agents by dermatologists has a direct effect on individual risk factors, which in turn results in specific recommendations for immunization. Dermatologists should therefore be familiar with these recommendations in order to be able to competently counsel their patients. One recent change relevant for dermatological patients has resulted from the approval of an adjuvanted inactivated herpes zoster subunit vaccine in 2018. Current STIKO recommendations provide for its standard use in individuals ≥ 60 years of age. It is indicated, the vaccine is also recommended for immunocompromised patients ≥ 50 [1, 2, 4, 5].

By prescribing immunomodulatory drugs, dermatologists directly influence individual recommendations for immunization.

Expert groups that include representatives from RKI and STIKO as well as from various medical societies have published detailed information on how to implement the STIKO recommendations in immunocompromised patients. Apart from a position paper outlining the basic principles [6], there are reviews specifically focusing on the issue of immunizations in patients with primary immunodeficiency and HIV [7], in individuals with autoimmune diseases and on immunomodulatory treatment [4], as well as in patients with malignancies, on antineoplastic treatment, status post organ or stem cell transplantation, or individuals with asplenia [8]. This CME article presents current recommendations on immunization, with a special focus on aspects relating to adult dermatological patients.

Situations that require the observance of special immunization recommendations

Various innate, disease-related or treatment-induced conditions are associated with a compromised immune system and thus require the observance of special immunization recommendations. Not only may this include the use of additional vaccines to avoid complications caused by vaccine-preventable diseases [1], but also the deliberate omission of live vaccines, as immunocompromised individuals may be harmed by exposure to live – albeit attenuated – pathogens [9–12]. Even though immunocompromised individuals in particular require adequate indication-based vaccinations, immunization rates in this group are lower than in the general population [6, 13], [14].

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Primary (innate) immunodeficiency

Infections are an important cause of morbidity and mortality in patients with primary immunodeficiency. Depending on the underlying condition, the ability to develop a sufficiently protective immune response may be significantly impaired [7]. Moreover, it is well known that exposure to live attenuated vaccines is associated with a significant risk for patients with severe immunodeficiency [9–12]. Thus, live vaccines are contraindicated in the majority of but not all patients with innate immunodeficiency. Individual vaccination counseling requires detailed knowledge about the patient's underlying immunodeficiency. A comprehensive review of the various immunodeficiencies would be beyond the scope of this article, even though

Live attenuated vaccines are contraindicated in many patients with severe innate immunodeficiency.

these disorders may present with cutaneous manifestations and may therefore be of interest to the practicing dermatologist. The reader is referred to the detailed recommendations for use of vaccines in patients with primary immunodeficiency developed in 2018 by an expert group from various medical societies as well as RKI and STIKO [7] and, of course, to current STIKO recommendations [1].

Chronic diseases associated with an increased risk of infections

There is a number of acquired, chronic diseases that are – irrespective of the type of immunomodulatory therapy required to treat them – associated with an increased risk of vaccine preventable infections or subsequent complications thereof (Table 1). In keeping with international guidelines, STIKO has therefore issued special immunization recommendations for individuals thus affected [1, 14].

Patients with *rheumatological diseases* are frequently treated by multiple different specialists. In patients with connective tissue disease or vasculitis predominantly characterized by cutaneous manifestations, dermatologists are often the primary coordinators of patient management. Depending on the individual disease and immune status, patients are recommended to undergo immunization against pneumococci and influenza, as well as herpes zoster (for individuals ≥ 50 years of age) [1, 14]. *Inflammatory bowel disease* as well as *HIV infection* are also frequently associated or complicated by cutaneous manifestations. The spectrum of non-routine vaccines recommended for HIV-positive patients is wider, especially if there are additional risk factors such as homosexual contacts, which constitute an indication for hepatitis A immunization [7]. While *chronic skin diseases,* such as atopic dermatitis, Darier's disease or cutaneous T-cell lymphoma, are associated with an increased incidence and severity of cutaneous infections, these are usually not vaccine preventable. STIKO recommends that adults with severe atopic dermatitis who have not previously had chickenpox be immunized with the live varicella vaccine [1]. There are as yet no STIKO recommendations with regard to the inactivated herpes zoster subunit vaccine in dermatological patients, even though a number of chronic skin conditions such as atopic dermatitis, psoriasis [2] and bullous autoimmune dermatoses are associated with a risk of severe herpes zoster infections [15]. Individuals with advanced *malignancies* are also considered to be immunocompromised. The recommendations for this patient group include annual flu shots [16, 17] as well as additional immunization against pneumococci and, if necessary, meningococci [8]. Detailed information on non-routine vaccines in patients with *other, predominantly internal medicine-related conditions* can be found in the current STIKO recommendations [1].

Individuals with underlying rheumatological diseases are recommended to undergo immunization against pneumococci and influenza, as well as herpes zoster (for patients ≥ 50 of age).

Many chronic skin diseases are associated with an increased incidence and severity of cutaneous infections.

Immunomodulatory treatment

If possible, a patient's vaccination status should be updated prior to initiating immunosuppressive therapy – this includes both standard and non-routine vaccinations recommended for immunocompromised patients [4]. However, as this goal is frequently unrealistic, e.g., because an active autoimmune disease requires rapid initiation of immunosuppressive treatment, it is essential to observe vaccine-specific instructions and contraindications. Table 2 (modified after [4]) shows a – by no means exhaustive – list of systemic treatments frequently prescribed by dermatologists. Prior to any immunization, it is imperative to consider any additional individual risk factors such as comorbidities and medications. *Combined treatment*

Table 1 Chronic conditions associated with an increased risk of vaccine-preventable infections.

Conditions	Remarks
Rheumatological diseases (e.g., arthritis, connective tissue disease, systemic vasculitis)	For the *majority* of patients with rheumatological diseases, EULAR recommends the same standard immunizations as for the general population, as well as non-routine immunization against influenza and pneumococci [14]. STIKO recommendations specifically include patients with rheumatoid arthritis and systemic lupus erythematosus (SLE) [1]. In these patients, the inactivated herpes zoster subunit vaccine is recommended for individuals ≥ 50 years, in addition to the aforementioned influenza and pneumococcal vaccination. Women with SLE have an increased risk of cervical dysplasia/cervical cancer and are therefore advised to undergo HPV vaccination [27], though there is currently no corresponding STIKO recommendation.
Inflammatory bowel disease (Crohn's disease, ulcerative colitis)	Inflammatory bowel disease does not cause immunodeficiency per se; any increased susceptibility to infection is attributed to protein deficiency, which is often associated with this type of disease, as well as to immunosuppressive treatment usually required to treat these patients [4, 35].
HIV infection	It is recommended that HIV patients be vaccinated against hepatitis B, herpes zoster, influenza, meningococci, and pneumococci; in case of additional risk factors, this also includes hepatitis A [7]. HPV immunization may likewise be indicated (case-by-case decision). The response to vaccination depends on disease stage/the number of $CD4^+$ T lymphocytes. Inactivated vaccines are not associated with any risk. Live vaccines are contraindicated in patients with a $CD4^+$ T-lymphocyte count < 200/µL [7].
Malignancies (e.g., melanoma, Merkel cell carcinoma, squamous cell carcinoma)	National guidelines for cutaneous malignancies do not include any recommendations for specific vaccinations in patients with advanced disease and/or on systemic anticancer treatment. Annual flu shots are recommended for cancer patients [16, 17]. STIKO recommends additional vaccinations against pneumococci (serial administration of PCV13 and PPSV23) [1] as well as meningococci (serogroups B and ACWY [8]. Patients with persistently compromised immune function after completed anticancer treatment may benefit from early booster shots of standard vaccines ('repeat vaccinations') [8].
Inflammatory skin diseases (e.g., atopic dermatitis, psoriasis, bullous autoimmune dermatoses)	Patients with severe atopic dermatitis have an increased risk of complications from chickenpox [36]. Various skin diseases such as atopic dermatitis, psoriasis [2] and bullous autoimmune dermatoses are a predisposing factor for severe herpes zoster [15]. STIKO recommends that adults with severe atopic dermatitis and without a history of chickenpox undergo immunization against varicella [1]. While there are currently no STIKO recommendations regarding the inactivated zoster vaccine for patients with chronic skin diseases, the choice of immunomodulatory treatment may determine whether the vaccine should be used.
Others (e.g., asplenia, chronic pulmonary disease, diabetes mellitus, cardiovascular disease, multiple sclerosis, chronic renal disease, patients who are status post organ or stem cell transplantation)	STIKO recommendations for specific vaccines can be found in [1] as well as in the respective review articles [8].

