National Medicines Information Centre
ST. JAMES'S HOSPITAL • DUBLIN 8
TEL 01-4730589 or 1850-727-727 • www.nmic.ie
VOLUME 23
NUMBER 5
2017

UPDATE ON PSORIASIS

- **Psoriasis is a chronic inflammatory skin condition, resulting from a complex interplay between the immune system, genetic susceptibility and environmental triggers**
- **Psoriasis is often associated with systemic co-morbidities, that may impact on management**
- **Topical therapies are the mainstay of treatment for mild to moderate localised disease**
- **Systemic pharmacotherapies (oral, biological) or phototherapy are needed for more severe disease, or for milder disease which fails to respond to topical therapies**

INTRODUCTION

Psoriasis is a chronic inflammatory skin condition that causes red, flaky, crusty patches of thickened skin (plaques) covered with silvery scales.[1,2] **The WHO has recognised it as a serious non-communicable disease**, affecting around 2% of people worldwide (similar incidence in males and females).[2,3,4] According to the recent Burden of Psoriasis Report (2015) there are around **73,000 patients with psoriasis in Ireland**.[5] Psoriasis can start at any age; the majority of cases occur before the age of 45 years, but some studies suggest a bimodal distribution (peaks during second and fifth decades).[3,6] It typically follows a **remitting and relapsing course**.[1] The severity of psoriasis varies greatly, ranging from mild symptoms to severe disease; however irrespective of the severity, psoriasis can have a negative impact on a person's quality of life.[5] Arthritis occurs in up to 30% of patients with psoriasis (prevalence increasing with severity and duration of disease) and patients are at increased risk of co-morbidities (inflammatory bowel disease (IBD) such as Crohn's disease; cardiovascular disease (CVD); diabetes mellitus and depression).[1,8,9] **There is no cure for psoriasis; therefore management requires a tailored approach appropriate to the patient's current disease pattern**.[1,3]
Treatment options for psoriasis have improved in recent years due to increased knowledge of the mechanisms of the disease. This bulletin (which updates a previous bulletin) will outline the current approach to the management of psoriasis.

PATHOGENESIS OF PSORIASIS

The cause of psoriasis is complex; recent research has confirmed that **psoriasis is a cell–mediated inflammatory disease** primarily driven by pathogenic T-lymphocytes that produce high levels of interleukins (e.g. IL-23 which stimulates IL-17).[10,11] The detrimental inflammatory events are not restricted to the skin and account for an increasing number of co-morbid systemic conditions.[10,12] These co-morbidities may account in part for the increased mortality reported in patients with psoriasis and they have substantial implications for disease management.[13]
The **initial trigger for psoriasis remains unclear**, however the aberrant immune response appears to be modified by **genetic susceptibility** and various **environmental stimuli**.[1,10] Studies have shown a greater incidence of psoriasis among first and second degree relatives and the risk of psoriasis is 2 to 3 times higher among monozygotic twins compared with dizygotic twins.[2] Multiple gene loci have been identified as conferring increased risk but no one single psoriasis gene exists.[6] In addition, environmental factors such as skin trauma, infections (especially ß-haemolytic Strep.), surgery, stress, obesity, smoking, alcohol and medicines (such as ACE inhibitors, lithium or ß-blockers) have all been associated with disease flares or exacerbations.[11,14]

CLINICAL FEATURES AND DIAGNOSIS

Plaque psoriasis is characterized by **well-demarcated, dry, bright-red plaques with thick, non-adherent, silvery-white scales** (resulting from a hyperproliferative epidermis), usually on extensor surfaces and the scalp.[2,15] In addition to the thickened epidermis, the **dermis has an inflammatory infiltrate**, which contributes to the **thickness** of the psoriatic lesions. **The redness of the lesions is due to the increased numbers of dilated capillaries**.[2] Plaque psoriasis is by far the commonest form of the condition (accounting for about 90% of cases).[1] Other types of psoriasis include guttate psoriasis and pustular (localised or generalised) forms (see Table 1). Distinctive nail changes (pits, oil spots, onycholysis) occur in around 50% of all those affected and are more common in people with psoriatic arthritis.[1,15]

Table 1: Clinical presentations of psoriasis[6,11]

Type	Clinical features	Course of disease
Plaque psoriasis (90% of cases, all ages)	Classic well-demarcated plaques	Relapsing–remitting disease (may be associated with co-morbidities)
Guttate psoriasis (children / adolescents)	Small plaques ("raindrops" <1cm) mostly on trunk (sometimes limbs) usually 2 weeks post ß-haemolytic Strep infection	Acute inflammatory response which usually clears spontaneously (20% may have background of plaque psoriasis)
Palmoplantar pustular psoriasis (F>M, 9:1; older age groups)	Crops of pustules on palms and soles that change colour and clear spontaneously	Relapsing–remitting disease, commoner in smokers (25% may have plaque psoriasis)
Generalised pustular psoriasis	Waves of skin pustules (may be wide-spread) - patient is systemically unwell	Medical emergency – risk of dehydration / septicaemia (may result from stopping potent oral or topical steroids)

