Review Article:

Beyond Biologics: Non-Biologic Systemic Treatments for Psoriasis-A Narrative Review

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Abstract

Background: Psoriasis is a chronic immune-mediated disorder affecting 2–3% of the global population. Although biologic therapies have transformed treatment paradigms, a substantial proportion of patients require or prefer non-biologic systemic therapies due to cost constraints, comorbidities, access limitations, pregnancy planning, or personal choice—particularly in resource-limited settings including Bangladesh where tuberculosis and hepatitis B coinfection remain prevalent. **Objective:** To comprehensively review the efficacy, safety, monitoring requirements, and clinical application of non-biologic systemic treatments for psoriasis across diverse healthcare settings. **Methods:** Narrative review of current evidence from clinical trials, guidelines, and real-world studies on systemic psoriasis therapy excluding biologics. **Key Findings:** Methotrexate, cyclosporine, and acitretin remain foundational therapies with robust long-term clinical experience. Modern small molecules—including apremilast, dimethyl fumarate, and the emerging TYK2 inhibitor deucravacitinib—offer improved safety profiles and reduced monitoring burden. Treatment selection requires individualized evaluation of disease severity, comorbidities, reproductive considerations, and patient accessibility.

Conclusion: Non-biologic systemic therapies remain essential tools in managing moderate-to-severe psoriasis globally. These agents provide cost-effective, flexible alternatives to biologics, with ongoing development of targeted oral therapies expanding therapeutic options. Judicious selection based on clinical phenotype and patient-specific factors optimizes outcomes while minimizing adverse effects.

Keywords: Psoriasis, systemic therapy, methotrexate, cyclosporine, apremilast, deucravacitinib, non-biologic therapy, small molecules

Introduction

Psoriasis is a chronic, immune-mediated inflammatory disorder characterized by cutaneous manifestations with significant systemic involvement1. Affecting approximately 2–3% of the global population, psoriasis carries substantial psychological, social, and economic burden1. The pathogenesis involves dysregulated Th17/Th1-mediated immune responses, with aberrant IL-23, TNF-α, and IL-17 signaling driving keratinocyte proliferation and cutaneous inflammation[1].

Over the past two decades, biologic immunosuppressive agents targeting specific cytokines have dramatically improved treatment efficacy. However, substantial barriers persist globally. In Bangladesh and other low-income countries, cost constitutes a prohibitive obstacle; biologic agents often exceed annual healthcare expenditure for most patients[2]. Additionally, contraindications such as active tuberculosis, hepatitis B/C coinfection, severe immunosuppression, and pregnancy remain highly relevant in endemic regions. Even in developed nations, treatment failure, loss of response, and serious adverse events necessitate alternative strategies.

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Non-biologic systemic therapies therefore retain critical relevance in contemporary psoriasis management. This narrative review synthesizes current evidence on traditional agents, modern small molecules, and emerging oral therapies, providing a comprehensive resource for clinicians across diverse healthcare settings.

Methods

This narrative review was conducted to synthesize current evidence regarding non-biologic systemic therapies for psoriasis management. A comprehensive literature search was performed using PubMed, Google Scholar, and MEDLINE databases, focusing on publications from 2010 onwards. Search terms included "psoriasis," "systemic therapy," "methotrexate," "cyclosporine," "acitretin," "apremilast," "dimethyl fumarate," "deucravacitinib," "JAK inhibitors," "small molecules," and "non-biologic treatment."

Inclusion criteria encompassed peer-reviewed original research, systematic reviews, clinical guidelines from major dermatology societies (American Academy of Dermatology, European Academy of Dermatology and Venereology, British Association of Dermatologists), and landmark clinical trials evaluating systemic non-biologic agents. Studies were selected based on relevance to clinical efficacy, safety profiles, monitoring requirements, and applicability to diverse healthcare settings, particularly resource-limited contexts.

