International Journal Of Health, Engineering And Technology (IJHET) *E-ISSN 2829 - 8683*
Volume 5, Number 4, November 2026, *Page. 3960 - 3977*
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Corticosteroid-Sparing Strategies For The Management Of Leprosy Reactions: A Systematic Review Of Emerging Therapeutic Approaches

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Abstract

Leprosy reactions are immune-mediated complications of leprosy and remain an important cause of nerve damage, disability, and impaired quality of life despite multidrug therapy. Systemic corticosteroids are used for severe reactions, but recurrent or chronic disease may require prolonged exposure and increase treatment-related toxicity. This systematic review evaluated established and emerging corticosteroid-sparing strategies for type 1 reactions and erythema nodosum leprosum (ENL). PubMed (MEDLINE), ScienceDirect, Cochrane Library, and ProQuest were searched for studies published between January 2017 and October 2026. Eligible trials and observational studies evaluated corticosteroid-sparing therapy in leprosy reactions. Study selection followed PRISMA 2020. Outcomes included clinical response, corticosteroid reduction or withdrawal, recurrence, neurological outcomes, and adverse events. Findings were synthesized qualitatively. Of 363 records identified, 83 duplicates were removed and 280 records were screened. Twelve reports were sought for retrieval, one could not be obtained, and 11 studies involving 722 patients were included. Nine studies focused on ENL, one on type 1 reactions, and one included both reaction types. Thalidomide showed the most consistent corticosteroid-sparing effect, with substantial prednisolone reduction and successful withdrawal reported across several studies. Minocycline achieved earlier ENL control than clofazimine but did not significantly reduce additional prednisolone requirements. Observational studies suggested benefit from methotrexate; however, the MaPs in ENL trial found no reduction in corticosteroid requirement or ENL flares. Etanercept, adalimumab, cyclophosphamide, and secukinumab showed promising activity in refractory ENL, although evidence was limited to small observational studies and case series. Corticosteroid-sparing therapy for leprosy reactions remains supported by heterogeneous and limited evidence, with more data available for ENL than for type 1 reactions. Thalidomide has the most consistent supporting evidence, whereas methotrexate lacks confirmed benefit in randomized data. Biologic and other immunomodulatory therapies remain promising but require larger controlled trials using standardized corticosteroid-sparing, relapse, neurological, and safety outcomes.

Keywords: Leprosy, Leprosy Reactions, Erythema Nodosum Leprosum, Corticosteroid-Sparing Therapy, Thalidomide, Immunomodulatory Therapy, Systematic Review

INTRODUCTION

Leprosy remains a clinically important neglected tropical disease despite the availability of effective multidrug therapy, largely because antimicrobial cure does not eliminate the risk of immune-mediated complications. Leprosy reactions may develop before treatment, during multidrug therapy, or after its completion and are estimated to affect a substantial proportion of individuals with the disease, particularly those with multibacillary forms. These acute inflammatory episodes represent a major determinant of morbidity because inflammation involving peripheral nerves can lead to irreversible sensory and motor impairment, deformity, and long-term disability. Their consequences extend beyond neurological injury; recurrent reactions are associated with pain, functional limitation, psychological distress, social exclusion, interruption of employment, and considerable economic hardship. The prevention and effective control of reactional episodes therefore remain central to preserving function and quality of life even after successful microbiological treatment of leprosy (Jaume *et al*., 2023; Putri *et al*., 2022; Mehta *et al*., 2025).

Leprosy reactions encompass immunologically and clinically distinct syndromes that require different therapeutic considerations. Type 1 reaction, or reversal reaction, occurs

predominantly within the borderline spectrum and is characterised by an abrupt enhancement of cell-mediated immune activity, producing inflammation of pre-existing skin lesions and peripheral nerves. The associated inflammatory oedema within anatomically constrained nerves can rapidly compromise neural function. Type 2 reaction, most commonly manifested as erythema nodosum leprosum (ENL), occurs primarily in borderline lepromatous and lepromatous disease and has a broader systemic phenotype, with painful erythematous nodules accompanied variably by fever, neuritis, arthritis, lymphadenitis, iridocyclitis, orchitis, and other organ involvement. Contemporary studies indicate that these syndromes involve complex interactions among T-cell subsets, neutrophils, immune complexes, complement pathways, tumour necrosis factor-α, interferons, and other inflammatory mediators, providing a biological basis for therapeutic strategies that extend beyond non-specific corticosteroid suppression (Dewi *et al*., 2023; Serrano-Coll *et al*., 2024; Mehta *et al*., 2025).

