Chapter

Medical Management of Chronic Plaque Psoriasis in the Modern Age

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Abstract

Despite its frequency, psoriasis is still a difficult pathology to manage, in no small part due to the wide number of therapeutic choices available. These range from topical medicine to systemic drugs to more targeted agents such as biological therapies. All medical personnel involved in the treatment of psoriasis patients should be aware of these methods and apply them accordingly. Even though all patients may benefit from specific treatment options, these differ in regard to posology, monitoring, interactions and contraindications. Moreover, due to the adverse effects and drug interactions of some of these agents, not all patients are suitable candidates for each of therapies discussed. Therefore, nurses, trainees, general practitioners and dermatologists must carefully select the most appropriate therapy based on the characteristics of each patient, severity of the pathology, comorbidities and coexistent medications. This review aims to offer an updated, pragmatic insight into the modern management of patients with moderate-to-severe psoriasis.

Keywords: psoriasis, T cells, immunomodulators, keratinocytes, phototherapy, systemic therapies, biologic agents

1. Introduction and short history

Psoriasis is defined as chronic inflammatory systemic ailment, affecting the teguments foremost, and characterized by important genetic and immune constituents. The most common form is represented by psoriasis vulgaris, affecting every race and all ages, most often between the ages of 50 and 69 years, concerning at least 100 million individuals worldwide [1, 2]. It is a potentially devastating disorder with a progressive natural course, associated with multiple comorbidities and typified by underlying immunologic and inflammatory elements [3]. Despite it being a convoluted pathology with an incompletely elucidated pathogenesis, it has been shown that the environment, immune system and genetic predisposition all play a decisive role in triggering the psoriasis cascade [4]. As of today, treating psoriasis remains a demanding endeavour, merely attending the symptoms and ignoring the principal cause. Medical management is satiated by a wide variety of choices with fluctuating efficiency, for example, topical therapies, phototherapy, systemic drugs and biological agents [5]. It is fathomable that choosing the most appropriate treatment scheme for each individual can oftentimes be perplexing or even disheartening. Nevertheless, the treatment involved should imply a multidisciplinary course

of action, with psychologists, rheumatologists and dermatologists collaborating in order to deliver the best possible care, with the most satisfactory outcome.

To properly understand the breakthroughs of modern treatment of psoriasis, it might be worthwhile to glance over the history of this complicated disease. The first reported cases were identified in ancient Greece, many of the description written by Hippocrates (460–377 BC) himself [6, 7]. Portrayals of psoriasis can also be traced back to the times of the Old Testament, wherein people suffering from such skin disorders were publicly ostracized since they were considered punished by divinity. Numerous historians acknowledge Celsus (ca. 25 BC–45 AD) as documenting the first clinical description of papulosquamous diseases, whereas Galen (133–200 AD) first utilized the term psoriasis [6, 8, 9]. However, his depiction was inconsistent regarding the disorder that we now know as psoriasis. He described it as a pruritic, scaly skin illness of the eyelids and scrotum, probably referred to as today as seborrheic dermatitis. Nevertheless, the unselective grouping together of all inflammatory skin disorders contributed to the stigmatization of psoriasis patients. During the Middle Ages, when it was believed that psoriasis was as contagious as leprosy, these patients were mandated to carry a chime or clapper that would announce their approach. Furthermore, they had to wear a special garment and could only eat or come into physical contact with others considered lepers.