Only under certain conditions may *live vaccines* be administered during

with more than one immunosuppressant – e.g., corticosteroids with a steroid-sparing DMARD – will in all likelihood lead to enhanced immunosuppression. Only under certain conditions should *live vaccines* be administered during immunosuppressive therapy. Current recommendations issued by the European League Against Rheumatism (EULAR) advocate the administration of *booster shots* of

Table 2 Vaccine-specific instructions of use and contraindications in dermatological patients on immunomodulatory therapy (as of May 2020).

Agent	Specific instructions regarding vaccinations
Apremilast	*Live vaccines:* The prescribing information does not contain any warnings regarding live vaccines. Experts agree that certain MMR vaccines, respectively varicella vaccines that is Priorix®, Priorix® Tetra and Varilrix® may be considered. On principle, however, it is recommended that an interval of at least four weeks be observed between a live vaccine and treatment initiation. During treatment, live vaccines should only be administered according to individual risk-benefit assessment [4]. *Inactivated vaccines:* Ideally, aimmunizations should be completed two or even better four weeks prior to treatment initiation; however, inactivated vaccines may be administered at any time during treatment with no increase in risk. *Additional remarks:* Live vaccines were explicitly permitted in the pivotal ESTEEM-1 trial [37].
Azathioprine	*Live vaccines:* The prescribing information of products containing azathioprine excludes the administration of live vaccines during treatment, irrespective of the dose. Their use is therefore not recommended in Germany (expert consensus [4]). By contrast, the EULAR immunization recommendations define a low-dose range (< 3 mg/kg/day) considered to result in 'mild' immunosuppression, which may permit administration especially of booster shots against measles [14]. Immunization with live vaccines should be concluded at least four weeks prior to treatment initiation and an interval of three months after the end of treatment should be observed. *Inactivated vaccines:* Ideally, vaccination should be concluded two or even better four weeks prior to treatment initiation; however, inactivated vaccines may be administered at any time during treatment with no increase in risk. *Additional remarks:* There have been reports of reduced immune responses to influenza, pneumococcal and tetanus vaccines in patients treated with azathioprine; however, the majority of patients did achieve sufficiently high (protective) antibody levels [38, 39]. Immunogenicity of the hepatitis B vaccine was also reduced in patients treated with azathioprine [40].
BRAF-Inhibitors (dabrafenib, vemurafenib, encorafenib)	The product-specific prescribing information does not contain any recommendations regarding vaccinations. In vitro data indicates a direct antiviral effect of vemurafenib against the influenza A virus [41].
Cyclosporine	*Live vaccines:* During low-dose therapy (≤ 2.5 mg/kg /day), administration of certain MMR or varicella vaccines that is Priorix®, Priorix® Tetra and Varilrix® may be considered, as the respective prescribing informations only list severe acquired immunodeficiency as a contraindication. The prescribing information for cyclosporine excludes the administration of live vaccines during treatment, irrespective of the dose. Thus, any use of the aforementioned vaccines constitutes off-label use. In cases of higher doses (> 2.5 mg/kg/day), live vaccines are always contraindicated. Vaccinations must be concluded at least four weeks prior to treatment initiation and an interval of three months must be observed after treatment has been discontinued. *Inactivated vaccines:* Ideally, vaccination should be concluded two or even better four weeks prior to treatment initiation; however, inactivated vaccines may be administered at any time during treatment with no increase in risk. *Additional remarks:* In patients receiving low-dose cyclosporine monotherapy, immunogenicity of vaccines does not appear to be substantially compromised [42].
Cyclophosphamide	*Live vaccines:* Live vaccines are contraindicated in patients treated with cyclophosphamide. These vaccines should be concluded at least four weeks prior to treatment initiation and an interval of three months must be observed after treatment has been discontinued [4]. *Inactivated vaccines:* Ideally, vaccination should be concluded two or even better four weeks prior to treatment initiation; however, inactivated vaccines may be administered at any time during treatment with no increase in risk.

Continued

Table 2 Continued.

Agent	Specific instructions regarding vaccinations
Dapsone	The product-specific prescribing information does not contain any references to vaccinations. Monotherapy does not appear to result in relevant immunosuppression.
Dimethyl fumarate	*Live vaccines:* The prescribing information for Skilarence® recommends that live vaccines during ongoing treatment only be administered after individual risk-benefit assessment, noting that there are insufficient data with respect to potential risks. These warnings are not contained in the prescribing information for Fumaderm®. According to expert consensus, certain MMR as well as varicella vaccines that is Priorix®, Priorix® Tetra and Varilrix® may be considered after individual risk-benefit assessment [4]. In particular, live vaccines should be avoided if relevant lymphocytopenia occurs during treatment with dimethyl fumarate (expert consensus [4]). *Inactivated vaccines:* Ideally, vaccination should be concluded two or even better four weeks prior to treatment initiation; however, inactivated vaccines may be administered at any time during treatment with no increase in risk. *Additional remarks:* Adequate immune responses after vaccination against tetanus/diphtheria, pneumococci (PPSV23) and meningococcal serogroup ACWY have been observed in patients treated with dimethyl fumarate [43].
Dupilumab	*Live vaccines:* According to the product-specific prescribing information, live vaccines are contraindicated during treatment with dupilumab, as there is insufficient data regarding efficacy and safety. Booster shots of necessary live vaccines are recommended prior to initiating dupilumab therapy. There is no mention of intervals to be observed. *Inactivated vaccines:* Administration of inactivated vaccines during ongoing treatment with dupilumab is specifically recommended in the prescribing information. *Additional remarks:* Decreased immunogenicity of tetanus/diphtheria or meningococcal ACWY vaccines during ongoing dupilumab treatment was not observed in a placebo-controlled trial [44].
Corticosteroids	*Live vaccines:* During low-dose therapy (< 10 mg prednisolone equivalent/day or < 0.2 mg/kg/day) or short-term treatment (< 2 weeks), all MMR and varicella vaccines approved in Germany may be administered. In case of higher doses (≥ 10 mg prednisolone equivalent/day) or intravenous pulse therapy, live vaccines are contraindicated. Vaccinations should be concluded two or even better four weeks prior to treatment initiation; the earliest date for subsequent vaccination is two months after treatment discontinuation. *Inactivated vaccines:* Ideally, vaccination should be concluded two or even better four weeks prior to treatment initiation; however, inactivated vaccines may be administered at any time during treatment with no increase in risk.
Hydroxychloroquine	*Live vaccines:* Administration of live vaccines is not limited during hydroxychloroquine monotherapy. The prescribing information does not contain any warnings or recommendations on intervals to be observed. *Inactivated vaccines:* Ideally, vaccination should be concluded two or even better four weeks prior to treatment initiation; however, inactivated vaccines may be administered at any time during treatment with no increase in risk. *Additional remarks:* Decreased immunogenicity of influenza [45], tetanus/diphtheria, measles, poliomyelitis, typhus or tuberculosis vaccines has not been observed [4].

Continued

Table 2 Continued.