Rapid control of inflammation is essential when reactions threaten nerve function or involve major systemic manifestations. Systemic corticosteroids, particularly prednisolone, consequently remain a principal treatment for severe type 1 reactions, acute neuritis, and many presentations of severe ENL. Their efficacy in suppressing inflammation is clinically valuable, but treatment frequently extends over several months and may require repeated or prolonged courses when symptoms recur during dose reduction. This problem is particularly pronounced in chronic and recurrent ENL, in which attempts to taper corticosteroids can precipitate further inflammatory episodes and progressively increase cumulative exposure. Thalidomide and clofazimine provide important non-corticosteroid options in ENL, but neither offers a universally applicable solution: thalidomide is limited by profound teratogenicity, peripheral neurotoxicity, regulatory restrictions, and variable accessibility, whereas the delayed anti-inflammatory effect and pigmentation associated with higher-dose clofazimine constrain its role in rapidly progressive disease (Costa *et al*., 2018; Mehta *et al*., 2025; Bathula *et al*., 2023).

The need to reduce corticosteroid exposure is not merely theoretical. Prolonged systemic corticosteroid therapy in people affected by leprosy has been associated with metabolic, infectious, gastrointestinal, ophthalmological, skeletal, and endocrine complications, with the greatest cumulative burden arising in patients requiring prolonged treatment for recurrent reactions. A recent systematic review encompassing 111 studies identified corticosteroid-induced lipodystrophy among the most frequently reported complications, while infections affected approximately 15% of treated individuals and accounted for most corticosteroid-associated deaths, predominantly through tuberculosis. Cataract and osteoporosis were also disproportionately represented among patients with ENL, reflecting the long treatment courses often required by this subgroup. These findings shift corticosteroid reduction from a matter of treatment convenience to a clinically meaningful therapeutic objective and highlight the importance of strategies that maintain inflammatory control while limiting cumulative glucocorticoid toxicity (Lun, de Barros and Walker, 2026).

Several corticosteroid-sparing approaches have consequently been explored, although their therapeutic positions remain unevenly defined. Thalidomide has the most established corticosteroid-sparing role in moderate-to-severe ENL and can induce relatively rapid clinical improvement, with observational data supporting reductions in corticosteroid requirements and recurrent disease activity. More recent studies suggest that lower-dose thalidomide regimens may retain clinically useful activity while potentially reducing treatment-related toxicity. High-dose clofazimine has also been used to control chronic or recurrent ENL and reduce corticosteroid dependence, although its slower onset limits its usefulness as monotherapy for acute severe inflammation. These experiences demonstrate

that corticosteroid-sparing therapy should not be viewed simply as substitution of one anti-inflammatory drug for another; successful strategies must simultaneously provide adequate control of acute inflammation, prevent recurrence, preserve nerve function, minimise treatment toxicity, and remain feasible in the resource-limited settings where leprosy is most prevalent (Upputuri *et al*., 2020; Bathula *et al*., 2023; Costa *et al*., 2018).

Immunomodulatory agents used in other chronic inflammatory disorders have broadened the therapeutic landscape, but the available evidence illustrates why apparent corticosteroid-sparing activity requires rigorous evaluation. Methotrexate initially appeared promising in case reports and small series involving both type 1 and type 2 reactions, and a French multicentre cohort reported complete clinical response in 61.5% of treated patients, with complete corticosteroid withdrawal achieved in more than half of those receiving glucocorticoids at methotrexate initiation. Earlier evidence was nevertheless dominated by small uncontrolled studies. Importantly, the recently completed international *MaPs in ENL* randomized controlled trial involving 137 adults with severe ENL found that adjunctive methotrexate did not delay ENL flares, reduce flare frequency or severity, or decrease the need for additional prednisolone compared with placebo. A similar caution is provided by the AZALEP trial, in which adding azathioprine to corticosteroid therapy did not improve overall outcomes in type 1 reactions. Collectively, these findings demonstrate the substantial discrepancy that may exist between encouraging observational evidence and comparative trial data (Pérez-Molina *et al*., 2020; Jaume *et al*., 2023; Lockwood *et al*., 2017; de Barros *et al*., 2026).