In the dawn of the nineteenth century, Willan expanded on Celsus's explanations of papulosquamous afflictions by describing characteristics we know considered compatible with psoriasis. Even so, he labelled modern psoriasis as 'lepra vulgaris', which maintained the confusion between these two distinct diseases [6, 7, 10]. Afterwards, there was an incongruity when referring to these pathologies, as authors could not properly agree on which term to use. Ultimately, Gibert corroborated Willan's description with the term psoriasis, putting an end to some of the perplexity and guiding to an improved awareness and understanding of psoriatic patients. Heinrich Auspitz (1835–1886) noticed the papillary bleeding that appeared after removing the scale of psoriatic lesions, currently referred to as the Auspitz sign (or bloody dew phenomenon) [6, 7, 11, 12]. In 1877, Heinrich Köbner (1838–1904) defined the sign that carries his name, specifically the occurrence of a psoriatic lesion within the location of a physical injury. After two more decades, in 1898, William Munro (1863–1908) described the microabscesses that appear in psoriasis, otherwise known as Munro's abscesses. The beginning of the twentieth century led to further advancements in the understanding of psoriatic lesions. In 1910, Leo von Zumbusch (1874–1940) was the first to note generalized pustular psoriasis, now called the von Zumbusch disease [6, 13]. Among other descriptions was also the one of the Russian dermatologist D.L. Woronoff in 1926 regarding a pale halo now known as the 'Woronoff ring' enclosing a plaque of psoriasis [7, 14]. The characterization of the Auspitz sign, Köbner's phenomenon, Munro's abscess, and pustular psoriasis, as well as the Woronoff ring made it possible for practitioners to more easily identify patients with psoriasis.

The next discoveries furthered our understanding of pathophysiology, especially concerning epidermal hyperplasia and keratinocytes' cell cycle shortening by van Scott and Ekel in 1963, followed by the role of the immune system by Gubner in 1951 and Muller in 1979 [6, 7]. However, there is still much to be learned about this complex disease and its intricate mechanisms.

The treatment of psoriasis also varied across the ages, from arsenic and ammoniated mercury in the nineteenth century (which both had a comparable toxic potential), to chrysarobin, anthralin and coal tars in the late nineteenth and early twentieth centuries, reaching to corticosteroids, methotrexate and PUVA in the middle of the last century [6, 7, 10, 15]. In what follows, we describe the modern forms of therapy which have been scientifically proven to ameliorate the symptoms in psoriasis.

2. Management of psoriasis

In the past few years, countless achievements have been made in grasping the intricate physiopathological contrivances of psoriasis. Studies repeatedly demonstrated that it is a chronic, systemic immune-mediated ailment, the dermatologic manifestation representing its most debilitating aspect, usually followed by joint involvement. However, the explicit mechanisms of this process have not been untangled. Even so, it appears that the myeloid dendritic cells begin producing interleukins such as IL-12, IL-23 and TNF-α prior to a minor traumatic injury that perform as chemoattractants for the T helper Th-1 and Th-17 cells [16, 17]. In the next step, these cells will raise the production of psoriatic cytokines such as IL-17 within the site of injury, hence increasing the keratinocytes' turnover and eventually piloting towards the cutaneous symptoms of psoriasis [18–21]. Also, the proinflammatory substances may extend into the bloodstream with a significant influence on insulin signalling, angiogenesis, lipogenesis or adipogenesis, which will ultimately lead to comorbidities such as obesity and dyslipidaemia, hypertension, depression and type 2 diabetes mellitus [3, 22]. Grasping the mechanisms of psoriasis is the utmost step in offering the best available therapy.

Topical therapy as the only form of treatment has demonstrated a mediocre rate of improvement, with patients often describing ongoing clinical symptoms, for instance, redness, pruritus or scales [23]. One survey targeted to such patients showed that 40% of cases with a mild disease, circa 50% of those with moderate psoriasis and well above 40% with the severe form were discontented with the recommended topical therapies. The lowermost treatment satisfaction quotients were found in the topical medications versus systemic and phototherapy group [24]. Should topical therapy in itself fail to achieve the expected outcome, practitioners have to be ready for alternative strategies, such as systemic and biological therapies.

2.1 Topical therapy

Topical therapies are recommended in mild psoriasis, when the affected body surface area is below 10% [25].

2.1.1 Anthralin

Anthralin via mitochondrial dysfunction might reduce the proliferation of keratinocytes and re-establish cell differentiation. As such, it is used to treat the localized plaques that are covered with thick scales localized either on body or the scalp that have failed to clear with other treatments. It is applied on the affected areas in concentration of 1%, and it is left between 20 min and 1 h before removal [26].

Among the adverse effects, the common is skin irritation or staining of the adjoining skin [25].

2.1.2 Coal tar

Coal tar seems to reduce hyperproliferation of keratinocytes by supressing DNA synthesis, and it has exhibited efficacy on chronic plaque psoriasis, palmoplantar psoriasis or scalp psoriasis, improving the general aspect of the psoriasis plaque after 1 month of treatment. It appears as though the remission period of the lesions persists longer than that with other topical treatments [25].