Agent	Specific instructions regarding vaccinations
IL-17 antagonists (brodalumab, ixekizumab, secukinumab)	*Live vaccines:* Live vaccines are contraindicated during treatment with IL-17 antagonists according to the product-specific prescribing information; there is no mention of intervals to be observed between live vaccines and treatment initiation. With respect to secukinumab, however, it is recommended to conclude vaccination with live vaccines at least four weeks prior to treatment initiation and to observe an interval of at least two months after treatment discontinuation (expert consensus [4]). *Inactivated vaccines:* Ideally, vaccination should be concluded two or even better four weeks prior to treatment initiation; however, inactivated vaccines may be administered at any time during treatment with no increase in risk. If possible, necessary vaccinations during ongoing treatment should be performed in the middle of the treatment interval (expert consensus on secukinumab [4]). *Additional remarks:* Immune responses following immunization against influenza and meningococcal serogroup C were not reduced two weeks after administration of a single dose of secukinumab [46]. Immunogenicity of tetanus and pneumococcal (PPSV23) vaccines was observed to be the same in patients treated with ixekizumab as in the control group [47].
IL-23 antagonists (guselkumab, risankizumab, tildrakizumab)	*Live vaccines:* Live vaccines are contraindicated during treatment with IL-23 antagonists. Product-specific minimum intervals are indicated in the prescribing information. After administration of a live vaccine, intervals of two weeks (guselkumab), respectively four weeks (risankizumab, tildrakizumab) are recommended prior to initiating treatment with the respective IL-23 antagonist. After discontinuation or interruption of treatment, intervals of 12 weeks (guselkumab), 21 weeks (risankizumab) and 17 weeks (tildrakizumab) must be observed before administration of a live vaccine. *Inactivated vaccines:* It is recommended to update the vaccination status prior to treatment initiation. The prescribing information mentions a lack of data regarding the immunogenicity of vaccines during treatment with IL-23 antagonists; however, use of inactivated vaccines is not explicitly prohibited.
Immune checkpoint inhibitors (anti-CTLA-4 antibody ipilimumab, anti-PD-1 antibodies nivolumab/ pembrolizumab, anti-PD-L1 antibody avelumab)	Based on current expert consensus, it is recommended to administer necessary vaccinations with *inactivated vaccines* during treatment with checkpoint inhibitors, whereas *live vaccines* should be avoided [8]. Immunogenicity of the influenza vaccine is not reduced during treatment with immune checkpoint inhibitors [48]. While there has been a debate about the potential increase in incidence or severity of immune-related adverse events [49], there is currently insufficient data for a conclusive assessment [8, 50].
Immunoglobulins	Neutralizing antibodies contained in immunoglobulin preparations compromise the response to immunization with attenuated *live vaccines* by inhibiting virus replication [6]. The product-specific prescribing information therefore recommends to avoid the use of live vaccines for three months (MMR-V: 8 months [8]) after administration of immunoglobulins. There is no mention of any intervals to be observed regarding *inactivated vaccines*; it is safe to assume that immunogenicity is sufficient [8].
MEK inhibitors (trametinib, cobimetinib, binimetinib)	The product-specific prescribing information does not contain any references to vaccines. In vitro data indicates that trametinib may exhibit direct antiviral activity against the influenza A virus [51].

Continued

Table 2 Continued.

Agent	Specific instructions regarding vaccinations
Methotrexate (MTX)	*Live vaccines:* During low-dose therapy (≤ 20 mg/week or ≤ 0.4 mg/kg/week), administration of certain MMR or varicella vaccines that is Priorix®, Priorix® Tetra and Varilrix® may be considered, as the respective prescribing informations only list severe acquired immunodeficiency as a contraindication [4]). The prescribing information for MTX, however, excludes the use of live vaccines during treatment, irrespective of the dose. Thus, any use of the aforementioned vaccines constitutes off-label use. During high-dose treatment (> 20 mg/week), live vaccines are always contraindicated. Vaccination should be concluded at least four weeks prior to treatment initiation, and an interval of at least two months after discontinuation must be observed. *Inactivated vaccines:* Ideally, vaccination should be concluded two or even better four weeks prior to treatment initiation; however, inactivated vaccines may be administered at any time during treatment with no increase in risk. *Additional remarks:* In general, studies do not indicate reduced immunogenicity of vaccines during MTX treatment [18, 19, 52, 53]. Immune response to pneumococcal vaccines (with PPSV23) however is thought to be reduced [53]. Immunogenicity of the influenza vaccine may be improved by interruption of MTX treatment [54].
Mycophenolate mofetil (MMF)/ mycophenolic acid (MA)	*Live vaccines:* During low-dose treatment (≤ 2 g/day), certain MMR and varicella vaccines that is Priorix®, Priorix® Tetra and Varilrix® may be considered, as the respective prescribing informations only list severe acquired immunodeficiency as a contraindication. The prescribing information for MMF/MA, however, exclude the use of live vaccines during treatment, irrespective of the dose. Thus, any use of the aforementioned vaccines constitutes off-label use. During high-dose therapy (> 2 g/day), live vaccines are always contraindicated. Vaccination should be concluded at least four weeks prior to treatment initiation, and an interval of at least two months after discontinuation must be observed. *Inactivated vaccines:* Ideally, vaccination should be concluded two or even better four weeks prior to treatment initiation; however, inactivated vaccines may be administered at any time during treatment with no increase in risk. *Additional remarks:* During ongoing treatment with mycophenolate mofetil, reduced immunogenicity of influenza vaccines [45] and HPV vaccines [55] was observed. Influenza vaccination according to national guidelines is explicitly recommended in the prescribing information for MMF/MA.
Rituximab	*Live vaccines:* Live vaccines are contraindicated during rituximab therapy. Any such vaccinations should be concluded at least four weeks prior to treatment initiation, and an interval of at least twelve months, as well as a normal B cell count, must be observed after treatment discontinuation. *Inactivated vaccines:* Necessary vaccinations should be concluded at least four weeks prior to treatment initiation. While an interval of only two weeks is acceptable if early treatment initiation is required, this constitutes off-label use. If vaccines are administered directly before or within six months after rituximab, substantial reduction in the humoral immune response must be expected. Even though there is no impact on safety, inactivated vaccines should also be avoided during this period. Sole exception is vaccination against the seasonal flu, which is also recommended within the six-month interval after rituximab treatment (expert consensus [4]). *Additional remarks:* Immune response to influenza vaccination administered within six months after rituximab therapy is markedly reduced but detectable [56]. Immune response to pneumococcal vaccination (PPSV23) was reduced when the vaccine was administered six months after combination treatment with rituximab and MTX, but immune response to tetanus vaccination was normal [57].

Continued

Table 2 Continued.

Agent	Specific instructions regarding vaccinations
TNFα inhibitors (adalimumab, certolizumab, etanercept, infliximab)	*Live vaccines:* Live vaccines are contraindicated during treatment with TNFα inhibitors. Any such vaccinations should be concluded at least four weeks prior to treatment initiation, and an interval of two months (infliximab: three months) must be observed after treatment discontinuation. *Inactivated vaccines:* Ideally, vaccination should be concluded two or even better four weeks prior to treatment initiation; however, inactivated vaccines may be administered at any time during treatment with no increase in risk. If possible, necessary vaccinations during ongoing treatment should be performed in the middle of the treatment interval (expert consensus [4]). *Additional remarks:* Immune response to influenza [58], pneumococcal (PPSV23) [58] and hepatitis B [59] vaccines was not reduced during adalimumab monotherapy, but immune response to pneumococcal (PPSV23) and influenza vaccines was somewhat reduced during combination treatment with adalimumab and other immunosuppressants [58]. Immune response to influenza and pneumococcal (PPSV23) vaccines was not reduced after initiation of certolizumab monotherapy, but combination with MTX resulted in a reduced response [60]. During treatment with etanercept, a somewhat reduced but still adequate immune response was observed after pneumococcal (PPSV23 [61, 62] or PCV13 [63]) and influenza A vaccination [64]; immune response to influenza B vaccination was reduced even further. A small case control study suggests that MMR vaccination in children is effective and safe when administered during etanercept treatment [19]. Reduced immune responses to influenza [65, 66], pneumococcal (PPSV23) [67] and hepatitis B [40, 59] vaccines were observed when administered during infliximab treatment.
Ustekinumab	*Live vaccines:* Live vaccines are contraindicated during treatment with ustekinumab. According to the product-specific prescribing information, any such vaccinations should be concluded at least two weeks prior to treatment initiation, and an interval of 15 weeks should be observed after discontinuation or interruption of treatment. *Inactivated vaccines:* Ideally, vaccination should be concluded two or even better four weeks prior to treatment initiation; however, inactivated vaccines may be administered at any time during treatment with no increase in risk. If possible, necessary vaccinations during ongoing treatment should be performed in the middle of the treatment interval (expert consensus [4]). *Additional remarks:* Immune response to pneumococcal (PPSV23) and tetanus vaccines was not reduced when administered during treatment with ustekinumab [68].

Inactivated vaccines are not associated with an increased risk of adverse effects in immunocompromised patients; however, the response to vaccines may be impaired.

