Simon Tso, William Hunt, Helen Frow and Andrew Ilchyshyn

Systemic agents for psoriasis and their relevance to primary care

INTRODUCTION

Psoriasis is a common chronic autoimmune inflammatory disease. There is an increasing range of systemic agents prescribed by specialists in the management of psoriasis. Thus, it is important for clinicians to become familiar with these medicines. This article aims to answer questions commonly asked about these medicines in relation to their side effects and their impact on vaccinations, preconception planning, breastfeeding, infection management, and major elective surgery.

WHAT ARE THE IMPORTANT SIDE EFFECTS OF SYSTEMIC AGENTS?

Box 1 provides a selected example of important side effects of systemic agents used in psoriasis. The list of side effects is not exhaustive and it is based on the authors' perceived importance even though they may be rare.

CAN VACCINATIONS BE GIVEN WITH SYSTEMIC AGENTS?

With the exception of acitretin, patients should complete all vaccinations prior to starting on systemic agents. If live vaccines are required, they should be given at least 4 weeks prior to starting methotrexate, biologics, and biosimilars.[3,4] Once patients are established on systemic agents, they should receive inactivated influenza vaccination every year and pneumococcal vaccine every 5 years. Patients should come off biologics or biosimilars for at least 6 months before receiving any live vaccination (except varicella zoster virus vaccine, which is 12 months).[3] Infants born to mothers receiving biologics should not receive live vaccines until after 6 months of age.[3] Patients on methotrexate, biologics, and biosimilars should avoid close contact with individuals receiving live vaccines for 4–6 weeks after vaccination.[4]

Box 1. Important side effects and preconception advice for systemic agents used in psoriasis

Drug	Side effects not to be missed	Time needed by patients to be off treatment before conception
Acitretin[a,b]	Hyperlipidaemia, hair loss, deranged liver enzymes, calcinosis in tendons	3 years for females
Ciclosporin	Infections,[a] hypertension, renal impairment, cancer risks[b]	Can be used during pregnancy if potential benefit outweighs the risks
Methotrexate	Infections,[a] agranulocytosis, liver and lung fibrosis, cancer risks[b]	At least 3 months for males and females
Dimethyl fumarate	Flushing, liver and renal impairment, diarrhoea, progressive multifocal leukoencephalopathy	No data
Apremilast	Diarrhoea, depression, weight loss	No data
Biologics and biosimilars	Infections,[a] cancer risks,[b] demyelinating disorders (anti-TNF-α)	Variable — up to 6 months for females

[a]Cancer risks of systemic agents are discussed by Geller and colleagues[1] and their skin cancer risks could be ranked as follows: ciclosporin > methotrexate > biologics. Acitretin is chemoprotective from skin cancers. [b]A Spanish registry study reported the incidence rates for serious infections with 95% confidence intervals (CI) per 1000 person-years were as follows: ciclosporin, 20 (8.3 to 47.9); infliximab, 18.9 (7.9 to 45.5); adalimumab, 9.8 (5.7 to 16.8); methotrexate, 9.6 (5.3 to 17.3); acitretin, 7.6 (2.8 to 20.2); ustekinumab, 5.9 (2.8 to 12.3).[2] TNF = tumour necrosis factor.

S Tso, MD, MRCP, dermatology specialty registrar year 6; **W Hunt**, BM BS, core medical trainee year 2; **A Ilchyshyn**, FRCP, consultant dermatologist, Department of Dermatology, University Hospitals Coventry and Warwickshire NHS Trust, Coventry. **H Frow**, MRCGP, GP and associate specialist dermatology, Royal Devon and Exeter NHS Foundation Trust, Exeter.

Address for correspondence

Simon Tso, Department of Dermatology, University Hospitals Coventry and Warwickshire NHS Trust, Coventry CV2 2DX, UK.

Email: simontso@doctors.org.uk

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WHAT PRECONCEPTION AND BREASTFEEDING ADVICE SHOULD BE GIVEN TO PATIENTS ON SYSTEMIC AGENTS?

Patients are counselled to avoid pregnancy, fathering a child, or breastfeeding while they are on systemic agents. Table 1 summarises the duration patients should come off systemic agents prior to pregnancy or fathering a child. Females on anti-TNF-α may continue their biologic treatment into the first or second trimester if potential benefit of continuation outweighs the risk to fetus (transplacental transfer of immunoglobulin G leads to immunosuppression after birth).[3] Females on methotrexate wishing to continue with pregnancy should be counselled about the risks of fetal neural tube defects and given folinic acid promptly. Females on adalimumab should not breastfeed until at least 5 months after the last adalimumab treatment according to manufacturer's information (www.medicines.org.uk/emc). For secukinumab this is 20 weeks (although not an absolute contraindication; www.medicines.org.uk/emc).

CAN SYSTEMIC AGENTS BE STOPPED WHEN A PATIENT DEVELOPS AN INFECTION?

Although there is no formal guideline, immunosuppressive systemic agents are typically stopped when patients develop severe or opportunistic (for example, *Mycobacterium* species) infections.[5] There is no consensus on the definition of 'severe infections' and it is the authors' view that patients with infections that failed a course of oral antimicrobial therapy, those requiring intravenous therapies (given at home or hospital), those requiring inpatient hospital admission, or patients with multiple comorbidities at risk of deterioration should have their immunosuppressive systemic agents stopped and restarted only after they have fully recovered from their infections.

DO SYSTEMIC AGENTS NEED TO BE STOPPED PRIOR TO ELECTIVE SURGERY?

The decision to stop immunosuppressive systemic agents should be undertaken by the surgical team in consultation with the prescriber. There is considerable variation in practices over what type of surgery warrants preoperative cessation of systemic agents as well as when to stop and reinitiate them. Biologics are often stopped for three to five half-lives of the drug before major elective surgery[3] (which roughly translates to 4–7 weeks for infliximab, 6–10 weeks for adalimumab, and 9–15 weeks for ustekinumab).

CONCLUSION

This article provides an overview of systemic agents used in psoriasis and their relevance to primary care services.

Provenance

Freely submitted; externally peer reviewed.

Competing interests

The authors have declared no competing interests.

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REFERENCES

1. Geller S, Xu H, Lebwohl M, *et al*. Malignancy risk and recurrence with psoriasis and its treatments: a concise update. *Am J Clin Dermatol* 2018; **19(3):** 363–375.
2. Dávila-Seijo P, Dauden E, Descalzo MA, *et al*. Infections in moderate to severe psoriasis patients treated with biological drugs compared to classic systemic drugs: findings from the BIOBADADERM Registry. *J Invest Dermatol* 2017; **137(2):** 313–321.
3. Smith CH, Jabbar-Lopez ZK, Yiu ZZ, *et al*. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2017. *Br J Dermatol* 2017; **177(3):** 628–636.
4. Warren RB, Weatherhead SC, Smith CH, *et al*. British Association of Dermatologists' guidelines for the safe and effective prescribing of methotrexate for skin disease 2016. *Br J Dermatol* 2016; **175(1):** 23–44.
5. Swoger JM, Regueiro M. Stopping, continuing, or restarting immunomodulators and biologics when an infection or malignancy develops. *Inflamm Bowel Dis* 2014; **20(5):** 926–935.