Adverse effects number odour, staining, contact dermatitis, erythema and folliculitis.

It can be used during pregnancy, but in children caution is advertised [27].

2.1.3 Salicylic acid

Salicylic acid triggers desquamation of corneocytes via lowering intracellular cohesion between the cells of the stratum corneum. It can be applied in creams, ointments or lotions in concentrations between 2 and 6%.

The most notable adverse effect mentioned while using salicylic acid is the potential systemic intoxication [28].

It is safe to utilize during pregnancy, but in children, because of the systemic absorption, it should be avoided [25].

2.1.4 Calcineurin

Calcineurin inhibitors like tacrolimus, pimecrolimus and sirolimus supress the production of the inflammatory substances that seem accountable for the skin lesions in psoriasis. It is found in concentration of 0.3% gel or 0.5% cream [29].

As side effects, the most common is stinging sensation or contact dermatitis.

It can be used in children older than 2 years old [25].

2.1.5 Topical retinoids tazarotene and bexarotene

Topical retinoids tazarotene and bexarotene downregulate the turnover by altering transcription of genes in keratinocytes upon transportation within the nucleus, after binding to retinoic acid on the cell membrane. Furthermore, it reduces the hyperproliferation of keratinocytes; it regulates the differentiation and reduces inflammation [30].

It can be applied as a cream in concentration of 0.1 and 0.05%, and when used on the nails, it seems to improve the onycholysis, pitting and salmon patches [25].

It is contraindicated during pregnancy, but it is permitted to be used in children [31].

2.1.6 Topical corticosteroids

Topical corticosteroids display immunosuppressive, anti-inflammatory, antiproliferative and vasoactive action. They are categorized based on their potency, from low-potency to very potent corticosteroids. When considering the potency and the vehicle, disease severity, patient preference and sites of lesions must be taken into account [25]. They can be found as creams, ointments, gel, solutions, nail lacquer, foams or shampoos applied on the skin, scalp or nails.

Skin atrophy, telangiectasia as well as secondary infection are the most notable side effects.

Corticosteroids can be used during pregnancy but are not recommended in children under 2 years old [32].

2.1.7 Vitamin D

Vitamin D analogues calcitriol, tacalcitol, maxacalcitol, paricalcitol and becocalcidiol decrease keratinocyte proliferation, inflammation or keratinization [33]. They can be applied on the skin, scalp or nails and are found as creams, ointments or scalp lotions.

The most common side effect is skin irritation. Very rare hypercalcemia, hypercalciuria and parathyroid hormone suppression have been described.

Vitamin D analogues are contraindicated in patients with hypercalcemia or in pregnancy, but they can be used in children while not exceeding the dose of 50 g/week [34].

2.2 Phototherapy in psoriasis

Ultraviolets either from the sun or artificial light play a significant role in treating psoriasis mainly by supressing activated T cells, independently on the cell subpopulation involved in the disease [25]. It has been shown that NB-UVB is the most utilized phototherapeutical approach, inducing clinical and histopathological resolution of moderate-to-severe plaque psoriasis by exerting a cytotoxic effect on epidermal T cells [35, 36]. This apoptotic effect on T cells depends mostly on the penetration of the NB-UVB within the lesion, penetration that on the one hand depends on the wavelength and on the other the depth of the skin lesion [37]. Understanding that the T cells responsible for psoriasis are situated along the dermal-epidermal junction and within the epidermis, it has been determined that the optimal wavelength spectrum should range between 290 and 313 nm [38]. Currently, NB-UVB is the most common approached used worldwide, and it can be regarded as the gold standard in therapy for treating moderate-to-severe plaque psoriasis [39].

2.3 Systemic therapies

2.3.1 Methotrexate

Methotrexate is a folic acid analogue employed in psoriasis for its anti-proliferative, anti-inflammatory and immunosuppressive actions [40].

Dosage and administration. Methotrexate comes as a self-injectable solution administered by the patient weekly, with the added proposal of coupling with folic acid supplements. Initiation dosage is typically 10–25 mg once per week. Maximum dose should not surpass 30 mg/week. Folate intake should be about 1–5 mg daily, except on the day of methotrexate intake [41].