More targeted immunomodulatory approaches have emerged for patients with persistent or treatment-refractory disease. Apremilast, an oral phosphodiesterase-4 inhibitor that modulates several pro-inflammatory pathways implicated in ENL, has shown clinical activity in case reports and a prospective pilot study of chronic or recurrent ENL, supporting further evaluation of its corticosteroid-sparing potential. Biological inhibition of tumour necrosis factor-α represents another mechanistically attractive strategy because TNF-α contributes substantially to the inflammatory milieu of reactional states. Small case series have described rapid improvement in otherwise refractory ENL treated with agents such as etanercept or adalimumab, including patients who had failed corticosteroids, thalidomide, or conventional immunosuppressants. These observations remain preliminary, and the potential for serious infection, reactivation or unmasking of mycobacterial disease, high cost, and requirements for specialised monitoring are particularly relevant in leprosy-endemic settings. The therapeutic promise of these agents must consequently be interpreted in relation to both the biological plausibility of their targets and the limited certainty of the clinical evidence supporting their use (Narang *et al*., 2021; Mendes *et al*., 2022; Mehta *et al*., 2025).

The expanding range of therapeutic alternatives has created a literature that is clinically important but methodologically fragmented. Evidence spans randomised trials, observational cohorts, pilot studies, case series, and individual reports; treatment populations differ substantially with respect to reaction type, severity, chronicity, previous therapy, and neurological involvement; and outcomes are inconsistently reported as clinical response, recurrence, corticosteroid reduction, corticosteroid discontinuation, nerve-function recovery, or adverse events. Recent discordance between observational experience and randomised evidence further emphasises that individual therapies cannot be judged solely from apparent response in refractory cases. A systematic appraisal that distinguishes type 1 reactions from ENL while integrating efficacy, corticosteroid-sparing capacity, recurrence, neurological outcomes, safety, and quality of evidence is therefore needed. This systematic review aims to critically evaluate established and emerging corticosteroid-sparing therapeutic strategies for leprosy reactions and to define the current evidence supporting

their clinical use, limitations, and priorities for future investigation (Mehta *et al*., 2025; Lun, de Barros and Walker, 2026; de Barros *et al*., 2026).

RESEARCH METHODS

This systematic review was conducted to systematically identify, evaluate, and synthesize the available evidence on corticosteroid-sparing therapeutic strategies for the management of leprosy reactions. The PICOS (*Population, Intervention, Comparison, Outcome, and Study design*) framework was used to define the review question and identify relevant studies. The literature search, study selection, and reporting process were performed in accordance with the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) 2020 guidelines.

Study Selection

Studies included in this systematic review were identified from the following online databases: *PubMed (MEDLINE)*, *ScienceDirect*, *Cochrane Library*, and *ProQuest*. Eligible studies evaluated corticosteroid-sparing therapeutic strategies in patients with leprosy reactions, including type 1 reaction (reversal reaction) and type 2 reaction or *erythema nodosum leprosum* (ENL). The study population comprised patients with a confirmed diagnosis of leprosy who developed acute, recurrent, chronic, or corticosteroid-dependent reactional episodes requiring anti-inflammatory or immunomodulatory treatment. Two reviewers independently screened titles and abstracts and subsequently assessed potentially eligible full-text articles. Disagreements regarding study eligibility were resolved through discussion and consensus.