Exclusion criteria Biologic agents (TNF-α inhibitors, IL 17/IL 23 inhibitors, JAK inhibitors used for autoimmune diseases unrelated to psoriasis), topical monotherapy, phototherapy-only interventions, and studies published in languages other than English.. Case reports of single patients and outdated publications (pre-2010) lacking contemporary clinical relevance were excluded.

Data extraction focused on: (1) mechanism of action, (2) efficacy endpoints (primarily PASI 75 response rates at standard time points), (3) onset of action, (4) adverse effect profiles, (5) monitoring requirements, (6) contraindications and special populations, and (7) clinical applicability in resource-limited settings including Bangladesh. Evidence was synthesized narratively by therapeutic class, with emphasis on practical clinical decision-making and treatment selection algorithms.

The manuscript followed the Preferred Reporting Items for Narrative Reviews (PRISMA-NR) guidelines to ensure systematic presentation and transparency. No meta-analysis was performed due to heterogeneity of study designs and outcome measures. The narrative review presents a comprehensive synthesis of available evidence to guide clinicians in selecting appropriate non-biologic systemic therapies tailored to individual patient characteristics and healthcare contexts.

Traditional Systemic Therapies

Methotrexate (MTX)

Mechanism of Action: Methotrexate is a folic acid analogue that competitively inhibits dihydrofolate reductase, impairing thymidylate and purine synthesis and thereby reducing proliferation of activated T lymphocytes and keratinocytes.[1,2]

At low weekly doses used in psoriasis, methotrexate exerts important anti inflammatory effects through increased adenosine release and modulation of multiple cytokines, contributing to its efficacy beyond simple antiproliferative activity.[1,3]

Efficacy: Guidelines and large series support methotrexate as a first line systemic agent for moderate to severe plaque psoriasis, with typical PASI 75 response rates of about 35–40% after 12–16 weeks at standard doses.[1,4]

Real world data confirm durable control in many patients and additional benefit in psoriatic arthritis, although responses may be slower and less complete than with newer biologics.[3,4]

Dosing and Monitoring: Methotrexate is given once weekly (oral, subcutaneous, or intramuscular) at doses usually ranging from 7.5–25 mg/week, with gradual titration according to efficacy and tolerability, and concomitant folic acid 1–5 mg on non MTX days to reduce toxicity.[1,4]

Baseline work up includes complete blood count, liver function tests, serum creatinine, hepatitis B/C and tuberculosis screening, pregnancy testing where appropriate, and ongoing monitoring with complete blood count, liver enzymes and renal function at least every 1–3 months, with more frequent testing early in therapy or in high risk patients.[1,5]

Side Effects: Common dose related adverse effects include nausea, vomiting, anorexia, fatigue, mucositis, and reversible cytopenias; long term use carries a risk of cumulative hepatotoxicity and, less commonly, pulmonary toxicity.[1,4,5]

Other important adverse effects are increased susceptibility to infection, hair thinning, photosensitivity, and, at higher cumulative doses, liver fibrosis, particularly in patients with obesity, diabetes, alcohol use, or pre existing liver disease.[1,4]

Drug Interactions: Concomitant use with other antifolate or myelosuppressive drugs (such as trimethoprim–sulfamethoxazole) markedly increases the risk of severe bone marrow suppression and should be avoided.[2,5]

Non steroidal anti inflammatory drugs, salicylates, some

antibiotics (for example penicillins), and drugs that impair renal function or tubular secretion can reduce methotrexate clearance and raise toxicity, so careful dose adjustment and monitoring are required.[2,4]

Advantages: MTX offers cost-effectiveness, extensive long-term safety data spanning decades, and documented efficacy in moderate-to-severe plaque psoriasis and psoriatic arthritis (PsA). It remains the standard first-line systemic agent in resource-limited settings.