Adverse effects. In case of pregnancy, it may lead to foetal death or to teratogenic effects; also, it can be toxic to the gastrointestinal tube, liver and kidneys, and it can cause myelosuppression, malignant lymphomas, pulmonary fibrosis, severe infections, fatigue, headaches, alopecia or oligospermia [42, 43].

Laboratory tests recommended. To start therapy with methotrexate correspondingly, the following evaluations are compulsory: physical exam, patient history, QuantiFERON-TB Gold for latent TB infection, complete blood count with differential and thrombocytes count, renal function tests, hepatic enzymes and pregnancy test.

Drug interactions. Methotrexate has been shown to interact with cyclosporine, proton pump inhibitors, oral antibiotics, salicylates, mercaptopurine, nonsteroidal anti-inflammatory drugs, cisplatin, probenecid, phenylbutazone, sulfonamides, theophylline, live vaccines, retinoids and azathioprine [43].

As anticipated, this drug is contraindicated in pregnancy and while breastfeeding due to its teratogenic effects. Therefore, the use of contraception is highly advocated in the course of treatment. Other contraindications include blood dyscrasia, chronic liver disease, immune deficiency syndromes or alcohol abuse [44].

2.3.2 Cyclosporine

Cyclosporine is a calcineurin inhibitor agent that is used in psoriasis for its immunosuppressing action and its capability to prevent the T cell proliferation

by reversibly inhibiting the activation of CD4+ T cells, leading to a block on the synthesis of interleukin 2 [45].

Dosage and administration. To induct psoriasis remission, the everyday dosage varies between 2.5 and 5 mg/kg, administered in two divided doses each day. Experts recommend it not be used continuously for longer than 1 whole year [46].

Adverse effects. Among the most important reported adverse effects of cyclosporine are renal toxicity, structural kidney damage, hypertension, liver toxicity, severe infections, high potassium levels, low magnesium levels, acne, tremors, headache, pneumonitis and gastrointestinal toxicity [47, 48].

Laboratory tests recommended. Physical exam, patient history, QuantiFERON-TB Gold for latent TB infection, renal function tests, complete blood count with differential and platelet count, magnesium level, potassium level, uric acid, lipids, glycaemia, bilirubin and liver enzymes are necessary before initiating therapy. The serum creatinine should be measured on two distinct occasions. Contraception has to be ensured.

Drug interactions. Cyclosporine interacts with a large number of drugs such as antibiotics (ciprofloxacin, gentamicin, tobramycin, vancomycin, trimethoprim with sulfamethoxazole, azithromycin, erythromycin), nonsteroidal anti-inflammatory drugs, antifungals (amphotericin B, ketoconazole, fluconazole, itraconazole, terbinafine), ranitidine, cimetidine, birth control pills, tacrolimus, methotrexate, methylprednisone, allopurinol, colchicine, fenofibrate, gemfibrozil, statins, calcium channel blockers, amiodarone, bromocriptine, anticonvulsants (carbamazepine, oxcarbazepine, phenobarbital), protease inhibitors (indinavir, nelfinavir, ritonavir, saquinavir) and octreotide [48].

It is contraindicated in the case of poorly controlled arterial hypertension, known malignancies or renal dysfunctions. As of yet, there have not been enough studies performed in humans to certify whether the drug affects the foetus or not. Nonetheless, the treatment is still to be avoided in pregnant women due to the role calcineurin inhibitors are believed to play in neural development. As such, cyclosporine should only be used in pregnancy if the benefits justify the hypothetical risk to the foetus [49].

2.3.3 Acitretin

Acitretin is a retinoid agent with substantial immunomodulatory and anti-inflammatory effects, advocated in psoriasis for its capacity to modulate the proliferation and differentiation of keratinocytes [50].

Dosage and administration. Acitretin is taken in a single oral dose, alongside the main meal. Therapeutic dosage varies between 25 and 50 mg/day. A simultaneous topical therapy is also suggested due to the slow onset of action, needing as long as 3–6 months for a maximal response to acitretin [51].

Adverse effects. It can cause serious teratogenic effects on the exposed foetus, mucocutaneous dryness, hypertriglyceridemia, hepatotoxicity, toxic hepatitis, pancreatitis, hyperostosis, intracranial hypertension, alopecia, arthralgia and fatigue [52].