Psoriasis is a clinical diagnosis, based on the presence of the classical skin features with or without associated co-morbidities. Psoriasis in moist flexural sites may lack scales.[6] Clues to the correct diagnosis include a history of scalp scale / dandruff, scaling in the ears, pruritus in the genital area or arthralgia, alongside a positive family history of psoriasis.[11] The **Koebner phenomenon** (development of psoriatic lesions at sites of trauma, e.g. surgery, abrasions, burns) may be helpful if present.[6] There are no specific blood tests available.[11] There are several different rating scales that can be used to assess the **severity of disease**; they are also used to monitor response to treatment.[16] The simplest is a global rating scale which evaluates the extent of disease according to the extent of *body surface area* (**BSA**) involvement (e.g. <5% BSA involvement = mild; 5 to 10% = moderate; >10% = severe);[6,17] however, BSA does not take into account the features of the disease such as itch, redness, scale, or thickness of plaques. The *Psoriasis Area and Severity Index* (**PASI**) is the best evaluated method of assessing severity.[16] It combines assessment of the area of involvement (in terms of %), the severity of scaling, plaque thickness and erythema using a scale of 0-4;[6,11] it is also used to monitor treatment response.[18] In addition, it is important to proactively check for the presence of **co-morbidities** known to be associated with psoriasis, especially in more severe / longer standing disease (see Table 2).

Table 2: Co-morbidities associated with psoriasis[8-10,19]

Psoriatic arthritis (seronegative arthritis, heterogeneous presentation)
Metabolic syndrome (obesity, hypertension, dyslipidaemia and diabetes), cardiovascular disease
Gastrointestinal disease (inflammatory bowel disease, especially Crohn's disease; non-alcoholic steatohepatitis)
Mood disorders (e.g. depression and anxiety)
Malignancy (e.g. non-melanoma skin cancer)

Psoriatic arthritis (PsA) may be difficult to identify in some patients, because of its heterogeneous presentation; there are no biomarkers.[19,20] Patients with psoriasis who do not have a diagnosis of PsA should be monitored, at least annually, using a validated screening tool for PsA (e.g. the *Psoriasis Epidemiology Screening Tool* (**PEST**)).[21]
All of the above screening tools are freely available to download from the British Association of Dermatologists website (**www.bad.org.uk**).

MANAGEMENT OF PSORIASIS

The goals of management are to (1) achieve long-term disease control (2) improve the patient's quality of life (QoL) and (3) minimise treatment-related adverse effects. Because it is a chronic often highly visible condition, low self-esteem and anxiety or depression are common in people with psoriasis (even with mild disease).[1,22] This can result in profound functional and psychological morbidity and reduced levels of employment;[1,3] psychological distress has been shown to be associated with lower adherence to treatment.[23] Validated patient self-assessment tools (e.g. the *Patient's Global Assessment* or *Dermatology Life Quality Index* (**DLQI**)) may be used in primary care to evaluate the **patient's perception of his/her disease** (available from **www.bad.org.uk** with advice on interpreting the results).[16,21]
Patients will require **education and ongoing advice** on how to manage their condition.[1] Patients with psoriasis should be made aware that **treatment will control (but not cure) their disease**. Their expectations of treatment should be discussed and a long-term management plan (tailored to their disease profile and needs) agreed with them prior to its initiation, in order to optimise adherence.[3,6,11] The management plan should also take into account treatment of co-morbidities (Table 2). Advice on **appropriate lifestyle changes for each individual patient** (including weight loss, exercise, reduced alcohol intake and smoking cessation) should be included in the management plan since such changes will be helpful in controlling the disease and co-morbidities, and in preventing disease flares.[4,14]
The treatment options for psoriasis include topical and systemic (oral and biological) pharmacotherapy and phototherapy.

TOPICAL THERAPY

Topical therapies are the mainstay of treatment for localised psoriasis and also may be used in combination with systemic therapies for selected body areas.[7,11] Table 3 outlines the topical therapies currently authorised for use in psoriasis. Patients should be instructed on how to apply each therapy correctly in order to optimise response and minimise toxicity.[6]

Table 3: Topical therapies authorised for use in psoriasis[1,24-34]