The humoral immune response is largely suppressed in patients treated with the anti-CD20 antibody rituximab.

the live-attenuated measles virus during low-dose immunosuppressive therapy, as they are supposed to be associated with a lower risk than the initial vaccine dose [14, 18, 19]. Recommendations on live vaccines, taking into account the various immunosuppressive agents available and their dosing, are discussed in detail in the above-mentioned review article [4] and are summarized in Table 2. *Inactivated vaccines* may be administered at any time without an increased risk of adverse effects [4]. While the response to vaccines may be impaired during immunosuppressive therapy, patients will usually develop sufficiently high antibody levels to be protected. An exception in this context is the administration of B cell and T cell-depleting antibodies, as they lead to significant suppression of the humoral or cellular immune response, thus rendering effective immunization impossible. One important such example in the field of dermatology is the anti-CD20 antibody *rituximab*, which was approved for the treatment of pemphigus vulgaris in 2019 [20, 21]. The anti-CD20 antibody *ocrelizumab* and the anti-CD52 antibody *alemtuzumab* are approved for the treatment of multiple sclerosis and are, at present, not recommended for dermatological use.

Table 3 Recommendations of the German Standing Committee on Vaccination for immunocompetent and immunocompromised adults [1].

Infectious disease (vaccine)	STIKO vaccination recommendation for immunocompetent adults	Recommendation for immunocompromised patients
Diphtheria, tetanus (inactivated vaccine)	Everyone without or with incomplete primary three-dose immunization, and/or everyone who has not been vaccinated for the last ten years	According to standard recommendation
Tick-borne encephalitis (TBE) (inactivated vaccine)	No standard vaccine. Recommended for individuals exposed to ticks in certain risk areas	According to recommendation for immunocompetent individuals
Haemophilus influenzae type B (inactivated vaccine)	No standard vaccine for adults	Single dose for patients with anatomical or functional asplenia
Hepatitis A (inactivated vaccine)	No standard vaccine for adults. Vaccination is recommended for risk groups (e.g., men who have sex with men, IV drug users, residents of psychiatric institutions) as well as for anyone with occupational exposure	According to recommendation for immunocompetent individuals
Hepatitis B (inactivated vaccine)	No standard vaccine for adults. Recommended for individuals with occupational and non-occupational exposure, as well as for travelers to certain risk areas	Individuals at risk for severe hepatitis B infection (e.g., concomitant infection with HIV or hepatitis C); the indication for vaccination should be based on the actual exposure risk [22]
Herpes zoster (inactivated vaccine)	Individuals ≥ 60 years of age	Individuals ≥ 50 years of age
Human Papillomavirus (inactivated vaccine)	No standard vaccine for adults	Consider for individuals with HIV infection or female patients with systemic lupus erythematosus
Influenza (inactivated vaccine)	Individuals ≥ 60 years, pregnant women from the 2nd trimester onwards, medical staff, household contacts of immunocompromised patients, individuals who have contact with wild birds, impending epidemic	Individuals ≥ 6 months of age
Measles (live vaccine)	Adults born after 1970 with unknown vaccination status as well those who have never been vaccinated or have received only one dose, especially in cases of occupational exposure [28]	According to standard recommendation *prior to* immunosuppressive therapy; may be contraindicated *during* immunosuppressive therapy depending on agent and dose
Meningococci (inactivated vaccines against serogroups ACWY and serogroup B)	No standard vaccine for adults; vaccination is recommended for laboratory staff exposed to meningococci (ACWY+B), during outbreaks (according to current recommendations), for travelers to certain risk areas (ACWY)	Individuals with – Complement/properdin deficiency – Eculizumab therapy – Hypogammaglobulinemia – Anatomical/functional asplenia(ACWY+B in all cases)
Mumps (live vaccine)	Adults born after 1970 with unknown or incomplete vaccination status, especially in cases of occupational exposure [28]	According to standard recommendation *prior to* immunosuppressive therapy; may be contraindicated *during* immunosuppressive therapy depending on agent and dose

Continued

Table 3 Continued.

Infectious disease (vaccine)	STIKO vaccination recommendation for immunocompetent adults	Recommendation for immunocompromised patients
Pertussis (inactivated vaccine)	Single booster vaccine for adults; medical staff, women of reproductive age and individuals who may have contact with neonates should be vaccinated at ten-year intervals	According to standard recommendation
Pneumococci (inactivated vaccines PPSV23 and PCV13)	Individuals ≥ 60 years (PPSV23); repeat vaccination after no less than six years according to individual circumstances	Sequential vaccination with PCV13, followed by PPSV23 after 6–12 (no less than 2) months; repeat vaccination with PPSV23 at six-year intervals; Individuals with chronic respiratory, metabolic, or neurological disorders not associated with immunosuppression are recommended to only receive the PPSV23 vaccine
Poliomyelitis (inactivated vaccine)	After completion of the primary immunization in childhood, a single booster dose during adolescence or adulthood	According to standard recommendation
Rubella (live vaccine)	Adults born after 1970 with unknown or incomplete vaccination status, especially women of reproductive age or in cases of occupational exposure [28]	According to standard recommendation *prior to* immunosuppressive therapy; may be contraindicated *during* immunosuppressive therapy depending on agent and dose
Varicella (live vaccine)	Vaccination is recommended for the following groups (if seronegative or no history of chickenpox in childhood): Women wanting to have children, severe atopic dermatitis, occupational exposure [28]	According to standard recommendation *prior to* immunosuppressive therapy; may be contraindicated *during* immunosuppressive therapy depending on agent and dose

Vaccine-specific recommendations for immunocompetent and immunocompromised adult individuals

Current vaccine-specific STIKO recommendations [1] for healthy and immunocompromised adult individuals are summarized in Table 3.

Diphtheria, tetanus

Adults should receive booster shots against tetanus and diphtheria every ten years, irrespective of their immune status.

This is a routine vaccine. Inactivated vaccines by various manufacturers are available. The immunization schedule recommends four doses within the first 14 months of life, usually as part of a combination vaccine against tetanus/diphtheria, pertussis, poliomyelitis, *Haemophilus influenzae* type B, and hepatitis B. Booster shots are recommended at the age of 5 or 6 and again between the ages of 9 and 16; for adults, every ten years. It is recommended that adults without any vaccination record receive two doses at an interval of 4–8 weeks, and a third shot after 6–12 months. There are no special recommendations for immunocompromised patients.

Tick-borne encephalitis (TBE)

The TBE vaccine is a non-standard vaccine for individuals exposed to ticks in certain risk areas.

This is a non-standard immunization for individuals exposed to ticks in certain risk areas. Following completion of the primary three-dose immunization, booster doses are recommended every five years, respectively every three years for individuals ≥ 50 years. Inactivated vaccines by various manufacturers are available. There are no special recommendations for immunocompromised patients.

Haemophilus influenzae type B

Severely immunocompromised adults with anatomical or functional asplenia are recommended to undergo immunization against *Haemophilus influenzae* type B (single dose).

Three, respectively four, doses, usually as part of a combination vaccine, are recommended for children within the first 14 months of life. There is no recommendation for immunization for immunocompetent adults. Severely immunocompromised adults, particularly those with anatomical or functional asplenia, should receive a single dose. Various monovalent vaccines may be obtained through international pharmacies.

Hepatitis A

This is a non-standard immunization. It is recommended for immunocompetent individuals who are at an increased individual risk (e.g., men who have sex with men, iv drug users, residents of psychiatric institutions) or for individuals with occupational exposure (e.g., health care personnel, employees at childcare centers or sewage plants). There are no special recommendations for immunocompromised patients.

Hepatitis B

Hepatitis B immunization is indicated for immunocompromised individuals with an increased risk of severe disease.

Antibody monitoring is required following hepatitis B immunization.

This is a standard vaccine recommended for everyone. Children should receive three, respectively four, doses within the first 14 months of life. For immunocompetent adults, the vaccine is recommended in cases of occupational and non-occupational exposure, and for travelers to certain high-risk areas. In addition, immunization is recommended for immunocompromised individuals with an increased risk of severe disease (e.g., concomitant infection with HIV or HCV). For immunocompromised individuals too, the indication for hepatitis B immunization is based on the actual exposure risk [22]. Serological tests prior to vaccination are not required, as the vaccine will be ineffective but safe for individuals with existing hepatitis B infection [1]. Antibody monitoring is recommended 4–8 weeks after the third dose to assess the effectiveness of the immunization [1]. The response to immunization is considered adequate if the anti-HBs titer is ≥ 100 IU/L. Additional doses and serological tests are recommended for *low-responders* (individuals with an insufficient increase in antibody levels; in *non-responders* (individuals who develop no antibodies at all), chronic infection should be ruled out. Additional antibody monitoring is required in individuals with humoral immunodeficiency (annually) and in those with a high risk of exposure (every ten years). Booster shots are recommended if the antibody titer drops below 100 IU/L.