Limitations and Contraindications: Key limitations are the need for regular laboratory monitoring, slow onset of action compared with cyclosporine, and concerns about hepatotoxicity, particularly in patients with metabolic risk factors or chronic viral hepatitis.[1,4,5]

Absolute contraindications include pregnancy and breastfeeding, significant hepatic or renal impairment, severe bone marrow suppression, uncontrolled infection, and chronic excessive alcohol intake; effective contraception is mandatory for both men and women during treatment and for a period after discontinuation.[1,4]

Cyclosporine (CSA)

Mechanism of Action: Cyclosporine is a calcineurin inhibitor that binds cyclophilin in T lymphocytes, blocking calcineurin dependent activation of nuclear factor of activated T cells (NFAT) and thereby reducing interleukin 2 transcription and T cell proliferation.[1,2]

This targeted immunosuppressive effect leads to rapid suppression of psoriatic inflammation and improvement in keratinocyte hyperproliferation.[1,3]

Efficacy: Cyclosporine is highly effective for moderate to severe plaque psoriasis, achieving PASI 75 responses in approximately 50–70% of patients within 4–8 weeks at standard doses.1,3

It is particularly useful for severe, unstable, erythrodermic or pustular psoriasis and is often employed as short term "rescue" or bridge therapy while transitioning to slower acting systemic agents.[1,2]

Dosing and Monitoring: Typical dosing in psoriasis is 2.5–5 mg/kg/day in two divided doses, with dose escalation based on clinical response and tolerability, and a preference for the lowest effective dose and intermittent short courses rather than continuous long term therapy.[1,3]

Baseline and follow up monitoring should include blood pressure, serum creatinine, estimated glomerular filtration rate, electrolytes (particularly potassium and magnesium), lipids, and liver enzymes, initially every 2–4 weeks and then at regular intervals; treatment duration is generally limited to 12–16 weeks or, at most, about one year in total to reduce cumulative nephrotoxicity.[1,2,4]

Side Effects: The most important adverse effect is dose dependent nephrotoxicity, which may present as reversible rises in serum creatinine but can progress to chronic irreversible renal damage if high doses or prolonged courses are used.1,2

Other frequent side effects include hypertension, hypertrichosis, gingival hyperplasia, tremor, paresthesias, hyperlipidaemia, and increased risk of infections and, with long term exposure, possible elevation in malignancy risk, especially cutaneous malignancies in previously phototreated patients.1,3

Drug Interactions: Cyclosporine is metabolized by CYP3A4 and is a substrate for P glycoprotein; strong inhibitors (such as azole antifungals, macrolide antibiotics, some calcium channel blockers) can raise cyclosporine levels and toxicity, whereas inducers (such as rifampicin) can reduce efficacy.2,4

Concomitant use with other nephrotoxic or photosensitizing drugs (for example non steroidal anti inflammatory drugs, aminoglycosides, methotrexate, or PUVA/UVB therapy) increases the risk of renal impairment or malignancy and should be avoided or undertaken only with very close monitoring.1,2

Advantages: Rapid clinical improvement and efficacy in severe, unstable presentations (erythrodermic or pustular psoriasis) allow CSA to serve effectively as bridge therapy during initiation of slower-acting agents.

Limitations and Contraindications: Limitations include its potential for nephrotoxicity and hypertension, the need for frequent monitoring, and the recommendation to avoid prolonged continuous therapy, which restrict its role mainly to short term control rather than long term maintenance.1,2

Cyclosporine is contraindicated in uncontrolled hypertension, significant renal impairment, uncontrolled infections, certain malignancies, and in patients receiving concomitant photochemotherapy; caution is required in patients with metabolic syndrome, elderly patients, and those with prior extensive phototherapy exposure.1–3

Acitretin

Mechanism of Action: Acitretin is an oral retinoid that binds nuclear retinoic acid receptors (RAR/RXR), normalizing epidermal differentiation, reducing keratinocyte hyperproliferation, and exerting immunomodulatory effects on inflammatory pathways involved in psoriasis.5,6

It does not have direct immunosuppressive activity, which distinguishes it from other systemic agents and contributes to its particular utility in patients at high infection risk.5,7