Drug	Mode of Action*	Notes on use in clinical practice*
Emollients	Hydration and softening of skin; anti-pruritic properties	Used to maintain hydration in stable psoriasis and may help ↓ irritation in acute inflammatory disease.
Vitamin D analogues calcipotriol / calcitriol (different formulations available)	↓ proliferation of keratinocytes (onset of action within 2 wks)	Applied twice daily to affected skin (↓ to once daily at 2 wks). Used for 4-6 wks (continued if good response). May cause irritation (especially on face, flexures and genitalia). Use of >max recommended dose* may lead to hypercalcemia.
Corticosteroids [TCS] **Mild** (eg hydrocortisone 1%) **Moderate** (eg alclometasone 0.05%) **Potent** (eg betamethasone 0.1%) **Very potent** (eg clobetasol 0.05%)	Anti-inflammatory, immunosuppressive and antiproliferative properties (rapid onset of action within days)	Apply 1-2 times/day; useful for "difficult to treat" psoriasis: localised psoriasis of face, neck, flexures, genitalia (mild - moderate TCS); scalp, palms or soles (potent TCS). Continuous use should be limited (see text). Risk of rebound on abrupt withdrawal and of skin atrophy or adrenal suppression with prolonged usage, especially with usage of >10% BSA.
Dithranol (0.1% to 2% strengths)	Inhibition of DNA replication	Applied to *affected* skin in subacute / chronic disease – start at lowest strength and ↑ strength weekly to optimum (and best tolerated) response. Used once daily (see individual SmPC* for recommended contact times) and then washed off. May cause irritation to normal skin and stains clothes.
Coal Tar (coal tar extract / lotion / shampoo)	Antipruritic, keratolytic and anti-inflammatory properties	Applied directly to skin (lotion) or added to bath (extract) twice daily to induce remission of inflammation in psoriasis (shampoo 1-2 times/week). May cause irritation. Extracts are messy, smelly and stain clothes.

*full prescribing information is available for each medicine in the Summary of Product Characteristics (SmPC) at: **www.hpra.ie**

The **vitamin (Vit) D analogues** are suitable for **localised stable plaque psoriasis**; they are convenient to use because they are odourless and colourless.[25,26]
Topical corticosteroids (TCS) have a rapid onset of action and the availability of varying strengths enables treatment to be adjusted to the severity of the psoriasis.[27-30] **TCS are especially useful for difficult-to-treat presentations of psoriasis** (see Table 3).[33] A recent review showed that TCS and Vit D analogues had similar outcomes when used for psoriasis but TCS were more effective for scalp psoriasis.[7] Patients should not be left on continuous TCS for prolonged periods; ideally there should be a break of 4 weeks between each course of TCS, with tapering of dose, rather than an abrupt discontinuation, to prevent flare-up of the psoriasis.[1] Continuous use of potent or very potent TCS may cause psoriasis to become unstable and/or lead to systemic side effects if used on >10% BSA.[1]
Older treatments (**dithranol** and **coal tar**) are more difficult for the patient to manage and therefore are **no longer first-line topical therapeutic options**, except for specific presentations (e.g. tar or tar/salicylic acid shampoos for **scalp psoriasis**).[6,34] They may be useful in difficult cases of plaque psoriasis (used in a day care or inpatient setting). These treatments may also be used with other topical (e.g. TCS) or systemic therapies or phototherapy to optimise response.[6,34]
The calcineurin inhibitor **tacrolimus** has been reported to be an effective alternative to TCS for treating flexural and facial psoriasis (unlicensed indication in Ireland).[1,6,34]
Combination topical therapy (typically TCS with Vit D analogues or coal tar) is recommended if topical monotherapy fails to achieve remission, prior to initiating the next line of treatment; this may **improve response and improve the safety profile** by enabling reduction of the dose of the individual preparations.[1] A recent systematic review found that TCS / Vit D analogue combination therapy was significantly more effective than either as monotherapy.[7]

SYSTEMIC THERAPY

Systemic therapies are used for patients (a) with extensive psoriasis or (b) whose psoriasis has failed to respond to, or who are intolerant of topical therapies, or (c) where the disease is having a significant impact on their physical, psychological or social wellbeing.[1,6,11] Systemic therapies should be under **specialist supervision**; patient preference should be taken into account, since they each have different toxicity profiles (e.g. teratogenicity, skin cancer risk) and patients will need **ongoing advice and**

supervision to optimise adherence and to minimise adverse outcomes.[1,3,34,35]

Oral Pharmacotherapies

The oral therapies currently authorised for use are presented in Table 4.

Table 4: Oral systemic therapies for psoriasis[34,36-41]

