MODERATE-TO-SEVERE PSORIASIS

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INTRODUCTION
Psoriasis is a chronic skin condition that can have a marked physical and psychological impact on those affected. While most patients have mild disease that can be managed in primary care, those with moderate-to-severe psoriasis require referral for specialist intervention and access to therapy such as biologics.

Biologics are an option for patients who have failed to respond to standard systemic therapy or in those for whom systemic therapy is unsuitable. The scope of this supplement is to enhance the understanding of biologics.

Dr Brian Malcolm provides his opinion on the role of the GP in the management of moderate-to-severe psoriasis.

Dr Rebecca Ellard and Dr Anshoo Sahota discuss the key elements of the diagnosis and management of moderate-to-severe psoriasis.

Dr Amy Foulkes and Dr Richard Warren focus on long-term control of psoriasis.

Dr Alia Ahmed and Dr Anthony Bewley present a case of a patient who was successfully treated with biologics.

Dr David Chandler and Dr Anthony Bewley provide a summary of the recently published NICE guideline on psoriasis.

Dr Justine Kluk, Dr Sandy McBride and Professor Malcolm Rustin present a management algorithm to aid the diagnosis, treatment and referral of patients with moderate-to-severe psoriasis.

Dr Paula Hensler, Editor, MIMS Dermatology

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Psoriasis is common, affecting approximately 2% of the UK population. Such prevalence demands that a GP should have an up-to-date knowledge of this condition, specifically the potential triggers, the treatments available and when to refer patients to secondary care.

**PHYSICAL AND PSYCHOLOGICAL DISTRESS**
Psoriasis can be very distressing. Patients can be significantly disabled by plantopalmar pustular psoriasis, severe scalp psoriasis, fissuring hyperkeratotic psoriasis of the hands, or rarely, acropustulosis. Genital involvement can also lead to high levels of sexual distress.

GPs are well placed to offer support and manage patient expectations about treatment outcomes.

**RECOGNISING TRIGGERS**
GPs should understand the pathogenesis of the psoriasis to avoid exacerbations with the use of prescribed drugs known to potentially worsen psoriasis. These include lithium, antimalarials and beta-blockers. GPs can also offer advice regarding exacerbating lifestyle factors such as alcohol, stress and smoking, especially as there is a growing recognition that psoriasis is an independent risk factor for cardiovascular disease.

**TREATMENT KNOWLEDGE**
It is important that GPs have a good understanding of topical treatments. GPs must also be aware that certain topical treatments, particularly steroids, may have systemic effects if they are used long term. Furthermore, the usefulness of simple emollients to keep skin hydrated should never be underestimated. Even if a patient is under specialist care, the GP still has a pivotal role in repeat prescribing and shared-care plans.

**SECOND-LINE TREATMENTS**
GPs should have understanding of the patient’s individual needs. Furthermore, there should be an awareness of commonly used second-line drugs and their implications, for example, family planning issues with the use of retinoids, alcohol intake with methotrexate, renal function, hypertension and a history of cancer with ciclosporin and a past history of infections, particularly TB, and cancer with biologics.

**REFERRAL TO SECONDARY CARE**
Referral should be considered when there is diagnostic doubt; when topical treatments have failed; in extensive disease and where there are difficult treatment sites. Erythrodermic or generalised pustular psoriasis also warrant referral, as does severe arthropathy. GPs have an important role in writing relevant and precise referral letters.

Even when a patient requires specialist care, there is potential for a knowledgeable GP to contribute to a holistic management approach.

Dr Brian Malcolm is associate specialist, GP principal and GPSI in dermatology in Barnstaple, Devon

**REFERENCES**
Diagnosis and management of moderate-to-severe psoriasis

Management should include early and continual assessment from first presentation through to specialist care, write Dr Rebecca Ellard and Dr Anshoo Sahota

Psoriasis is a chronic disease that affects approximately 1-3% of the population, with or without psoriatic arthritis. Patients typically present with 'unsightly' lesions which are sometimes itchy; for many there is no identifiable cause. Psoriasis can have a profound effect on quality of life and is also associated with cardiovascular disease. Recent NICE guidance states that management should include early and continual assessment of psoriasis from first presentation in primary care through to specialist care. The guidance focuses on disease severity, physical and psychological effect, assessment for referral and treatment choice.