Efficacy: Acitretin is moderately effective in chronic

plaque psoriasis, with PASI 75 responses in roughly 23–30% of patients as monotherapy at standard doses, but it is especially valuable in pustular and erythrodermic psoriasis and in combination with phototherapy.[5,7]

Combination regimens with narrowband UVB or PUVA enhance efficacy and allow lower acitretin doses, improving tolerability while maintaining good clinical responses.[5,6]

Dosing and Monitoring: For plaque psoriasis, acitretin is usually started at 10–20 mg/day with food and titrated over several weeks to 25–50 mg/day depending on response and adverse effects, using the lowest effective maintenance dose once disease is controlled.[5,6]

Baseline and periodic monitoring should include liver function tests and fasting lipid profile, with additional assessment of renal function, glucose and, where appropriate, pregnancy testing; laboratory monitoring is typically performed every 1–3 months during treatment.[5–7]

Side Effects: Dose dependent mucocutaneous adverse effects are very common and include cheilitis, xerosis, epistaxis, hair thinning, and nail fragility, together with photosensitivity and pruritus.[5,6]

Metabolic and systemic effects such as hypertriglyceridaemia, elevated liver enzymes, skeletal changes with very long term use, and potential mood changes can occur and require regular monitoring and dose adjustment or discontinuation in severe cases.[5–7]

Drug Interactions: Concomitant use with other hepatotoxic drugs (for example high dose methotrexate or chronic alcohol intake) may increase the risk of liver injury and should be avoided or minimized.[5,7]

Co administration with tetracyclines or high dose vitamin A derivatives increases the risk of pseudotumor cerebri, and acitretin is contraindicated with ethanol because of in vivo re esterification to etretinate, which has a much longer half life and prolongs teratogenic risk.[5,6]

Advantages: Acitretin offers non-immunosuppressive mechanism, exceptional efficacy for pustular psoriasis, and can be combined synergistically with phototherapy1.

Limitations and Contraindications: The major limitation of acitretin is its strong teratogenicity; pregnancy is absolutely contraindicated during treatment and for a prolonged period after discontinuation, and strict contraception (often two concurrent methods) and regular pregnancy testing are mandatory in women of childbearing potential.[5,6,8]

Acitretin is contraindicated in pregnancy, breastfeeding, severe hepatic or renal impairment, uncontrolled hyperlipidaemia, and in patients with chronic excessive alcohol use; its mucocutaneous and metabolic side effect profile also limits use in patients with poorly controlled cardiovascular risk factors.[5–7]

Modern Non-Biologic Small Molecules

Apremilast (PDE-4 Inhibitor)

Mechanism and Efficacy: Apremilast inhibits phosphodiesterase-4, increasing intracellular cAMP and reducing production of pro-inflammatory cytokines including TNF-α, IL-17, and IL-232. PASI 75 response approximates 33% at 16 weeks.

Dosing and Monitoring: Standard dose is 30 mg twice daily after a 5-day titration schedule. Notably, apremilast requires no routine laboratory monitoring—only weight assessment and mood screening for depression².

Advantages: Oral administration, favorable safety profile, minimal monitoring burden, and suitability across diverse patient populations (including pregnancy with caution) represent significant advantages. Apremilast bridges traditional and biologic efficacy ranges, offering patients a middle-ground option.

Limitations: Lower efficacy compared to methotrexate and biologics, gastrointestinal intolerance (particularly diarrhea and nausea), and frequent weight loss limit acceptability in some patients.

Dimethyl Fumarate (DMF)

Mechanism and Efficacy: Dimethyl fumarate activates the nuclear factor erythroid 2–related factor 2 (Nrf2) pathway, conferring anti-inflammatory and cytoprotective properties2. PASI 75 response rates of approximately 50% are observed at 8–16 weeks; long-term remission is achievable in subset of responders².