Drug	Dosage regimen	Adverse effects include*	Special warnings include**
Methotrexate (immuno-suppressant)	10 to 25mg **once weekly** titrated to patient response (onset of action 1 to 7 wks). **Folic acid** 5mg/wk may ↓ GI toxicity, but not taken on same day. (S/C route may be used as alternative)	↑ risk of infections, ↓ WCC, GI upset (nausea very common), ↑ LFTs → risk of liver fibrosis (when total dose > 1.5g), headache, ↓ renal function, **teratogenic**. Risk of drug interactions.	**Ensure adequate contraception** (males + females). Regular LFTs and U&E (weekly initially); check type III procollagen (marker of liver fibrosis) at baseline and quarterly during treatment. Avoid / reduce alcohol intake during use.
Ciclosporin (immuno-suppressant)	2.5 to 5mg/kg/day titrated to patient response and baseline renal function. Blood level affected by many drugs	↓ WCC, ↑ lipids, ↑ LFTs (+ bilirubin) renal dysfunction, headache, GI upset, photosensitivity and ↑ BP. **Risk of multiple drug interactions.**	Regular U&E, LFTs, FBC and BP monitoring. Avoid other nephrotoxic drugs. **Should not be used with phototherapy**.
Acitretin (vitamin A analogue)	25 to 50mg/day titrated to patient response. (not licensed for continued use > 6 months)	Skin / mucosal dryness, skin atrophy, pruritus, flushing, ↑ LFTs and ↑ lipids, arthralgia, myalgia. **Teratogenic.**	**Ensure adequate contraception** during and for 3 years after use, due to teratogenicity risk. C/I during breast-feeding. Regular LFTs / blood lipid tests required.
Apremilast (PDE4 inhibitor)	30mg every 12 hours (titrated from 10mg daily – see SmPC) (*second line systemic therapy*; no experience beyond 52 wks)	Upper RTI, insomnia, depression, headache, cough, diarrhoea, nausea, vomiting, anorexia, back pain, fatigue, tiredness.	Monitoring for changes in mood required (see text). Monitor weight regularly. Dose ↓ (30mg/day) needed in severe renal dysfunction. C/I in some hereditary diseases.
Dimethyl fumarate (immuno-modulator)	Dose titrated ↑ from 30mg daily until response / max tolerated dose; max dose is 720mg daily. *(second line systemic therapy)*	↓ or ↑ WCC, ↑ eosinophils, ↑LFTs headache, diarrhoea, constipation, abdominal pain, nausea, vomiting, skin redness and pruritus, fatigue.	Regular FBC and LFTs. Monitoring for opportunistic infections required (see text); treatment should be discontinued if this occurs.

*only common / very common ADRs shown here; refer to full listing (**section 4.8**) in each Summary of Product Characteristics (SmPC) at www.hpra.ie.
full details in **section 4.4 of each SmPC. BP=blood pressure; C/I=contraindicated; FBC=full blood count; GI=gastrointestinal; LFTs=liver function tests; PDE4= phosphodiesterase type-4 inhibitor; RTI=respiratory tract infection; S/C=subcutaneous; U&E=urea and electrolytes; WCC=white cell count.

Methotrexate (MTX) is regarded as the **first-line oral systemic pharmacotherapy for psoriasis**.[1,11] It has been shown to produce 75% reduction in PASI in up to 40% patients.[36] **It is also effective in patients with PsA**.[11] MTX can be used as maintenance (long-term) management, where it should be used at the lowest effective dose with regular hepatic monitoring (Table 4). **Patients need to be educated about the MTX once-weekly regimen**.[36]

Ciclosporin is also effective (especially for acute flares or palmoplantar psoriasis) and has a rapid onset of action; however it is not suitable for long-term management, due to its toxicity (Table 4).[11,38]

Acitretin has a slower onset of action but is well tolerated by patients; it is particularly useful for palmoplantar pustular psoriasis.[11,39] However as a vitamin A analogue it is **highly teratogenic** and requires strict pregnancy prevention measures (Table 4); there is no apparent effect on sperm.[39]

Apremilast exerts its anti-inflammatory effect by modulating the expression of cytokines and mediators associated with psoriasis (Table 4).[41] It is **recommended for use when other oral systemic therapies have failed or are not tolerated**.[40] It is also effective in PsA.[43] Cases of **depression** and **suicidality** have been reported with its use; therefore, patients on apremilast should be carefully monitored for mood changes.[40]

Dimethyl fumarate is currently **recommended for use in severe psoriasis which has failed to respond to phototherapy or other oral systemic therapies, or where such treatments are not tolerated**.[41] A recent appraisal noted that dimethyl fumarate showed efficacy in severe psoriasis which appeared to be less effective than systemic biological therapies or apremilast.[44] Patients should be **monitored for the development of opportunistic infections** as cases of progressive multifocal leukoencephalopathy (**PML**) have been reported in patients taking dimethyl fumarate.[41] Renal dysfunction (including Fanconi Syndrome) has been reported with other fumaric acid ester-containing products.[45]

Biological Pharmacotherapies

Biological pharmacotherapies ("**biologics**") include monoclonal antibodies and a variety of protein-based medicines, which work by targeting the activity of the specific immune mediators, known to be involved in the pathogenesis of psoriasis.[2,10,11] These are normally used to treat moderate or severe psoriasis following failure of other systemic therapies or where a patient is intolerant of other systemic therapies.[1,18] All biologics require **specialist initiation and ongoing patient supervision**. In view of their different safety profiles, prescribers are advised to consult the individual Summary of Product Characteristics (SmPC) to inform clinical decision making for individual patients.[18] Table 5 lists the biologics authorised for psoriasis; many are also authorised for PsA. It is not possible to present all the complex prescribing and safety details for each biologic in this bulletin; the SmPC for each of the listed medicines contains full prescribing information and is available at: **www.hpra.ie**.