The interventions of interest included pharmacological therapies administered as alternatives or adjuncts to systemic corticosteroids with the potential to reduce corticosteroid exposure, such as thalidomide, clofazimine, methotrexate, azathioprine, apremilast, biological agents, and other immunomodulatory therapies. Comparator groups, when available, included systemic corticosteroid therapy alone, placebo, standard care, or alternative corticosteroid-sparing regimens. The primary outcomes assessed were clinical response or resolution of leprosy reactions and reduction in corticosteroid requirement. Secondary outcomes included cumulative corticosteroid dose, successful corticosteroid tapering or discontinuation, recurrence or flare of reactional episodes, changes in peripheral nerve function, treatment-related adverse events, and treatment discontinuation.

Randomized controlled trials, non-randomized interventional studies, cohort studies, case-control studies, and case series reporting clinically relevant outcomes of corticosteroid-sparing treatment were considered eligible for inclusion. Studies were excluded if they: (1) did not include patients with type 1 or type 2 leprosy reactions; (2) evaluated corticosteroids without assessment of a corticosteroid-sparing intervention; (3) focused exclusively on the antimicrobial treatment of leprosy without reporting outcomes related to reactional episodes; (4) consisted of reviews, editorials, letters without original clinical data, conference abstracts, animal studies, or *in vitro* studies; (5) did not report relevant clinical efficacy, corticosteroid-sparing, recurrence, neurological, or safety outcomes; or (6) were published outside the predefined study period.

Study Search

Relevant studies were identified using search terms derived from the PICOS framework to maximize the sensitivity of the literature search. Medical Subject Headings (MeSH) and corresponding free-text terms were first identified and subsequently combined using advanced search techniques, bibliographic searching, and Boolean operators (AND and OR). The search was conducted across *PubMed (MEDLINE)*, *ScienceDirect*, *Cochrane Library*, and *ProQuest*. Because leprosy reactions are indexed using several related terms,

both type 1 reaction and type 2 reaction terminology were incorporated into the search strategy. The search was restricted to studies published between 1 January 2017 and 4 October 2026. The final database search was conducted on 4 October 2026. The following search terms were used and adapted according to the indexing system of each database:

"(((*Leprosy* [MeSH] OR *leprosy* OR *Hansen disease* OR *Hansen's disease*) AND (*leprosy reaction* OR *leprosy reactions* OR *type 1 reaction* OR *reversal reaction* OR *type 2 reaction* OR *erythema nodosum leprosum* OR *ENL*)) AND (*corticosteroid-sparing* OR *steroid-sparing* OR *immunomodulator* OR *immunosuppressive therapy* OR *thalidomide* OR *clofazimine* OR *methotrexate* OR *azathioprine* OR *minocycline* OR *apremilast* OR *cyclosporine* OR *ciclosporin* OR *cyclophosphamide* OR *etanercept* OR *adalimumab* OR *infliximab* OR *secukinumab* OR *tumor necrosis factor inhibitor* OR *TNF inhibitor* OR *biologic therapy*))"

Data Extraction and Quality Assessment

Data from all eligible studies were systematically extracted using a standardized data extraction form. Extracted information included the first author, year of publication, country, study design, sample size, characteristics of the study population, type of leprosy reaction, corticosteroid-sparing intervention, comparator when applicable, treatment duration, corticosteroid regimen, clinical response, corticosteroid dose reduction or discontinuation, recurrence of leprosy reactions, neurological outcomes, and treatment-related adverse events. Data extraction was performed independently by two reviewers, and any discrepancies were resolved through discussion and consensus.

The methodological quality and risk of bias of the included studies were assessed according to study design. Randomized controlled trials were evaluated using the *RoB 2: A Revised Cochrane Risk-of-Bias Tool for Randomized Trials*, covering bias arising from the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Non-randomized comparative or interventional studies were assessed using the *Risk Of Bias In Non-randomized Studies of Interventions* (ROBINS-I), whereas observational studies and case series were evaluated using the appropriate *Joanna Briggs Institute* (JBI) Critical Appraisal Tools. Because these instruments differ in their domains and judgment categories, risk-of-bias findings were summarized separately according to study design and were not pooled into a single cross-design risk-of-bias estimate.