Herpes zoster

STIKO recommends that immunocompromised adults ≥ 50 years receive the adjuvanted inactivated herpes zoster subunit vaccine (approved in 2018).

Current STIKO recommendations advocate immunization with the adjuvanted inactivated herpes zoster subunit vaccine (approved on 2018) for all immunocompetent adults ≥ 60 years and for all immunocompromised individuals ≥ 50 years [5].

This recommendation presupposes that the majority of people in this age group have previously had chickenpox; serological tests prior to vaccination are not required [1]. The goal is to boost the T cell-mediated immune response and thus to prevent reactivation of latent *varicella zoster* virus in dorsal root ganglia. Two doses of the vaccine are administered intramuscularly at an interval of 2–6 months. While there is limited evidence for the effectiveness in individuals with a prior history of herpes zoster, the data available indicates the vaccine to be sufficiently immunogenic and also safe [5, 23]. Therefore, the aforementioned recommendations also apply to individuals with a prior history of herpes zoster [24]. At the time of vaccination, patients should not exhibit any signs of herpes zoster. An interval of twelve months between the actual disease and vaccination appears appropriate.

The recommendation for immunization with the inactivated herpes zoster vaccine also applies to individuals with a prior history of herpes zoster.

Human papillomavirus (HPV)

This is a standard vaccine recommended to all children and adolescents aged 9–14. Two doses are given at an interval of at least five months; a third dose is required if the vaccination is started at a later age. The vaccine is not recommended for immunocompetent adults. HIV-positive adults should be vaccinated according to expert consensus [7], considering the increased prevalence of HPV in men having sex with men [25] and the increased risk of high-grade anal dysplasia and anal carcinoma in patients with HIV [26]. Female patients with systemic lupus erythematosus (SLE) are also advised to receive HPV vaccination, as this patient group has a significantly increased risk of genital HPV infection, cervical dysplasia and cervical carcinoma [27]. Given that there is currently no explicit STIKO recommendation for adult patients, it is recommended to inquire prior to vaccination whether the vaccine will be covered by the competent statutory health insurance fund.

HPV vaccination in adult women with systemic lupus erythematosus reduces the risk of developing cervical carcinoma.

Influenza

This is a standard vaccine recommended for immunocompetent adults ≥ 60 years. In addition, STIKO also recommends its use for immunocompromised individuals ≥ 6 months, for those with occupational and non-occupational exposure, residents of nursing homes, pregnant women from the 2nd trimester onwards, and for those who are in close contact with high-risk individuals (e.g., in the same household). The vaccine is administered annually in the fall, using a quadrivalent inactivated vaccine containing the antigen combination recommended by the World Health Organization (WHO) for that particular year.

Annual flu shots are recommended for immunocompromised individuals ≥ 6 months.

Measles

This is a standard vaccine. Immunocompetent children receive two doses, starting at the age of eleven months (or nine months if admission to a communal facility is imminent). Since March1, 2020, the German government has mandated that all children be immunized against measles. Proof of complete immunization is therefore required before a child can be admitted to a communal facility (e.g., childcare center) or school. Live vaccines are available from various manufacturers, always in combination with live vaccines against mumps and rubella (MMR) and, if required, also against varicella (MMR-V). Adults born after 1970 with incomplete or insufficiently documented vaccination records are advised to undergo catch-up vaccination against MMR (two documented doses are recommended) [28]). Vaccination is explicitly required in cases of occupational exposure (including medical staff, personnel at technical colleges, vocational schools or universities, individuals

Since March1, 2020, the German government has mandated that all children be immunized against measles.

Adults born after 1970 with incomplete immunization are advised to undergo catch-up vaccination with a combined MMR vaccine.

working in communal facilities including housing facilities for asylum seekers, refugees or late repatriates [28]). This particular recommendation for immunization does not apply to individuals born before 1970, as it is safe to assume that they have a history of prior exposure [29]. While there are no special recommendations for immunocompromised patients, certain limitations/contraindications regarding live vaccines do have to be observed.

Meningococci

Various manufacturers offer inactivated vaccines, either against meningococcal serogroup C (single-dose standard vaccine at age 11–23 months) or against meningococcal serogroups ACWY and B. Vaccination is recommended for immunocompetent adults at risk of exposure (laboratory staff; ACWY+B), during epidemics (according to current recommendations) as well as for travelers to certain high-risk countries (ACWY). The vaccine is also recommended as non-standard vaccine for severely immunocompromised patients (asplenia, complement/properdin deficiency, hypogammaglobulinemia, treatment with the monoclonal antibody eculizumab directed against the N-terminal complement component C5 [30]). While routine vaccination against meningococci is currently not required for dermatological patients, it may become necessary in the future due to the development of novel drugs, e.g., use of complement inhibitors in the treatment of bullous pemphigoid [31].

Vaccination against meningococcal serogroups ACWY and B is required in cases of severe immunodeficiency, e.g., patents with asplenia or complement/properdin deficiency.

Mumps

There is no monovalent mumps vaccine available; however, there are various live combination vaccines against measles/mumps/rubella (MMR) and, if required, also against varicella (MMR-V). Immunocompetent children receive two doses, starting at the age of eleven months. Recommendations for catch-up vaccination in adults born after 1970 are the same as for measles (see above). While there are no special recommendations for immunocompromised patients, certain limitations/contraindications regarding live vaccines do have to be observed.

Pertussis

This is a standard vaccine administered in childhood and adolescence. Given that there is no monovalent pertussis vaccine, immunization is performed in combination with the tetanus and diphtheria vaccine (see above). Adults are recommended to undergo one-time immunization with a TDaP vaccine next time they are up for a tetanus/diphtheria shot. Individuals with occupational exposure, women of reproductive age, and persons in close contact with neonates are advised to receive booster shots every ten years. There are no special recommendations for immunocompromised patients.

Adults are recommended to undergo one-time immunization with a TDaP vaccine next time they are up for a tetanus/diphtheria shot.

Pneumococci

Term infants receive three doses of the 13-valent conjugate vaccine PCV13 within the first 14 months of life; preterm infants get one additional dose starting at the age of two months. Immunocompetent individuals ≥ 60 years are supposed to receive at least one dose of the 23-valent polysaccharide vaccine PPSV23. Booster shots at intervals of at least six years may be considered based on individual circumstances. Immunocompromised children, adolescents and adults are recommended to receive sequential vaccination, first with the PCV13 vaccine and af-

In immunocompromised individuals, use of the 13-valent conjugate vaccine PCV13 in series with the 23-valent polysaccharide vaccine PPSV23 is recommended.

Supply shortages for pneumococcal vaccines have occurred due to the COVID-19 pandemic.

ter 6–12 months (at least 2 months) with the PPSV23 vaccine; the latter should not be administered to anyone ≤ 2 years. Booster shots with the PPSV23 vaccine should be administered every six years in immunocompromised patients. Adults with chronic respiratory, metabolic and neurological diseases not associated with immunosuppression are advised to receive PPSV23 immunization only. Due to the COVID-19 pandemic, there have been supply shortages and some of the aforementioned recommendations have had to be modified accordingly (use of PCV13; or if not available, use of a 10-valent conjugate vaccine only for primary immunization, standard vaccination with PPSV23 only in individuals ≥ 70 years).

Poliomyelitis

This is a standard vaccine that should be administered three to four times between the 2nd and the 14th month of life, usually in the form of a combination vaccine. Today, the only poliomyelitis vaccine used is the inactivated (injectable) IPV vaccine. A single booster shot is required during adolescence or adulthood; incomplete primary vaccination must be completed. Individuals at increased risk of exposure (residents of communal facilities, medical staff in close contact with patients, laboratory staff at risk of infection) should receive booster shots every ten years.

Rubella (German measles)

There is no monovalent rubella vaccine available; however, there are various live combination vaccines against measles/mumps/rubella (MMR) and, if required, also against varicella (MMR-V). Immunocompetent children ≥ 11 months receive two doses. Recommendations for catch-up vaccination of adults born after 1970 are the same as for measles (see section on 'measles'). It is explicitly required that women of reproductive age be vaccinated against rubella. While there are no special recommendations for immunocompromised patients, certain limitations/contraindications regarding live vaccines do have to be observed.