Table 5: Biologics authorised for use in psoriasis[46-52]

Authorised medicines (route)	Class precautions for use
Tumour Necrosis Factor α [TNF-α] inhibitors* • Adalimumab (S/C injection) • Etanercept (S/C injection)** • Infliximab (I/V infusion)**	Pre-treatment screening and ongoing monitoring for TB and HBV is required. ↑ risk of infections and risk of worsening HF → monitoring required during treatment. Periodic skin exam while on treatment (potential ↑ risk of non-melanoma skin cancers especially with prior phototherapy or immunosuppression). Risk of blood dyscrasias → patients advised to seek medical attention if they develop signs and/or symptoms. Live vaccines should not be given while on treatment. Use only after full B/R assessment in patients with demyelinating disease; d/c should be considered if signs of demyelination occur.
Interleukin [IL] inhibitors (all via S/C injection) • Brodalumab • Ixekizumab • Secukinumab* • Ustekinumab*	Pre-treatment screening to rule out TB is required. ↑ risk of infection therefore patients advised to seek medical attention if they develop signs / symptoms. ↓ WCC may occur. Periodic skin exam while on treatment (potential ↑ risk of non-melanoma skin cancers with prior phototherapy / patients >60 yrs old). Live vaccines should not be given while on treatment. [Suicidal ideation and behaviour reported with brodalumab usage; patients need screening and then regular review].

*these agents are also authorised for use in psoriatic arthritis. **biosimilars are currently available for these biological agents. B/R=benefit/risk. HBV=hepatitis B virus; HF=heart failure; I/V=intravenous; S/C=subcutaneous; TB=tuberculosis; WCC=white cell count; d/c=discontinuation.

Clinical guidance on the use of biologics: The British Association of Dermatologists currently recommends that **biologics should be used in patients with moderate to severe psoriasis who have failed to respond to, or who have a contra-indication to, or are intolerant of, other systemic therapies and/or phototherapy** – see next section).[1,11,18]

TNF-α inhibitors have been used for the treatment of **psoriasis and PsA** for several years. Clinical guidelines recommend **adalimumab** as a potential first-line anti-TNF-α option, due to its reported superior benefit/risk profile, compared with the others;[53,54] **infliximab** is recommended for very severe psoriasis or for subsequent usage (high efficacy but poorer tolerability).[18,53,55]

The IL-inhibitors inhibit various interleukins thought to be implicated in the development of psoriasis. **Secukinumab** and **ustekinumab** are recommended as potential first-line options because of their positive benefit/risk profile; they are also licensed for PsA.[1,18] *Candida* infections have been reported with use of certain IL-inhibitors (particularly IL-17 inhibitors).[56]

Sequential treatment with biologics: Patients not responding to treatment (despite optimum dosing) or experiencing toxicity with one biologic should be offered a second agent, either from within the same class or another class as an alternative treatment.[35] A recent review of patients (n=2,980) receiving biologic therapy for psoriasis reported that 34% had experienced treatment modifications during the first year of treatment; these included a change to, or discontinuation of a biological therapy, and / or concomitant use of oral therapies.[57] There was no difference between biologic-naïve and non-naïve patients in terms of treatment modification.

The duration of biological treatment: Following response to biological treatment, patients should be reviewed at 6-monthly intervals; the decision to continue treatment should be weighed against the potential risks of long-term usage (e.g. risk of immunogenicity, parenteral administration issues, other precautions see Table 5) versus the potential for relapse, and following consultation with the patient.[1,18,58] Etanercept, adalimumab and ustekinumab appear to be generally well tolerated with long-term use (up to 4 years).[59] A recent review of long-term psoriasis registry data did not show an increased non-skin cancer risk with use of these agents; non-melanoma skin cancer risk is confounded by the nature of the disease and potential risk associated with other treatments such as phototherapy.[53] Table 6 summarises the recommended process for choosing a biological agent for a patient with psoriasis.

Table 6: Guidance on use of biological therapy for psoriasis[18,53]

1. Offer biological therapy to patients with moderate to severe psoriasis requiring systemic therapy if MTX and ciclosporin (or phototherapy) have failed, are not tolerated or are contraindicated, or psoriasis involves difficult-to-treat sites (face, scalp, nails).
2. Take into account the patient's disease status, co-morbidities (e.g. PsA, HF, IBD, demyelinating disease), treatment goals, patient preference (e.g. administration regimen) when choosing the first-line biologic; provide appropriate patient information.
3. Assess initial response to therapy (e.g. using PASI* and DQLI**) at the time point appropriate to the biologic prescribed (between 10 and 20 weeks as per SmPC for each biologic); if successful response, review every 6 months.
4. If no response (*primary failure*) despite optimal dosage or if a biologic is not tolerated, offer another biologic (taking note of point 2).
5. If initial response is followed by subsequent relapse (*secondary failure*), offer another biologic (taking note of point 2).
6. If no response to second biologic, check for modifiable patient factors (e.g. poor adherence, obesity); optimise adjunctive therapy (e.g. add in MTX, change from PO to S/C MTX if already on MTX) or offer another biologic.
7. If no response at this stage, consider other approaches (e.g. in-patient management, oral systemic therapies, phototherapy).