Data Analysis

Data analysis was performed by systematically integrating and describing the findings of all included studies through a qualitative synthesis. Extracted data included study characteristics such as first author, year of publication, country, study design, sample size, duration of follow-up, type of leprosy reaction, therapeutic intervention, comparator, and treatment duration, as well as population characteristics including age, sex, and relevant clinical features. The principal outcomes assessed were clinical response, reduction or discontinuation of corticosteroid therapy, recurrence or flare of leprosy reactions, changes in peripheral nerve function, and treatment-related adverse events. The extracted data were organized in a structured synthesis matrix to facilitate comparison across studies. Findings were narratively synthesized according to the type of leprosy reaction and corticosteroid-sparing intervention, with consideration of the direction and consistency of treatment effects, safety outcomes, and methodological quality of the included studies. No quantitative data pooling or meta-analysis was performed.

RESULTS AND DISCUSSION

Study Search

The systematic search of *PubMed (MEDLINE)*, *ScienceDirect*, *Cochrane Library*, and *ProQuest* identified 363 records, comprising 144 records from PubMed, 62 from ScienceDirect, 56 from Cochrane Library, and 101 from ProQuest. After removal of 83 duplicate records, 280 records underwent title and abstract screening, of which 268 were excluded because they did not meet the predefined eligibility criteria. Twelve reports were subsequently sought for full-text retrieval. One report could not be retrieved, leaving 11 reports for full-text eligibility assessment. No additional studies were excluded after full-text assessment, resulting in 11 studies included in the qualitative synthesis. The included studies evaluated corticosteroid-sparing strategies including azathioprine, thalidomide, clofazimine, methotrexate, minocycline, tumour necrosis factor-α inhibitors, cyclophosphamide, and other biological therapies. The study selection process is presented in accordance with the PRISMA 2020 framework in Figure 1.