Varicella (chickenpox)

This is a standard vaccine. It is recommended that immunocompetent children ≥ 11 months receive two doses. While this may be done using a combination vaccine (measles/mumps/rubella/varicella; MMR-V), separate immunization with a monovalent live varicella vaccine is thought to be better tolerated, especially when given for the first time [32]. Given that a reported history of chickenpox is considered to be very reliable [33], serological tests or subsequent immunization are not required [1]. Indications for varicella vaccination in adults without a history of chickenpox include: seronegative women wanting to have children; patients before initiation of immunosuppressive therapy; patients with severe atopic dermatitis, as well as individuals in close contact with the latter two groups. For individuals with occupational exposure, recommendations are the same as for measles. In immunocompromised patients, the usual limitations/contraindications for live vaccines must be observed.

A reported history of chickenpox is considered to be very reliable.

Patients with severe atopic dermatitis and no prior history of chickenpox should be vaccinated against varicella.

Implementation of immunization recommendations in dermatological patient care

Figure 1 shows a flow chart for managing vaccinations in patients who are either receiving immunosuppressive therapy or who may require such treatment in the

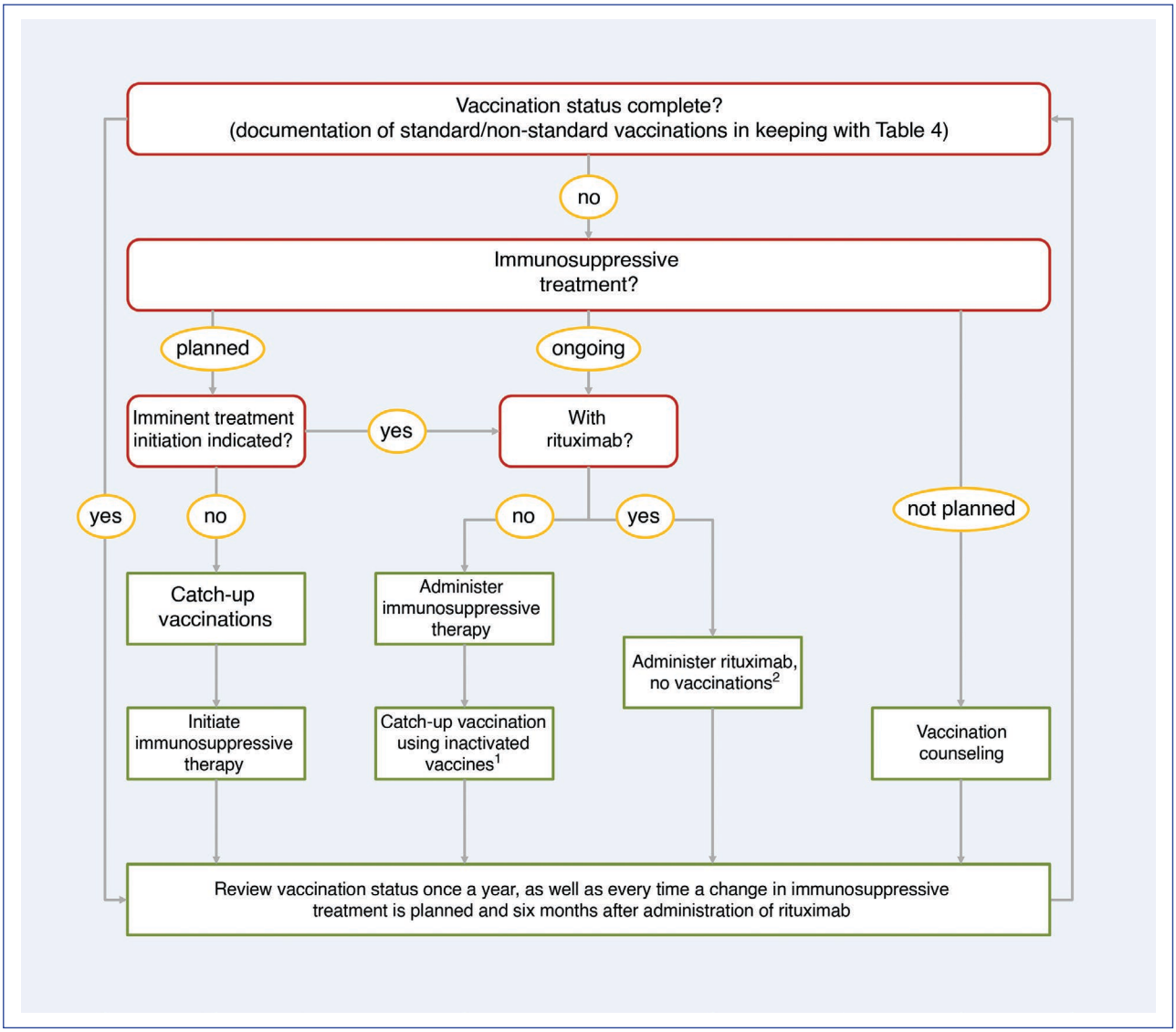

Figure 1 Algorithm for the management of vaccinations depending on the type of immunosuppressive therapy used. [1]Live-attenuated MMR and varicella vaccinations may be administered during low-dose corticosteroid therapy (< 10 mg of prednisolone equivalent per day). Following individual risk/benefit assessment, administration of certain vaccines (Priorix®, Priorix® Tetra, and Varilrix®) may be considered during treatment with apremilast, dimethyl fumarate, as well as on low-dose cyclosporine (≤ 2.5 mg/kg per day), methotrexate (≤ 0.4 mg/kg per week), or mycophenolate mofetil (≤ 2 g per day) therapy. [2]Annual influenza vaccination is also recommended within the first six months following rituximab therapy.

STIKO recommendations for standard vaccinations also apply to dermatological patients.

future. As a first step, the *individual vaccination status should be reviewed*, using available documentation or the vaccination certificate. Standardized text blocks or worksheets (as illustrated in Table 4) have proven useful for the *documentation in patient files*. All recommendations for *standard vaccinations* presented in the previous chapter and summarized in Table 3 also apply to dermatological patients. Following adequate counseling, these standard immunizations can usually be delegated to the patient's general practitioner, particularly if no immunosuppressive treatment is planned in the near future. If immunosuppressive therapy is intended or has already been initiated, the issue of *non-standard vaccines* needs to be addressed, such as the seasonal influenza vaccine, pneumococcal vaccination,

Table 4 Standardized documentation of vaccinations (worksheet).

Last name, first name: _____	**Diagnosis:** _____			**Date:** _____	
Date of birth: _____	**Medication/Dose:** _____			**Next review:** _____	
Vaccine-preventable disease	**Current vaccination status**			**Last vaccination (date)**	**Recommendation[1] (free text)**
	complete	**incomplete**	**not required**		
STANDARD VACCINES					
Diphtheria/Tetanus	O	O			
Pertussis	O	O			
Polio	O	O			
MMR (live vaccine)[2]	O	O	O		
VACCINES INDICATED FOR IMMUNOCOMPROMISED PATIENTS					
Pneumococci					
PCV13	O	O	O		
PPSV23	O	O	O		
Herpes zoster	O	O	O		
Influenza	O	O	O		
VACCINES INDICATED BASED ON INDIVIDUAL CIRCUMSTANCES					
Varicella (live vaccine)[3]	O	O	O		
Hepatitis B[4]	O	O	O		
Meningococci[5]					
Serogroups ACWY	O	O	O		
Serogroups B	O	O	O		
Haemophilus influenzae type B[6]	O	O	O		

[1]List any necessary vaccinations (non-standard vaccines, catch-up vaccinations, booster doses).
[2]Recommendation for individuals born after 1970. Observe any limitations for administration of live vaccines!
[3]Recommendation regarding varicella vaccination for the following (seronegative) groups: Women wanting to have children; patients *prior to* initiation of immunosuppressive treatment; individuals with severe atopic dermatitis; social contacts of the aforementioned groups. Observe any limitations for administration of live vaccines!
[4]Recommendation regarding hepatitis B vaccination in cases of occupational and non-occupational exposure and/or if there is a risk of severe infections.
[5]Recommendation regarding meningococcal vaccination in cases of asplenia, complement/properdin deficiency, hypogammaglobulinemia and/or individual exposure.
[6]Recommendation regarding *Haemophilus* influenzae type B vaccination for patients with anatomical or functional asplenia.