Dosing and Monitoring: Dosing typically escalates from 120 mg daily to maintenance of 240–720 mg daily depending on formulation. CBC (particularly lymphocyte counts) and LFTs require baseline and periodic monitoring.

Advantages: Effective oral agent with established long-term safety profile in European and Asian populations. DMF offers good tolerability in maintenance therapy and can be combined with phototherapy.

Limitations: Transient gastrointestinal side effects (flushing, diarrhea), lymphopenia (occasionally requiring discontinuation), and variable efficacy across ethnic populations present challenges. Limited availability outside Europe and Asia constrains global accessibility.

Conventional Immunomodulators (Emerging/Off-Label Use)

Mycophenolate Mofetil (MMF)

Mycophenolate mofetil inhibits inosine monophosphate dehydrogenase, reducing T- and B-lymphocyte proliferation. Dosing of 1–3 g daily in divided doses addresses refractory pustular or erythrodermic psoriasis, particularly in patients with renal disease or MTX

intolerance. Monitoring includes CBC, renal function, and LFTs. Gastrointestinal upset and infection risk limit broader adoption[3].

Hydroxyurea

Hydroxyurea inhibits ribonucleotide reductase, suppressing DNA synthesis. Dosing of 500–1500 mg daily has demonstrated efficacy in refractory psoriasis, particularly in resource-limited settings where cost is critical. Adverse effects including cytopenias, pigmentation changes, and theoretical carcinogenic potential restrict long-term use1.

Azathioprine

Azathioprine is a purine analogue and prodrug that converts to 6-mercaptopurine, acting as an antimetabolite to inhibit DNA and RNA synthesis. It exerts immunosuppressive effects by specifically inhibiting the proliferation of rapidly dividing T- and B-lymphocytes and inducing T-cell apoptosis. Clinical improvement typically follows a slow onset, often requiring 6-12 weeks for significant benefit. It can be particularly useful in maintaining remission after induction with faster-acting agents, and intermittent "pulse" dosing protocols have shown promise in prolonging remission periods.

Emerging Oral Targeted Therapies

Deucravacitinib (TYK2 Inhibitor)

Deucravacitinib is a first-in-class oral TYK2 inhibitor that modulates IL-23, IL-12, and type I interferon pathways via allosteric inhibition of the TYK2 regulatory domain, thereby sparing broader JAK1–3–mediated functions.4 In phase III trials of moderate-to-severe plaque psoriasis, it achieved PASI 75 response rates of about 58–69% at week 16, consistently outperforming apremilast and approaching the efficacy of traditional systemic agents, with durable responses and higher PASI 90 and sPGA 0/1 rates versus apremilast.[4]

Deucravacitinib is given as a fixed once-daily oral dose without titration, simplifying use in routine practice and making it suitable for patients eligible for systemic therapy or phototherapy in whom conventional agents are contraindicated, poorly tolerated, or insufficient.2,4. Its high selectivity for TYK2 appears to avoid many class warnings associated with broader JAK inhibitors; trials mainly report mild to moderate events such as upper respiratory tract infection, nasopharyngitis, acne, and headache, and there is no requirement for intensive laboratory monitoring beyond standard baseline screening.[2,4]

Within treatment algorithms, deucravacitinib represents an attractive oral option for patients who prefer tablets over injections, for those at higher risk of organ toxicity with methotrexate or cyclosporine, or when access to biologics is limited, offering a balance of convenient dosing, robust efficacy, and a favorable safety profile that positions it between traditional systemics and biologics.[1,2,4]

JAK Inhibitors

Tofacitinib (JAK1/3 inhibitor) is approved for psoriatic arthritis but its psoriasis indication has been withdrawn in some regions, and it is now used off-label for plaque psoriasis only in selected settings.[2,3]

Baricitinib (JAK1/2 inhibitor) demonstrated clinically meaningful PASI and Physician's Global Assessment responses in a phase 2b randomized trial of moderate-to-severe plaque psoriasis, confirming that JAK–STAT modulation is an effective therapeutic strategy; however, subsequent development and regulatory approvals have focused on rheumatoid arthritis, atopic dermatitis, and alopecia areata rather than psoriasis, so it is not routinely used as a standard psoriasis therapy11,12.