ASSESSMENT OF PSORIASIS

Various tools can be used to measure physical severity or functional severity of psoriasis. Physical severity is categorised as clear, mild, severe or very severe, as outlined in the Physicians' Global Assessment (PGA) or more precisely with the Psoriasis Area and Severity Index (PASI). Doctors should also note when nails, face, scalp or genitals are affected as these are particularly difficult to treat, along with symptoms or signs of psoriatic arthritis.

The PASI divides the body into head, arms, trunk and legs and notes the amount of redness, thickness and scale, along with percentage of area affected. A score maximum of 72 is given, and can help assess a patient's response to treatment pre- and post intervention. The majority of patients will have mild disease (<3% body affected) which can be successfully managed with topical therapy. More extensive disease (>10% body affected or PASI score >12) usually needs specialist input.

Functional severity can be measured with quality-of-life tools such as the Dermatology Life Quality Index (DLQI). Psychological morbidity is not well represented with these tools, but can be an important marker for disease impact. NICE guidelines suggest assessing impact on daily living, ability to cope with the treatment regimen, change in mood and impact on family or carers.

STEPWISE APPROACH TO MANAGEMENT

Management of chronic illness such as psoriasis should include physical and psychological aspects. It is helpful to manage expectations at an early stage and allow the patient control over their treatment, particularly with topical therapy. There is often the need to combine topical and systemic treatments.

The first step is topical treatment including the daily use of emollients. Patients should be reassured that almost any emollient is useful even if not prescribed or 'dermatological' in nature. Most patients will also need intermittent topical corticosteroid, with or without a vitamin D analogue, or a coal tar preparation.
Less commonly used products such as dithranol might be best used under specialist supervision. Second-line is phototherapy where narrow-band UVB has become the first choice followed by psoralen with UVA (PUVA). Some patients find the time commitment for phototherapy (typically 20-30 treatments in two-months) too onerous and will move to the third step.

Third-line treatments, for adult patients only, include ciclosporin, methotrexate and acitretin. These can be very effective although side-effects, including renal and hepatic toxicity, mean that patients should be monitored by a specialist. NICE guidance suggests methotrexate as the first choice in adults with moderate-to-severe psoriasis where topical therapies and phototherapy have not worked and where there is functional impairment and high levels of distress. Where psoriatic arthritis is present, a systemic agent should be chosen in discussion with a rheumatologist.

Adults with moderate-to-severe psoriasis who have failed to respond to, or cannot tolerate two systemic drugs should be offered the fourth step of biological agents including TNF-antagonists such as adalimumab, etanercept and infliximab, and an anti-IL-12/23 monoclonal antibody such as ustekinumab. These drugs are generally well tolerated in the majority of people.

**TRIGGERS AND ASSOCIATIONS**

In a newly-diagnosed patient, it is important to consider triggers, such as a streptococcal infection causing guttate psoriasis. Patients should be asked about common triggers such as high alcohol intake and stress, as it may be possible to prevent the use of systemic agents by avoiding such triggers. A specific trigger for palmoplantar pustular psoriasis is cigarette smoking (especially in women in their fourth or fifth decade of life) so patients should be made aware of this association.

**FLARES**

When psoriasis flares it can mean there is more of the disease or, less commonly, it can indicate the disease has become unstable and may become a systemic problem. In these patients specialist input should be sought. An inpatient stay may be necessary, particularly if the psoriasis is unstable. Traditional treatments such as bed rest and bland emollients can be helpful and rapidly working systemic agents such as ciclosporin may be useful in the short-term until the flare settles.

With the increasing recognition of the health, economic and psychological burden of psoriasis, the recent NICE guidance is a helpful resource. With the knowledge of a few simple principles of management, psoriasis can be gratifying to treat.

Dr Rebecca Ellard is a foundation doctor and Dr Anshoo Sahota is a consultant dermatologist, Barts Health NHS Trust

**REFERENCES**

The management of psoriasis can be interesting and rewarding. Optimal use of psoriasis treatments can lead to a vast improvement in a patient’s quality of life. It is, however, important to be honest with patients and explain that treatment is non-curative but aims to allow regression of psoriasis plaques to normal-looking skin. Whilst guidelines exist for the various severities of psoriasis, treatment options should be tailored to the individual. This review will briefly discuss new guidance and newer therapies in the treatment of severe psoriasis.