If immunosuppressive therapy is intended or has already been initiated, the issue of *non-standard vaccines* needs to be addressed, such as the seasonal influenza vaccine, pneumococcal vaccination, and the herpes zoster vaccine for individuals ≥ 50 years.

and the herpes zoster vaccine for individuals ≥ 50 years. The indication for other vaccines, e.g., against varicella, *Haemophilus influenzae* type B, hepatitis B, and meningococci, depends on the patient's comorbidities and individual exposure risk and should thus be reviewed on a case-by-case basis (Table 4). If immunosuppressive therapy is planned for the foreseeable future but is not required at the moment, the patient's vaccination status should be updated/completed prior to starting him/her on immunosuppressive agents. The interval recommended between vaccination and immunosuppression depends on the particular immunosuppressant to be

administered (Table 2). If immunosuppressive therapy is imminent or the patient is already taking an immunosuppressive agent, necessary vaccinations with inactivated vaccines should be completed but live vaccines should usually be avoided. An exception in this context is the urgently required administration of the B cell-depleting agent rituximab, e.g., for treating severe pemphigus vulgaris. With the exception of the annual flu shot (expert consensus [4]), inactivated vaccines should also only be administered no sooner than six months after rituximab has been discontinued (live vaccines: 12 months) in order to ensure sufficiently high antibody levels (protective immune response) (Table 2). As a consequence, controls of vaccination status and, if necessary, booster shots are recommended every six months during rituximab treatment, and once a year for all other patients [14] as well as always before switching treatments.

Controls of vaccination status and, if necessary, booster shots should be performed at least once a year in patients on immunosuppressive therapy.

Answers to frequently asked questions

How to manage patients with unknown vaccination status

Patients who can present neither a vaccination certificate nor any other medical documentation of prior immunizations are treated as if they have never been vaccinated at all. Consequently, they are required to undergo all vaccinations based on the currently recommended STIKO immunization schedule. Patient reports or vague memories of vaccinations in the past are not sufficient. While serological tests to confirm whether catch-up vaccinations are required are usually not indicated [1], they are recommended for women wanting to have children who cannot reliably remember if they have had chickenpox.

Undocumented vaccinations are considered to have never been performed.

What to do if a vaccination has not been completed as recommended?

The intervals recommended for primary immunization are minimum intervals to be observed to ensure an optimum immune response. Missed vaccine doses should be administered as soon as possible. Repeat administration of doses previously given is not indicated, even if the interval has been substantially exceeded ("every vaccine dose counts" [1]).

Every vaccine dose counts.

Is "over-immunization" harmful?

Additional vaccine doses are not associated with an increased risk of severe adverse effects [1]. Thus, if the vaccination status regarding a particular vaccine is unknown or insufficiently documented, administration of that vaccine is explicitly recommended, even if this may result in medically unnecessary or premature repeat vaccination. Patients with high serum antibody levels after recent vaccination with tetanus/diphtheria toxoids, repeat vaccination may result in painful local reactions (Arthus reaction), which are, however, usually self-limiting [1].

Additional vaccine doses pose no medical risk.

How to manage immunocompromised patients who have been vaccinated with PPSV23 but not yet with PCV13

Immunocompromised patients are recommended to receive sequential vaccination, first with PCV13 and 6–12 (at least two) months later with PPSV23.

Minimum intervals must be observed for pneumococcal vaccination using PCV13 and PPSV23.

Immunocompetent individuals ≥ 60 years are advised to undergo PPSV23 vaccination only. This frequently results in the situation that older immunocompromised patients have previously been vaccinated with PPSV23 but not with PCV13. Thus, the recommended sequence cannot be maintained. If the PPSV23 vaccine was given less than six years ago, PCV13 should be administered at least twelve months after the PPSV23 dose. If the PPSV23 vaccine was administered more than six years ago, patients should be vaccinated with PCV13 immediately, followed by PPSV23 vaccination 6–12 months later.

How to manage patients from abroad

STIKO recommendations apply to everyone, irrespective of their country of birth or origin.

Individuals who come to Germany from other EU or non-EU countries are recommended to receive the same vaccinations as persons born in Germany. Again: Only documented immunizations are considered to have actually been performed. Any undocumented vaccination needs to be administered according to STIKO recommendations.

Are there any special recommendations for social contacts of immunocompromised patients?

Live-attenuated viruses contained in the MMR vaccine are not transmissible to social contacts.

Individuals living in the same household as immunocompromised patients, as well as any other close social contacts, are advised to keep their STIKO-recommended standard vaccinations up-to-date and receive annual flu shots [4, 7, 14]. In particular, given that the live vaccine viruses are not transmissible, immunocompetent social contacts can and should receive MMR immunization according to guidelines [4]. Immunocompromised individuals should observe rigorous hand hygiene when caring for infants recently vaccinated with a live rotavirus vaccine, and they should avoid any contact following varicella vaccination (14 days) and nasal influenza vaccination (seven days).

What are the regulations regarding cost coverage?

All STIKIO-recommended vaccinations are covered by statutory health insurance funds.

The German Federal Joint Committee (*Gemeinsamer Bundesausschuss, G-BA)* specifies details regarding the delivery of immunization services in its vaccination guidelines, based on Article 20, Section 2 of the German Protection against Infections Act. Any STIKO-recommended vaccine will be covered by statutory health insurance funds, once it has been included in the G-BA vaccination guidelines. The current version of the guidelines (in German) can be accessed on the G-BA website (https://www.g-ba.de/richtlinien/60/). With respect to vaccines not listed in these guidelines or those intended to be given outside their approved indication, it is recommended to contact the patient's health insurer in advance and inquire whether the intended vaccination will be covered.

Who is permitted to administer vaccines?

Physicians of all specialties are permitted to administer vaccines.

According to Article 20, Section 4 of the German Protection against Infection Act, necessary vaccinations may be administered by any physician, irrespective of his/her specialty. Dermatologists are therefore considered qualified to administer any missing vaccination. The German Academy of Dermatology (DDA) offers certification on the topic of "Vaccinations by dermatologists" (https://akademie-dda.de/zertifikate/).

Conclusion

Immunosuppressive treatment of dermatological patients requires that their vaccination status (in keeping with STIKO recommendations) be reviewed and updated on a regular basis. Not only should dermatologists be familiar with the necessary standard immunizations as well as recommended non-standard vaccinations, but also with any potential limitations of their use in immunocompromised individuals. This will ensure the best possible protection of this vulnerable patient group from vaccine-preventable infections.

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[CME-Questions/Lernerfolgskontrolle]

1. Welche der folgenden Aussagen trifft zu?

a) Impfempfehlungen werden einmal jährlich durch das Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) im deutschen Ärzteblatt veröffentlicht.
b) Die Ständige Impfkommission (STIKO) ist eine gemeinsame Arbeitsgruppe der national führenden Hersteller von Impfstoffen.
c) Für immunsupprimierte Personen gelten dieselben Impfempfehlungen wie für Immungesunde.
d) Die Impfquote bei immunkompromittierten Personen ist aktuell niedriger als in der immungesunden Bevölkerung.
e) Eine immunsuppressive Therapie darf bei unvollständigem Impfstatus nicht eingeleitet werden.

2. Was ist eine Indikationsimpfung?

a) Jede entsprechend Empfehlungen der Ständigen Impfkommission (STIKO) indizierte Impfung.
b) Eine Impfung mit einem in Deutschland zugelassenen Impfstoff.
c) Eine Impfung, die für eine spezielle Indikation neu entwickelt wird (zum Beispiel COVID-19-Pandemie).
d) Eine Impfung mit Indikation für eine bestimmte Personengruppe (zum Beispiel aufgrund eines in dieser Gruppe erhöhten Erkrankungs- oder Komplikationsrisikos).
e) Eine nach Ermessen des behandelnden Arztes notwendige Impfung

3. Welche der folgenden Aussagen zu Impfungen von Patienten unter systemischer Therapie einer Psoriasis ist nicht korrekt?

a) Vor Gabe von Lebendimpfstoffen unter Therapie mit Dimethylfumarat wird eine individuelle Risikonutzenabwägung angeraten.
b) Die Gabe von Lebendimpfstoffen wird in den Fachinformationen MTX-haltiger Präparate als kontraindiziert eingeordnet.
c) Die Gabe von Totimpfstoffen kann unter bereits laufender Therapie mit Guselkumab nachgeholt werden.
d) In Studien wurde nach Impfung gegen Pneumokokken (PPSV23) und Tetanus unter Therapie mit Ustekinumab eine regelhafte Immunantwort dokumentiert.
e) Die Therapie mit Infliximab ist ohne Einfluss auf die Entwicklung einer protektiven Immunantwort nach Impfungen.