Upadacitinib (selective JAK1 inhibitor) shows strong efficacy in psoriatic arthritis, with dedicated psoriasis trials ongoing, but like other systemic JAK inhibitors it requires robust laboratory monitoring (CBC, LFTs, lipids) and carries class warnings for serious infections, venous thromboembolism, major adverse cardiovascular events, and malignancy, which, together with the availability of safer alternatives such as apremilast and the selective TYK2 inhibitor deucravacitinib, limit its role in routine psoriasis management.[2,3,13]

Phototherapy as a Bridge to Systemic Therapy

While not the primary focus of this review on non-biologic systemic agents, systemic phototherapy—particularly PUVA (psoralen plus UVA)—remains a critical adjunct or alternative to oral therapies, especially in resource-limited settings like Bangladesh where access to advanced systemic options may be constrained.

PUVA combines oral psoralens (0.6-0.8 mg/kg 8-methoxypsoralen) with controlled UVA exposure (2-3 sessions/week), achieving PASI 75 rates of 80-90% after 12-20 weeks through DNA cross-linking and T-cell apoptosis. It serves effectively as bridge therapy during systemic agent titration or for maintenance post-remission, offering extended disease-free intervals superior to narrowband UVB alone.

Treatment Selection Considerations

Optimal phototherapy integration requires evaluating disease phenotype (pustular/erythrodermic variants respond best), comorbidities (avoid in photosensitivity disorders), cost/accessibility (clinic-based infrastructure needed), pregnancy status (relative contraindication), monitoring tolerance, need for rapid onset, and prior treatment failures.

Advantages: High efficacy for thick plaques, cost-effectiveness relative to biologics, and favorable long-term remission in resource-poor settings.
Limitations: Cumulative skin cancer risk (SCC >200 treatments), nausea from psoralens, mandatory eye protection, and logistical demands of frequent visits limit broad applicability.

Summary Table of Non-Biologic Systemic Therapies

Drug	Mechanism	PASI 75 (%)	Onset	Key Adverse Effects	Monitoring
Methotrexate	Folate antagonist	35–40%	8–12 weeks	Hepatotoxicity, cytopenias	CBC, LFTs, creatinine
Cyclosporine	Calcineurin inhibitor	50–70%	4–6 weeks	Nephrotoxicity, hypertension	Blood pressure, creatinine
Acitretin	Retinoid	23–30%	8–12 weeks	Dyslipidaemia, teratogenicity	Lipid profile, LFTs
Apremilast	PDE4 inhibitor	33%	4–8 weeks	Gastrointestinal upset, weight loss	Clinical monitoring (no routine labs)
Dimethyl fumarate	odulator	50%	8–16 weeks	Lymphopenia, flushing	CBC
Deucravacitinib	TYK2 inhibitor	58–69%	4–8 weeks	Upper respiratory infection, acne	Minimal laboratory monitoring

Table 1. Comparative efficacy, safety profile, and monitoring requirements of non-biologic systemic agents for psoriasis management. PASI 75, 75% reduction in Psoriasis Area Severity Index; LFTs, liver function tests; CBC, complete blood count; PDE4, phosphodiesterase-4; TYK2, tyrosine kinase.[21,2,4,6]

Combination Approaches and Treatment Selection

Synergistic Combinations:

- Methotrexate + narrowband UVB phototherapy: Enhanced efficacy with dose reduction
- Acitretin + phototherapy: Particularly effective for pustular variants
- Fumarates + phototherapy: Supported by European evidence-based guidelines

Combinations to Avoid:

- Methotrexate + cyclosporine: Risk of cumulative hepatotoxicity and nephrotoxicity
- Any traditional systemic + biologics: Additive immunosuppression and infection risk