*Psoriasis Area and Severity Index. ** Dermatology Life Quality Index. MTX=methotrexate; PsA=psoriatic arthritis; HF=heart failure; IBD=inflammatory bowel disease.

PHOTOTHERAPY

Phototherapy is a **valuable first-line systemic therapy** used to treat **widespread, severe or refractory psoriasis**.[1,11] It has a rapid onset of action and is highly effective; it may be combined with any of the topical therapies to improve response and prolong remission.[1,3,11] It requires specialist dermatology facilities, therefore it may not be available for all patients with psoriasis in Ireland.

Narrowband ultraviolet B (**NB-UVB**) is administered 3 times weekly, typically for 6 to 8 weeks; side effects include skin burning, photosensitivity and photoageing.[11,60] **PUVA** combines the use of a photosensitiser (topical or oral **P**soralen) with **UVA** radiation therapy; this is a particularly effective treatment for palmoplantar pustular psoriasis.[1,11] PUVA is administered twice weekly and side effects include skin burning, photosensitivity, severe nausea and headache (thought to be related to oral psoralen).[11] There is a potential risk of skin cancer with cumulative dosage, (especially with PUVA) in patients who have received >150 treatments.[1]

SUMMARY

Psoriasis is a chronic condition, requiring life-long management. While many patients can be managed successfully in primary care, others will require specialist input in treating the skin manifestations, or associated co-morbidities such as PsA, CVD or inflammatory bowel disease. Patient involvement at all stages of the treatment process and ongoing education are essential to ensure adherence to therapy and optimise quality of life.[1,6,23] Figure 1 outlines a structured approach to managing psoriasis.

Figure 1: Management plan for psoriasis[1,3,6,11,18]

Evaluate the extent of skin involvement / severity of psoriasis and look for presence of co-morbidities

Localised / mild to moderate disease	**Extensive or severe disease**	**If co-morbidities present**
↓ Topical therapies appropriate to site of disease ↓ Vit D analogue / TCS / coal tar / dithranol ↓ Combination topical therapy may be used if inadequate response to monotherapy ↓ If no response, or the degree of psoriasis / patient circumstances warrants ↓ →Specialist referral for systemic therapy→ [**see next column**]	↓ Specialist referral for systemic pharmacotherapy or phototherapy 1. **Oral** (non-biological) agents (MTX, ciclosporin, acitretin) ↓ 2. **Biologics** if oral agents fail or there is intolerance of or C/I to oral therapies (TNF-α inhibitors; IL-inhibitors) **Phototherapy** is a useful alternative therapy especially for severe / refractory disease	↓ Appropriate specialist referral (PsA* / IBD / CVD) ↓ Multidisciplinary team input as per disease manifestation(s) ↓ Co-morbidities will impact on systemic pharmacotherapy choice for psoriasis (e.g. many agents are authorised for PsA and IBD as well as psoriasis; some co-morbidities (e.g. CVD) may C/I use of certain medicines)

*urgent rheumatology referral recommended if psoriatic arthritis is present. PsA=psoriatic arthritis; IBD=inflammatory bowel disease; CVD=cardiovascular disease; TCS=topical corticosteroids; C/I=contraindicated.

List of references available on request. Date of preparation: November 2017

UPDATE ON PSORIASIS 2017; Volume 23: Number 5

1. Psoriasis: assessment and management: Clinical guideline National Institute for Health and Care Excellence. nice.org.uk/guidance/cg153. [Published: 24 October 2012, updated September 2017]. Available online at: www.nice.org.uk. Accessed 8th November 2017

2. Nestle F et al, Mechanisms of Disease: Psoriasis. NEJM 2009; 361: 496-509.

3. Psoriasis. Health A-Z, Health Services Executive. Available online at: http://www.hse.ie/eng/health/az/P/Psoriasis/ . Accessed 19th October 2017

4. Global report on Psoriasis, World Health Organisation 2016. Available online at: http://apps.who.int/iris/bitstream/10665/204417/1/9789241565189_eng.pdf. Accessed 29 November 2017 T

5. The Burden of Psoriasis: Epidemiology, Quality of Life, Co-morbidities and Treatment Goals. Irish Skin Foundation (date of preparation April 2015). Available online at: https://irishskin.ie/wp-content/uploads/2016/08/Burden_of_Psoriasis_Report_final.pdf. Accessed 29 November 2017.