**TIMELY REFERRAL**

NICE have recently published guidelines on the management of psoriasis from primary through to tertiary care. Useful elements for the primary care physician include referral recommendations for specialist advice where:

- psoriasis is severe or extensive, for example more than 10% of body surface area (BSA; the size of the palm is approximately 1% BSA)
- there is diagnostic uncertainty
- psoriasis cannot be controlled with topical therapy
- there is acute guttate psoriasis that requires phototherapy
- nail disease has a major functional or cosmetic impact
- where any type of psoriasis is having a major impact on a person’s physical, psychological or social wellbeing.

NICE additionally recommend using a recognised questionnaire, such as the Psoriasis Epidemiology Screening Tool (PEST) to screen for the presence of psoriatic arthritis (PsA).

**BIOLOGICS**

The major advance in the management of severe psoriasis in the past decade has been the introduction of injectable biologic therapies, of which there are two approved groups in the treatment of psoriasis: TNF inhibitor agents (adalimumab, etanercept and infliximab) and those inhibiting interleukins (IL)-12 and IL-23 (ustekinumab).

Strict eligibility criteria are applied for use of all biologics, including:

- history of chronic psoriasis (more than six months);
- documented failure or unsuitability for traditional systemic therapies and phototherapy and;
- physical severity and quality of life detriment above a certain threshold.

RCTs have shown that TNF inhibitors are a good therapeutic option for PsA and etanercept is now approved for the management of severe psoriasis in children.

**EVIDENCE BASE**

The most recent biologic in use is ustekinumab, a fully humanised monoclonal antibody to the p40 subunit, common to IL-12 and IL-23. Large RCTs have demonstrated that ustekinumab is effective in psoriasis with a rapid onset of action and high response rates. The Psoriasis Area Severity Index (PASI) is a validated composite score of psoriasis severity, where a 75% improvement from baseline score is termed a PASI 75 response. In a RCT of 1,230 patients with moderate to severe psoriasis, 67% of patients receiving a 45mg dose and 76% of those receiving a 90mg
Treatment aims to regress psoriasis plaques

dose reached a PASI 75 at week 12, compared with 4% of those receiving placebo. After dose loading, ustekinumab is injected every 12 weeks. These short-term data are impressive and are supported by significant improvements in patient quality of life. Ustekinumab was generally well tolerated, without evidence of cumulative toxicity with increased duration of exposure.

However, extensions of clinical trials are not able to tell the full story about the safety of a therapy as any clinical trial has significant selection bias in the first instance. Thus, further safety data on all biologic therapies will come from large-scale registries that capture key data from those patients commencing systemic and biologic therapies. One of the best registries worldwide is being conducted in the UK, the British Association of Dermatologists’ (BAD) Biologic Interventions Register (BADBIR). Thus far, more than 3,500 biologic patients and 2,000 systemic patients have been recruited to BADBIR.

Whilst the majority of patients will have mild disease that can be managed effectively in primary care, an appreciation of newer therapies is crucial, as these can be life changing for those with severe disease.

Dr Amy Foulkes is dermatology specialist registrar and Dr Richard Warren is NIHR Senior Clinical Lecturer and Honorary Consultant Dermatologist, Salford Royal NHS Foundation Trust.

REFERENCES
Successful management of psoriasis can be challenging, write Dr Alia Ahmed and Dr Anthony Bewley

CLINICAL HISTORY
AC is a 65-year-old male with moderate-to-severe psoriasis. In the last ten years he had been trialled on a number of treatments, including hydroxyurea and methotrexate, with limited success. The patient also responded poorly to etanercept, with their Psoriasis Area Severity Index (PASI) dropping from 25 to only 22.4 over six months. A similar picture occurred with adalimumab (PASI dropping from 24 to 20.8 in six months). AC’s Dermatology Life Questionnaire Index scores (DLQI) ranged from 18 to 24 during this time. Ciclosporin was not given due to the patient’s high blood pressure.

The next step was to treat with ustekinumab (45mg 12-weekly). Within five months the PASI and DLQI scores dropped to zero, indicating disease clearance. To date, AC remains stable on ustekinumab, with no major side effects.