4. Welche der folgenden Aussagen zu Impfungen im Zusammenhang mit der Therapie mit Rituximab ist nicht zutreffend?

a) Auf die Gabe von Totimpfstoffen sollte innerhalb von sechs Monaten nach Therapie mit Rituximab verzichtet werden, da das Risiko für impfassoziierte Nebenwirkungen in diesem Zeitraum deutlich erhöht ist.
b) Vor Therapiebeginn anstehende Impfungen mit Totimpfstoffen sollten nach Möglichkeit vier, minimal aber zwei Wochen vor Erstgabe von Rituximab abgeschlossen sein.
c) Aufgrund der B-Zell-Depletion mit Suppression der humoralen Immunantwort ist der Erfolg von Impfungen, die innerhalb von sechs Monaten nach Rituximab-Therapie gegeben werden, deutlich eingeschränkt.
d) Die Impfung gegen Influenza wird auch innerhalb des 6-Monats-Intervalls nach Therapie mit Rituximab angeraten, wenn die Grippesaison in diese Zeit fällt.
e) Lebendimpfungen sollten mindestens vier Wochen vor Therapiebeginn abgeschlossen sein und sind frühestens zwölf Monate nach Therapieende wieder möglich.

5. Ihre 40-jährige Patientin (Geburtsjahrgang 1980) mit subakut-kutanem Lupus erythematodes wird seit zwei Jahren mit Hydroxychloroquin (400 mg täglich) behandelt. Bei Einsicht ihres Impfpasses stellen Sie fest, dass der Impfstatus bezüglich Standardimpfungen unvollständig ist. Insbesondere ist keine Impfung gegen Masern dokumentiert, und die letzte Impfung gegen Diphtherie und Tetanus erfolgte vor 15 Jahren. Welche der folgenden Aussagen ist richtig?

a) Die fehlenden Impfungen gegen Diphtherie, Tetanus und Masern können jederzeit nachgeholt werden.
b) Eine Impfung gegen Masern ist bei Patienten dieses Geburtsjahrgangs nicht erforderlich, da man davon ausgehen kann, dass diese durchgemacht wurden.
c) Eine Impfung gegen Masern (Lebendimpfstoff) ist aufgrund der laufenden Therapie mit Hydroxychloroquin kontraindiziert.
d) Vor Impfung gegen Diphtherie und Tetanus sollte Hydroxychloroquin über mindestens vier Wochen pausiert werden.
e) Da unter Therapie mit Hydroxychloroquin mit einer deutlich verminderten Impfantwort zu rechnen ist, werden serologische Kontrollen angeraten.

6. Ihr 38-jähriger Patient erhält eine Monotherapie mit Prednisolon

in einer Tagesdosis von 5 mg. Welche Aussage zu Lebendimpfstoffen ist in dieser Situation richtig?

a) Die in Deutschland zugelassenen Impfstoffe gegen Masern, Mumps, Röteln und Varizellen können gegeben werden.
b) Nur die Handelspräparate bestimmter Hersteller von Impfstoffen gegen Masern, Mumps, Röteln und Varizellen dürfen gegeben werden.
c) Erlaubt ist nur die Impfung gegen Varizellen. Die Gabe von Impfstoffen gegen Masern, Mumps und Röteln ist kontraindiziert.
d) Erlaubt ist nur die Impfung gegen Masern, Mumps und Röteln. Die Impfung gegen Varizellen ist kontraindiziert.
e) Alle Impfungen gegen Masern, Mumps, Röteln und Varizellen sind kontraindiziert.

7. Sie planen bei Ihrem 72-jährigen Patienten mit Erstdiagnose eines bullösen Pemphigoids zeitnah den Beginn einer Therapie mit Azathioprin. Der Patient hat alle altersentsprechenden Standardimpfungen erhalten. Eine einmalige Impfung mit dem 23-valenten Pneumokokken-Polysaccharidimpfstoff (PPSV23) erfolgte vor drei Jahren, die Impfung gegen die saisonale Grippe steht für die aktuell anstehende Saison noch aus. Welche Aussage trifft zu?

a) Die Einleitung der Therapie mit Azathioprin sollte im Abstand von mindestens acht Wochen zu allen notwendigen Impfungen erfolgen.
b) Die Impfung mit PPSV23 sollte zeitnah wiederholt werden.
c) Eine MMR-Impfung ist indiziert.
d) Die anstehende Impfung gegen Influenza kann und sollte auch unter Therapie mit Azathioprin durchgeführt werden.
e) Es sind keine Impfungen erforderlich.

8. Welche der folgenden Aussagen zur Pneumokokkenimpfung trifft **nicht zu?**

a) Personen über 60 Jahren wird eine Impfung mit dem 23-valenten Pneumokokken-Polysaccharid-Impfstoff (PPSV23) angeraten.
b) Immunsupprimierte Personen sollten sequenziell mit dem 13-valenten Pneumokokken-Konjugatimpfstoff (PCV13) und nach 6–12 Monaten mit PPSV23 geimpft werden.
c) Auffrischungen der Impfung mit PPSV23 sind unter immunsuppressiver Therapie nicht erforderlich.
d) Die STIKO spricht eine Impfempfehlung für Krebspatienten aus.
e) PPSV13 und PPSV23 sind Totimpfstoffe, die auch unter immunsuppressiver Therapie ohne Risiko gegeben werden können.

9. Ein 39-jähriger Familienvater unter immunsuppressiver Kombinationstherapie bei Pemphigus vulgaris (Rituximab, Mycophenolatmofetil, Prednisolon) hat Fragen zu Impfungen, die sein unmittelbares Umfeld betreffen. Welche der folgenden Empfehlungen sind **nicht zutreffend?**

a) Bei Ehefrau und Kindern sollte auf einen aktuellen Impfschutz entsprechend STIKO-Impfungen geachtet werden.
b) Eine Impfung der 38-jährigen immungesunden Ehefrau gegen die saisonale Grippe ist sinnvoll.
c) Die bei der 6-jährigen Tochter noch ausstehende MMR-Nachholimpfung sollte verschoben werden, um den immunkompromittierten Vater nicht durch die attenuierten Impfviren zu gefährden.
d) Im Anschluss an die Rotavirus-Schluckimpfung des zehn Wochen alten Sohnes sollten besondere Hygienemaßnahmen beachtet werden.
e) Der Kontakt zum zwölf Monate alten Nachbarsjungen sollte über zwei Wochen vermieden werden, nachdem dieser eine Lebendimpfung gegen Varizellen erhalten hat.

10. Welche Aussage zu Impfungen gegen Varizellen / Herpes zoster trifft **nicht zu?**

a) Seronegativen Frauen mit Kinderwunsch wird eine Impfung gegen Varizellen angeraten.
b) Seronegativen Personen mit schwerem atopischen Ekzem wird eine Impfung gegen Varizellen angeraten.
c) Die STIKO rät immungesunden Erwachsenen ab dem 60. Lebensjahr zu einer Impfung mit dem Herpes-zoster-*subunit*-Totimpfstoff.
d) Immunsupprimierten Personen wird bereits ab dem 50. Lebensjahr eine Impfung mit dem Herpes-zoster-*subunit*-Totimpfstoff angeraten.
e) Personen, die einen Herpes zoster durchgemacht haben, bleiben dauerhaft immun und sollten daher nicht mehr gegen Herpes zoster geimpft werden.

Liebe Leserinnen und Leser,
der Einsendeschluss an die DDA für diese Ausgabe ist der 11. September 2020. Die richtige Lösung zum Thema „Die Linienmuster der Haut und ihre Dermatosen“ in Heft 4 (April 2020) ist: (1a, 2e, 3b, 4a, 5c, 6c, 7b, 8a, 9a, 10b).

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