6. Psoriasis in The Oxford Handbook of Medical Dermatology (second ddition). Eds. Susan Burge, Rubeta Marin, Dinny Wallis. Oxford University Press, 2016. Chapter 9, pps 190-209

7. Mason AR, Mason J, Cork M, Dooley G, Hancock H. Topical treatments for chronic plaque psoriasis. Cochrane Database of Systematic Reviews 2013, Issue 3. Art. No.: CD005028. DOI: 10.1002/14651858.CD005028.pub3. [review]

8. Takeshita J et al, Psoriasis and comorbid diseases: Implications for management. J Am Acad Dermatol 2017;76:393-403

9. Gisondi P et al, Psoriasis and the metabolic syndrome. Clinics in Dermatology 2017; doi: 10.1016/j.clindermatol.2017.09.005

10. Hawkes JE et al, Psoriasis pathogenesis and the development of novel targeted immune therapies. J Allergy Clin Immunol 2017;140:645-53

11. Higgins E, Psoriasis. Medicine 2017; 45 (6): 368-78

12. Takeshita J et al, Psoriasis and comorbid diseases: Epidemiology. J Am Acad Dermatol 2017;76:377-90

13. Noe et al, Objective Measures of Psoriasis Severity Predict Mortality: A Prospective Population-Based Cohort Study. J Invest Dermatol. 2017 (Aug 23) doi: 10.1016/j.jid.2017.07.841. [Epub ahead of print]

14. Chi CC, Ko SH, Yeh ML, Wang SH, Tsai YS, Hsu MY. Lifestyle changes for treating psoriasis. Cochrane Database of Systematic Reviews 2015, Issue 11. Art. No.: CD011972. DOI: 10.1002/14651858.CD011972. [protocol]

15. Guttman-Yassky E et al, Contrasting pathogenesis of atopic dermatitis and psoriasis—Part I: Clinical and pathologic concepts. J Allergy Clin Immunol 2011;127:1110-8.

16. Bachmann F, Evaluation of disease severity: clinical scores and questionnaires *in* Psoriasis, Diagnosis and Management. (2015) Eds. W Sterry, R Sabat, S Phillipp. Publishers John Wiley & Sons Ltd. UK. Pps 129-139

17. Armstrong A et al, From the medical board of the national psoriasis foundation: treatment targets for plaque psoriasis. J Am Acad Dermatol 2017; 76: 290-8

18. Smith CH et al, British Association of Dermatologists guidelines for biologic therapy for psoriasis 2017. British Journal of Dermatology 2017; 177: 628–636

19. Nwe S and Gordon K, Psoriasis and Associated Diseases in Psoriasis, Diagnosis and Management. (2015) Eds. W Sterry, R Sabat, S Phillipp.Publishers John Wiley & Sons Ltd. UK. Pps 143-57

20. Ritchlin C et al, Psoriatic Arthritis. NEJM 2017; 376: 957-70.

21. Tools for diagnosis in psoriasis, British Association of Dermatologists. Available online at: http://www.bad.org.uk/healthcare-professionals/psoriasis. Accessed 14 November 2017

22. Shah K et al, Real-world burden of comorbidities in US patients with psoriasis. J Am Acad Dermatol 2017; 77: 287-92

23. Thorneloe RJ et al, Adherence to medication in patients with psoriasis: a systematic literature review. British Association of Dermatologists 2013 168, pp20–31

24. Oilatum emollient preparations® Summaries of Product Characteristics. Available online at: www.hpra.ie. Accessed 14th November 2017.

25. Dovonex® (calcipotriol). Summary of Product Characteristics. Available online at: www.medicines.ie. Accessed 16th October 2017

26. Silkis® (calcitriol) Summary of Product Characteristics. Available online at: www.hpra.ie. Accessed 16th October 2017

27. Hydrocortisone 1% cream. Summary of Product Characteristics. Available online at: www.hpra.ie. Accessed 10th November 2017

28. Modrasone Cream 0.05% w/w® Summary of Product Characteristics. Available online at: www.hpra.ie. Accessed 10th November 2017

29. Betnovate Cream 0.1% w/w® Summary of Product Characteristics. Available online at: www.hpra.ie. Accessed 10th November 2017

30. Dermovate Cream® Summary of Product Characteristics. Available online at: www.hpra.ie. Accessed 23rd October 2017

31. Dithrocream® Summary of Product Characteristics. Available online at: www.hpra.ie. Accessed 16th October 2017

32. Psoriderm® (cream, bath emulsion, scalp lotion) Summary of Product Characteristics. Available online at: www.hpra.ie. Accessed 16th October 2017

33. Skin [management of skin conditions] *in* British National formulary Number 67 (March – September 2014). Chapter 13 pps 763-810

34. Kragballe K et al, Treatment of plaque psoriasis *in* Psoriasis, Diagnosis and Management. (2015) Eds. W Sterry, R Sabat, S Phillipp.Publishers John Wiley & Sons Ltd. UK. Pps 163-213