COMMENT
Treatment of moderate-to-severe psoriasis can be challenging. Topical therapy and conventional systemic agents are not always successful and may be associated with adverse side effects. In these circumstances, treatment with biologics is necessary. TNF-alpha and the interleukins (IL-12 and 23) have been identified as therapeutic targets in psoriasis. Biologic agents used for treatment of psoriasis include etanercept, adalimumab, infliximab and ustekinumab.

Ustekinumab is a monoclonal antibody directed against IL-12 and IL-23, and its efficacy has been evaluated in high-quality trials. A systematic review has suggested continuous treatment with biologic agents to control psoriasis.

NICE guidance has suggested initiation of ustekinumab in patients with severe psoriasis that have not responded to systemic therapy, or where there is an intolerance or contraindication. The guidance also suggests treatment should be stopped at 16 weeks if there is <75% reduction in PASI or there is <50% reduction in PASI plus <5 point reduction in DLQI from baseline.

The physician must first assess the reasons for non-response to treatment and rule out confounding factors such as adherence, infection, natural variation in disease and stress. The benefit-risk profile needs consideration for every patient, coupled with close monitoring.

Dr Alia Ahmed is clinical research fellow in dermatology and Dr Anthony Bewley is consultant dermatologist, Barts Health NHS Trust.

REFERENCES
This new guideline recommends holistic management, say Dr David Chandler and Dr Anthony Bewley

The new NICE guideline for psoriasis highlights key priorities for implementation, with the aim of improving the delivery of care.

**ASSESSMENT AND REFERRAL**

All patients with psoriasis should receive a complete and holistic assessment. Assessment of severity is based on clinical examination, and the Psoriasis Area and Severity Index (PASI). Assessment should be tailored to the individual, and it is vital to assess health-related quality of life. A recommended tool is the Dermatology Life Quality Index (DLQI).

The majority of patients are managed in primary care. Referral should be considered when there is diagnostic uncertainty, extensive disease, nail disease that has a functional and cosmetic impact, failure of topical treatments or the need for phototherapy, and where there are concerns about the patient’s wellbeing.

**COMORBIDITIES**

Psoriasis can be complicated by arthritis in up to 30% of patients. The use of a validated tool, for example the Psoriasis Epidemiological Screening Tool (PEST), is recommended to assess adults. Urgent referral to a rheumatologist is necessary if severe psoriatic arthritis is suspected.

Risk factors for cardiovascular disease are more prevalent in patients with psoriasis. Advice should be tailored to the individual and, where appropriate, include information about risk factor modification.

**TREATMENTS**

Patients should be involved in all treatment decisions. Topical therapy should be offered as first-line treatment and practical advice on their use should be provided. Initial treatment for adults with psoriasis affecting the trunk or limbs should consist of a corticosteroid plus vitamin D (combination) or a vitamin D analogue.

Narrowband UVB should be considered for plaque or guttate psoriasis that is unresponsive to topical treatments.

Conventional systemic agents can be offered where topical treatments and phototherapy have failed, with extensive disease (PASI>10), or with localised disease with functional impairment. Methotrexate is the first choice.

Biologics can be used when other systemic agents have failed. An alternative biologic should be considered if: the psoriasis does not respond to a first biologic (at 10 weeks for infliximab, 12 weeks for etanercept, and 16 weeks for adalimumab and ustekinumab); or the psoriasis improves but subsequently loses this response; or the biologic is not tolerated or is contraindicated.

These recommendations have been incorporated into a helpful ‘NICE pathway’.

Dr David Chandler is a medical SHO and Dr Anthony Bewley is a consultant dermatologist, Barts Health NHS Trust.

**REFERENCES**

By Dr Justine Kluk and Dr Shantini Rice, dermatology registrars, and Dr Sandy McBride and Professor Malcolm Rustin, consultant dermatologists, Royal Free London NHS Foundation Trust.