Individualized selection algorithm for non-biologic systemic therapy in psoriasis

Clinical Scenario	Preferred Treatment	Rationale
Rapid disease control needed	Cyclosporine	Onset 4–6 weeks; bridge therapy potential
hepatitis B	Apremilast or deucravacitinib	Minimal immunosuppression; safer profile
Hepatic impairment	Apremilast or deucravacitinib	Avoid MTX and acitretin (hepatic metabolism risk)
Renal disease	Apremilast or MTX (dose-adjusted)	Avoid cyclosporine (nephrotoxicity)
Women of childbearing age	Apremilast, deucravacitinib (with caution)	Avoid acitretin (teratogenic) and MTX
Pustular or erythrodermic psoriasis	Acitretin or cyclosporine	Disease-phenotype efficacy
Resource-limited settings	Methotrexate or acitretin	Cost-effectiveness and availability
Severe metabolic syndrome	Apremilast or MTX (cautious)	Cyclosporine worsens hypertension and lipids

Table 2. Individualized selection algorithm for non-biologic systemic therapies based on clinical scenario and comorbidities1-4.

Monitoring Protocols and Safety Considerations

Baseline Assessment (All Patients):

- Clinical photographs and PASI scoring
- CBC, comprehensive metabolic panel, LFTs, renal function
- Lipid panel; glucose screening
- Blood pressure; weight; BMI
- Tuberculin skin test or IGRA and hepatitis B/C serologies (essential in Bangladesh)

Monitoring Frequency by Agent:

- Methotrexate: Monthly CBC/LFTs for first 3 months, then every 8–12 weeks; annual NASH assessment
- Cyclosporine: Bi-weekly blood pressure and creatinine for 4 weeks, then monthly
- Acitretin: Baseline and 4-week lipid panel; then every 3 months
- Apremilast/DMF: Quarterly clinical review; DMF requires 3–6 monthly CBC
- Deucravacitinib: Minimal routine monitoring; clinical assessment every 4 weeks initially

Adherence and Patient Education:
Structured counseling on medication adherence, adverse effect recognition, and contraception (for teratogenic agents) significantly improves outcomes. Written instructions regarding environmental decontamination and concomitant topical therapy enhance overall efficacy[2].

Recent Advances and Future Perspectives

The therapeutic landscape for non-biologic systemic psoriasis therapy continues to evolve. Novel oral agents targeting specific molecular pathways (PI3K-δ inhibitors, selective NLRP3 inflammasome inhibitors) are in clinical development. Integration of pharmacogenomic testing to predict MTX metabolism and tolerability may optimize traditional agent selection. Real-world evidence initiatives are documenting long-term safety and efficacy beyond controlled trial settings, particularly in resource-limited populations where generalizability remains critical[1].

Limitations

This narrative review synthesizes literature without systematic search methodology; selection bias may exist. Evidence quality varies across agents due to differing research prioritization by pharmaceutical industry. Limited head-to-head comparative trials between traditional and modern agents restrict definitive efficacy rankings. Regional variations in drug availability, regulatory status, and healthcare infrastructure affect clinical applicability globally.

Conclusion

Non-biologic systemic therapies remain essential in psoriasis management, particularly where biologics are inaccessible or contraindicated.[1,2] Traditional agents such as methotrexate, cyclosporine, and acitretin provide cost effective options when used with appropriate monitoring and patient selection.[2,3] Modern small molecules, including apremilast and dimethyl fumarate, add safer oral choices for patients with complex comorbidities.[2,5,6]

Deucravacitinib has emerged as an innovative oral TYK2 inhibitor offering promising efficacy and safety, with clinical trials showing higher rates of skin clearance than existing oral therapies and a novel, highly selective mechanism that may limit systemic adverse effects.4 Optimal outcomes depend on individualized treatment choices that account for phenotype, comorbidities, reproductive plans, and resource constraints, especially in regions with high tuberculosis and hepatitis B burdens.[1,2]

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