35. Leman J and Burden AD, Sequential use of biologics in the treatment of moderate-to-severe plaque psoriasis. British Journal of Dermatology 2012 167 (Suppl. 3), 12–20

36. Warren RB et al, British Association of Dermatologists' guidelines for the safe and effective prescribing of methotrexate for skin disease 2016. British Journal of Dermatology (2016) 175, pp 23–44

37. Methotrexate 2.5mg Summary of Product Characteristics. Available online at: www.hpra.ie. Accessed 16th October 2017 [hospira mercury orion]

38. Sandimmun® (ciclosporin) Summary of Product Characteristics. Available online at: www.hpra.ie. Accessed 16th October 2017

39. Neotigason® (acitretin) Summary of Product Characteristics. Available online at: www.hpra.ie. Accessed 16th October 2017

40. Otezla® (apremilast) Summary of Product Characteristics. Available online at www.ema.europa.eu. Accessed 16th October 2017

41. Skilarence® (Dimethyl fumarate). Summary of Product Characteristics. Available online at www.ema.europa.eu. Accessed 17th October 2017

42. Apremilast for treating moderate to severe plaque psoriasis. National Institute for Health and Care Excellence. Technology appraisal guidance Published: 23 November 2016. Available online at: https://www.nice.org.uk/guidance/ta419/resources/apremilast-for-treating-moderate-to-severe-plaque-psoriasis-pdf-82604611623877. Accessed 26th October 2017

43. Apremilast for treating active psoriatic arthritis. National Institute for Health and Care Excellence. Technology appraisal guidance Published: 22 February 2017. Available online at: https://www.nice.org.uk/guidance/ta433/resources/apremilast-for-treating-active-psoriatic-arthritis-pdf-82604722478533. Accessed 26th October 2017

44. Dimethyl fumarate for treating moderate to severe plaque psoriasis. Technology appraisal guidance (nice.org.uk/guidance/ta475). Published: 6 September 2017. Available online at: www.nice.org.uk. Accessed 14 November 2017

45. Balak DMW et al, Efficacy, effectiveness and safety of fumaric acid esters in the treatment of psoriasis: a systematic review of randomised and observational studies. Brit J Dermatol 2016; 175: 250-62

46. Humira® Summary of Product Characteristics. Available online at www.ema.europa.eu. Accessed 16th October 2017

47. Enbrel® Summary of Product Characteristics. Available online at www.ema.europa.eu. Accessed 16th October 2017

48. Remicade® Summary of Product Characteristics. Available online at www.ema.europa.eu. Accessed 16th October 2017

49. Kyntheum® (brodalumab). Summary of Product Characteristics. Available online at www.ema.europa.eu. Accessed 17th October 2017

50. Taltz® (Ixekizumab) Summary of Product Characteristics. Available online at www.ema.europa.eu. Accessed 16th October 2017

51. Costentyx® (secukinumab) Summary of Product Characteristics. Available online at: www.medicines.ie. Accessed 16th October 2017

52. Stelara® (ustekinumab) Summary of Product Characteristics. Available online at www.ema.europa.eu. Accessed 16th October 2017

53. Guidelines for biologic therapy for psoriasis: Methods, evidence and recommendations. [FULL VERSION] British Association of Dermatologists, April 2017. .Available online at: www.bad.org.uk. Accessed 1st November 2017

54. Adalimumab for the treatment of adults with psoriasis. Technology appraisal guidance. Published: 25 June 2008 nice.org.uk/guidance/ta146. Available at: www.nice.org.uk. Accessed 6 november 2017

55. Infliximab for the treatment of adults with psoriasis Technology appraisal guidance Published: 23 January 2008 nice.org.uk/guidance/ta134 . Available at: www.nice.org.uk. Accessed 6 november 2017

56. Saunte DM et al, Candida infections in patients with psoriasis and psoriatic arthritis treated with interleukin-17 inhibitors and their practical management. British Journal of Dermatology (2017) 177, pp47–62

57. Iskandar IYK et al, Patterns of biologic therapy use in the management of psoriasis: cohort study from the British Association of Dermatologists Biologic Interventions Register (BADBIR)*. British Journal of Dermatology (2017) 176, pp1297–1307

58. De Mozzi P et al, Psoriasis: an evidence-based update. Report of the 9th Evidenced Based Update Meeting, 12 May 2011, Loughborough, U.K. British Association of Dermatologists 2012 166, pp252–260

59. Rustin MHA, Long-term safety of biologics in the treatment of moderate-to-severe plaque psoriasis: review of current data. British Journal of Dermatology 2012 167 (Suppl. 3), 3–11.

60. Moseley H et al, Guidelines on the measurement of ultraviolet radiation levels in ultraviolet phototherapy: report issued by the British Association of Dermatologists and British Photodermatology Group 2015. British Journal of Dermatology (2015) 173, pp333–350.