Laboratory tests recommended. It is compulsory to take a pregnancy test before initiating the treatment; liver enzymes, lipid profile, renal function and complete blood count should also be included.

Drug interactions. Acitretin interacts with retinoic acid supplements, methotrexate, doxycycline, oral retinoids and phenytoin [53].

The high teratogenicity of retinoids severely restricts their use in fertile women who should be appropriately counselled on the methods and importance of contraception [54]. Moreover, pregnancy should be circumvented for at least 3 years after

halting treatment. A pregnancy test is to be performed regularly every 3 months during the course of therapy.

2.3.4 Fumaric acid esters and dimethyl fumarate

Fumaric acid esters and dimethyl fumarate have been employed in the treatment of psoriasis for five decades, with substantial outcomes for patients [55]. Seemingly, dimethyl fumarate affects multiple cytokines and lymphocyte pathways, i.e. inhibiting the nuclear translocation and the transcriptional activity of the nuclear factor kappa-light-chain-enhancer of activated B-cells through its interaction with the intracellular reduced glutathione. It also transforms the T helper cells from the Th1 and the Th17 profile to a Th2 phenotype, subsequently reducing cytokine production and the proliferation of epithelial cells [56].

Dosage and administration. It is available as gastro-resistant tablets, being recommended to start with a low initial dose that may be subsequently increased in the following manner: in the first week, it is advised to take one 30 mg tablet, in the second week one 30 mg tablet can be taken twice daily, and during the third week one 30 mg tablet is taken three times per day. From the fourth week onwards, it can be switched to one 120 mg tablet, taken in the evening. Depending on the results, this dose can be increased with one 120 mg tablet per week, but the maximum daily dose should not exceed 720 mg [57].

Adverse effects. Among more regularly reported events are gastrointestinal disorders, flushing, haematological disturbances (lymphopenia, leukopenia, eosinophilia), loss of appetite, headache, paraesthesia, proteinuria, renal failure, Fanconi syndrome and fatigue [58].

Reference tests. Complete blood count, renal function and liver enzymes should be included.

Drug interactions. Fumaric acid esters may interact with live vaccines, methotrexate, retinoids, cyclosporine, aminoglycosides, lithium, diuretics and nonsteroidal anti-inflammatory drugs [59].

2.3.5 Apremilast

Apremilast, operating as a selective inhibitor of phosphodiesterase 4, on the one hand downregulates the expression of specific proinflammatory cytokines like IL-17, IL-23 and TNF-α that each plays a crucial role in the pathophysiological chain of events in psoriasis. On the other hand, using the same mechanism, it increases the expression of anti-inflammatory cytokines such as IL-10 [59].

Dosage and administration. Presented in tablet form, apremilast is administered orally, with an indicated dose of 30 mg two times per day. The treatment should begin with a low starting dose of 10 mg in the morning, and then from the second day of therapy onward the dosage is increased daily by 10 mg until reaching the therapeutic dose of 30 mg twice daily [60, 61].

Adverse effects. Diarrhoea, nausea and vomiting, depression and weight loss are the most frequently noted adverse effects of apremilast [62].

Laboratory tests recommended. Physical exam, patient history (with an emphasis on psychiatric disorders such as depression), renal function and liver enzymes should be performed.

Drug interactions. Apremilast interacts with cytochrome P450 enzyme inducers such as rifampin, phenobarbital, carbamazepine and phenytoin [61].

Patients over 65 years old appear to be more vulnerable to develop the aforementioned side effects. Hence, supervision is very important in these cases, patients being warned regarding undesirable events. They should also be

instructed not to reduce or suspend the medication by themselves, but to address their treating physician [62].

2.4 Biologic therapies

2.4.1 The anti-TNF-α agents

The anti-TNF-α agents etanercept, adalimumab, infliximab and certolizumab have been developed to expressly inhibit the TNF-α signalling pathway, thereby lessening its inflammatory properties. Etanercept is a recombinant TNF-α receptor that impedes TNF-α function by operating as a decoy receptor that attaches to TNF. Adalimumab is an entirely humanized antibody of TNF-α, where infliximab is a mouse-human chimeric antibody. Certolizumab represents a distinctive anti-TNF-α antibody that does not include the Fc portion [63, 64].