REFERENCES
STELARA® 45 mg solution for injection in pre-filled syringe

PRESCRIBING INFORMATION

ACTIVE INGREDIENT(S): Ustekinumab. Please refer to Summary of Product Characteristics (SmPC) before prescribing. INDICATION(S): Treatment of moderate to severe plaque psoriasis in adults who failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapies including ciclosporin, methotrexate and PUVA. DOSAGE & ADMINISTRATION: Under the guidance and supervision of a physician experienced in diagnosis and treatment of psoriasis. Subcutaneous injection. Avoid areas with psoriasis. For self-injecting patients ensure appropriate training, follow-up and monitoring during treatment. Adults & Elderly: Patients ≤ 100kg, 45 mg at week 0 followed by a 45 mg dose at week 4, then every 12 weeks. Patients >100 kg, 90 mg at week 0 followed by a 90 mg dose at week 4, then every 12 weeks (45 mg was less effective in these patients). Consider discontinuation if no response after 28 weeks. Children <18 years: Not recommended. Renal & Hepatic impairment: Not studied. CONTRAINDICATIONS: Hypersensitivity to product; clinically important, active infection. SPECIAL WARNINGS & PRECAUTIONS: Infections: Potential to increase risk of infections and reactivate latent infections. Caution in patients with a chronic infection or history of recurrent infection, particularly TB. Patients should be evaluated for tuberculosis prior to initiation of STELARA. Consider anti-tuberculosis therapy prior to initiation of STELARA in patients with past history of latent or active tuberculosis. Patients should seek medical advice if signs or symptoms suggestive of an infection occur. If a serious infection develops, they should be closely monitored and STELARA should not be administered until infection resolves. Malignancies: Potential to increase the risk of malignancy. No studies in patients with a history of malignancy or in patients who develop malignancy while receiving STELARA. Monitor all patients, in particular those older than 60, patients with a medical history of prolonged immunosuppressant therapy or those with a history of PUVA treatment for non-melanoma skin cancer. Concomitant immunosuppressive therapy: Caution, including when changing immunosuppressive biologic agents. Hypersensitivity reactions: Serious hypersensitivity reactions (anaphylaxis and angioedema) reported, in some cases several days after treatment. If these occur, discontinue STELARA immediately and institute appropriate therapy. Immunotherapy: Not known whether STELARA affects allergy immunotherapy. Latex sensitivity: Needle cover contains natural rubber (latex), may cause allergic reactions. SIDE EFFECTS: Serious side effects: Serious infections, malignancies. Very common: upper respiratory tract infection, nasopharyngitis. Common: hypersensitivity reactions (rash, urticaria), cellulitis, viral upper respiratory tract infection, depression, dizziness, headache, pharyngolaryngeal pain, nasal congestion, diarrhoea, pruritus, back pain, myalgia, arthralgia, fatigue, injection site erythema, antibodies to ustekinumab. Uncommon: herpes zoster infection, injection site reactions. Rare: serious hypersensitivity reactions (including anaphylaxis, angioedema), facial palsy Refer to SmPC for other side effects. FERTILITY: The effect of ustekinumab has not been evaluated.

PREGNANCY: Should be avoided. Women of childbearing potential: Use effective contraception during treatment and for at least 15 weeks post-treatment. LACTATION: Limited data in humans. INTERACTIONS: In vitro, STELARA had no effect on CYP450 activities. Vaccinations: Live vaccines should not be given concurrently with STELARA, and should be withheld for at least 15 weeks after last dose of STELARA. STELARA can resume at least 2 weeks after such vaccinations. No data on secondary transmission of infection by live vaccines in patients receiving STELARA. Concomitant immunosuppressive therapy: The safety and efficacy of STELARA in combination with other immunosuppressants, including biologics, or phototherapy have not been evaluated. LEGAL CATEGORY: POM PRESENTATIONS, PACK SIZES, PRODUCT LICENCE NUMBERS & BASIC NHS COSTS: STELARA 45mg: 1 x 0.5ml pre-filled syringe. EU/1/08/494/003. £2147 MARKETING AUTHORISATION HOLDER: JANSSEN-CILAG INTERNATIONAL NV, Turnhoutseweg 30, B-2340 Beerse, Belgium. FURTHER INFORMATION IS AVAILABLE FROM: Janssen-Cilag Ltd, 50 – 100 Holmers Farm Way, High Wycombe, Buckinghamshire, HP12 4EG UK. © Janssen-Cilag Ltd 2013

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Indicated for the treatment of moderate to severe plaque psoriasis in adults who have failed to respond to, or have a contraindication to, or are intolerant to other systemic therapies including ciclosporin, methotrexate and PUVA.

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