Dosage and administration. Etanercept, adalimumab and certolizumab are given via subcutaneous injection either weekly or once every two weeks. Infliximab is administered via intravenous infusion every 8 weeks. **Table 1** presents the dosage and the administration method for the abovementioned anti-TNF-α agents [65–68].

Adverse effects. Among the serious side effects encountered while using any of the mentioned anti-TNF-α agents are severe infections, lymphomas or other malignancies and even the reactivation of the tuberculosis or hepatitis B virus. While using etanercept, adalimumab or certolizumab, the most usual local reactions are pain, swelling, haemorrhage or erythema at the place of injection; however, the intensity of these symptoms will diminish with continued treatment. Patients should be advised not to accept taking live vaccinations for the duration of the therapy. There have been reported cases of CNS demyelinating pathologies (e.g. multiple sclerosis, optic neuritis) or peripheral nerve demyelinating disease (Guillain-Barré syndrome). Patients are advised to suspend the therapy in these cases [3, 65–68].

Laboratory tests recommended. Physical exam and history, complete blood count, liver function, renal function, viral hepatitis screening and tuberculosis testing should be performed prior to anti-TNF-α treatment initiation.

Drug interactions. Other biologic therapies, live vaccines, anakinra and abatacept, were noticed to interact with anti-TNF-α drugs [65–68].

Certolizumab has been approved by the FDA for pregnant women. Data collected thus far has validated neither additional teratogenic effects when compared to the general population, nor a greater risk of foetal death [69].

2.4.2 The anti-IL-12/23 agents

The anti-IL-12/23 agents comprise ustekinumab, guselkumab and tildrakizumab. Il-23 is a heterodimeric cytokine incorporating two subunits: the p19 subunit, which is connected to the p40 subunit, the latest being shared with IL-12. Il-23 is the main actor prompting the activation of the T helper 17 inflammatory pathway, whereas IL-12 plays the chief role in Th-1 differentiation and proliferation. Ustekinumab is a biologic agent aiming for the p40 common domain of IL-12 and IL-23, hence preventing their interaction with their receptor. Contrariwise, guselkumab and tildrakizumab target the p19 subunit of IL-23, thus obstructing the signalling pathway associated with the immunopathogenesis of psoriasis [70–72].

Dosage and administration. Ustekinumab, guselkumab and tildrakizumab are delivered as prefilled syringes with subcutaneous administration. The induction phase lasts 1 month, being then ensued by the maintenance phase. In this phase, an injection is administered once every 8 or 12 weeks. **Table 2** presents the respective posology for the aforementioned biologic agents [73–75].

Biologic agent	Posology
Etanercept	50 mg × 1 twice a week during the induction phase (the first 3 months), thereafter only one injection weekly
Adalimumab	40 mg × 2 at week 0, afterwards 40 mg × 1 administered every 14 days
Infliximab	5 mg/kg is administered via intravenous infusion at weeks 0, 2 and 6 and after that every 8 weeks
Certolizumab	200 mg × 2 administered subcutaneously at weeks 2 and 4, followed by a 200 mg × 1 dose weekly

Table 1.
Anti-TNF-α agents. Posology.

Biologic agent	Posology
Ustekinumab	45 mg × 1 administered at weeks 0 and 4 and at every 12 weeks subsequently
Guselkumab	100 mg × 1 administered at weeks 0 and 4 and at every 8 weeks afterwards
Tildrakizumab	100 mg × 1 administered at week 0 and 4 and every 12 weeks thereafter

Table 2.
Anti-IL-22/anti-IL-23 agents. Posology.

Adverse effects. The most notable and grave adverse effects include severe infections, tuberculosis, malignancies, hypersensitivity reactions, headache, fatigue, injection site reaction, joint pain and gastroenteritis [73–75].

Laboratory tests recommended. Physical exam, patient history, complete blood count, liver function, renal function and tuberculosis testing have to be performed before treatment can begin.

Drug interactions. These agents have been noticed to interact with live vaccines. Therefore, it is contraindicated to receive any such vaccines during therapy [3, 73–75].

2.4.3 Ixekizumab, secukinumab and brodalumab

Ixekizumab, secukinumab and brodalumab are systemic anti-IL-17 agents that carry out their roles by expressly inhibiting the IL-17 signalling pathway. Ixekizumab is a humanized IgG4 antibody with a high affinity for IL-17A [76]. Secukinumab is a fully human IgG1 antibody that also blocks IL-17A. Last but not least, brodalumab is a fully human IgG2 antibody that impedes the IL-17 pathway at the receptor level, i.e. by binding to the IL-17RA, a receptor shared by IL-17A and other IL-17 cytokines. For this reason, its effect is broader but more unspecific [77].

Dosage and administration. Ixekizumab, secukinumab and brodalumab are administered as prefilled subcutaneous injections. The induction phase varies from 3 to 12 weeks, followed by the maintenance phase with one or two injections either every second or monthly. **Table 3** illustrates the posology of these therapies [78–80].

Adverse effects. Anti-IL-17 agents may cause serious infections, headache, joint pain, hypertension, diarrhoea, injection site reaction (oedema, pain, erythema, ecchymosis), musculoskeletal pain and hypersensitivity reactions [81].

Laboratory tests recommended. Physical exam, patient history, complete blood count, liver function, renal function and tuberculosis testing must be performed before these therapies as well.

Drug interaction. These agents may interact with drugs that are metabolized by cytochrome P450, e.g. warfarin or cyclosporine [78–80].

Biologic agent	Posology
Ixekizumab	80 mg × 2 at week 0 followed by 80 mg at weeks 2, 4, 6, 8, 10 and 12 and at every 4 weeks afterwards
Secukinumab	150 mg × 2 at weeks 0, 1, 2, 3 and 4 and after the induction phase, 150 mg × 2 is administered once every month
Brodalumab	210 mg × 1 at week 0, 1 and 2, followed by 210 mg × 1 administered every 2 weeks subsequently

Table 3.
Anti-IL-17 agents. Posology.

3. Biological therapies and pregnancy

Despite their presently being no curative remedies for psoriasis, a wide assortment of specific molecular agents exist that are able to ameliorate the symptoms and produce remission. Delivering any of the aforementioned drugs varies primarily on the proficiency of the treating practitioner and only afterwards on the patient's personal choice. It is of utmost importance that women during childbearing age are aware that no studies have been conducted on whether or not these therapies are safe to use while pregnant. Consequently, should any of the biological treatments mentioned except for certolizumab be taken, they must be discontinued prior to conceiving a child. Considering certolizumab, as of writing this chapter, it is ostensibly the only discovered biological agent that fails to cross the maternal-placental barrier, and no adverse or teratogenic consequences were discovered if taken while pregnant [69]. In **Table 4**, we illustrate the minimal time interval suggested between discontinuing the medication and child conception [82].

Therapeutic agent	Contraception
Methotrexate	During pregnancy and at least 3–6 months after
Cyclosporine	Contraception only during the therapy
Acitretin	During pregnancy and at least 3 years after
Fumaric acid esters	During pregnancy and at least 2 weeks after
Apremilast	During pregnancy and 28 days after
Adalimumab	During pregnancy and minimum 5 months after
Etanercept	During pregnancy and 3 weeks after
Ustekinumab	During pregnancy and at least 15 weeks after
Ixekizumab	During pregnancy and at least 6 months after
Secukinumab	During pregnancy and minimum 20 weeks after

Table 4.
Systemic therapy and pregnancy interval.

4. Conclusions

Psoriasis is a debilitating disease with the potential to cause severe psychological damage. In spite of the plentiful advances vis-à-vis treatment, we are still a long way off from obtaining an actual cure. It is crucial to remember that current management strategies only address the symptoms, and not the cause. Therefore,

those affected should be closely monitored even in the case of stationary disease or have regression. Moreover, not all therapies correspond to every patient due to possible comorbidities and drug interactions, and thus the notion of a miracle agent in psoriasis appears more and more illusory. This chapter aimed to provide a synopsis of modern treatment options of psoriasis, so that practitioners are sensitized of their uses, contraindications and adverse effects in order to choose the best available strategy.

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Conflict of interest

The authors declare no conflict of interest.

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