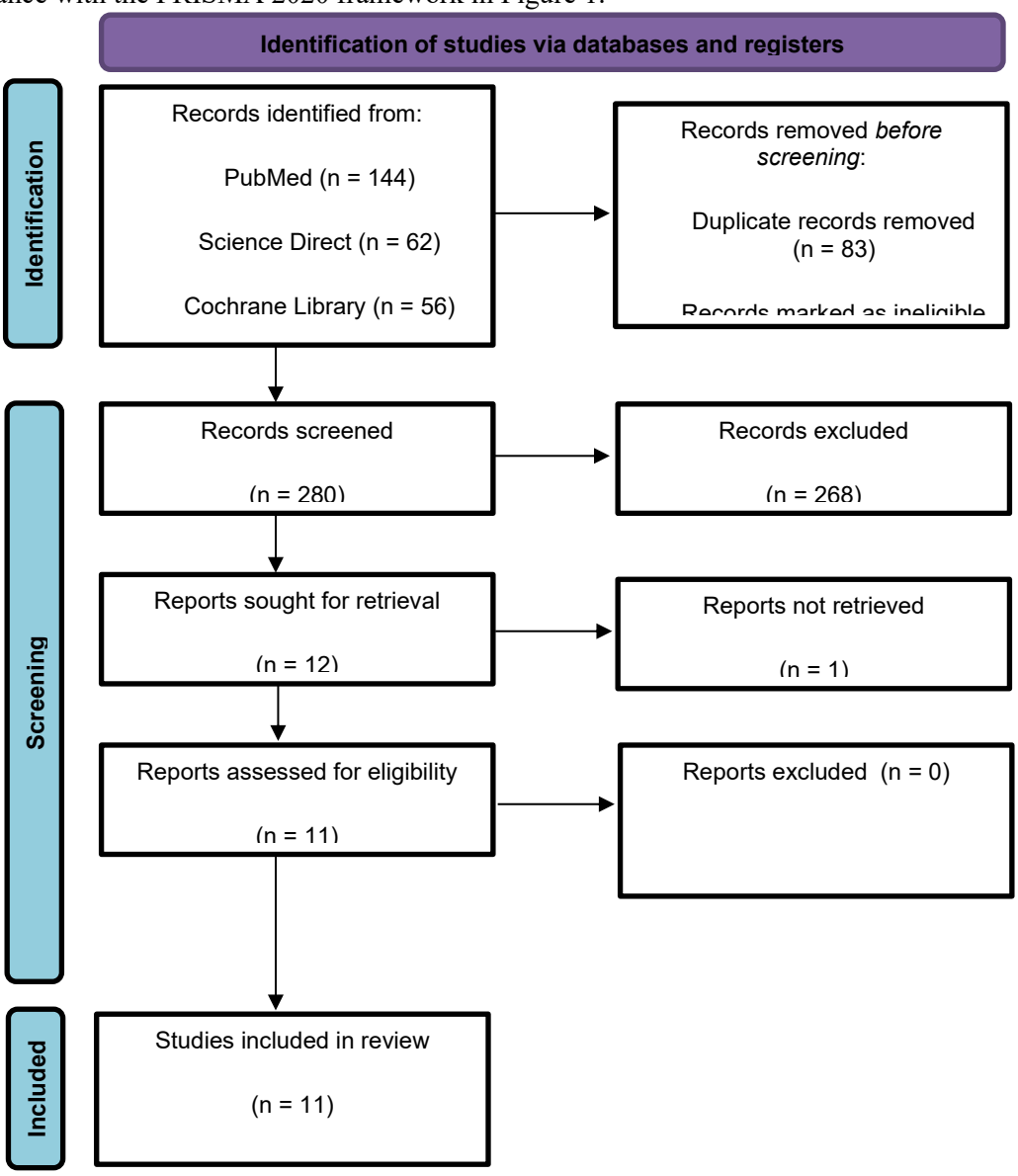


Figure 1. PRISMA *Flowchart*

Study Characteristics

A total of 11 studies were included in this systematic review, comprising randomized controlled trials, comparative interventional studies, retrospective cohort studies, and case

series. Most studies were conducted in India (n = 6), followed by Brazil (n = 3) and France (n = 1), while one multicentre randomized controlled trial recruited participants from India, Ethiopia, Indonesia, and Nepal. Across all included studies, 722 patients were evaluated, with individual study sample sizes ranging from 4 to 345 participants. Three studies were randomized controlled trials, while the remaining studies consisted of non-randomized comparative studies, retrospective observational studies, and case series.

Most included studies focused on type 2 leprosy reaction or erythema nodosum leprosum (ENL) (n = 9), whereas one study exclusively evaluated type 1 or reversal reactions and one study included patients with both reversal reactions and ENL. The corticosteroid-sparing interventions investigated included azathioprine, thalidomide, clofazimine, minocycline, methotrexate, etanercept, adalimumab, cyclophosphamide, and secukinumab. The study populations predominantly consisted of patients with chronic, recurrent, severe, or corticosteroid-dependent leprosy reactions, particularly ENL, in whom prolonged corticosteroid exposure represented an important therapeutic concern. The complete characteristics of the included studies are presented in Table 1.

Table 1. Study Characteristic

No	First author, year	Study design	Country	Intervention	Control	Intervention duration	Mean age Of intervention group (years)	Mean Age Of control group (years)	Sample population
1	Lockwood et al., 2017	Randomized Controlled trial	India	Azathioprine 50 mg /day + prednisolone	Placebo + Prednisolone	Prednisolone for 20 weeks; azathioprine for 24, 36, or 48 weeks	NR (overall Range 15–60)	NR	345 Patients with a new type 1 leprosy Reaction Involving the skin and/or peripheral nerves
2	Upputuri et al., 2020	Five-year Retrospective record-based study	India	Thalidomide	N/A	Mean 9.4 ± 8.6 months	34.4 ± 11.5	N/A	102 Patients With ENL; Predominantl multibacillary disease, with most receiving thalidomide for corticosteroid dependence
3	Hanumanthu et al., 2021	Prospective Randomized clinical trial	India	Minocycline 100 mg once daily + prednisolone	Clofazimine 100 mg three times daily predniso	12 weeks; follow-up for 6 months	NR	NR	60 Patients With chronic or recurrent ENL

					lone				
4	Sahani et al., 2022	Retrospe ctive study	India	Etanercept 25–50 mg SC weekly + background therapy	N/A	1–9 weekly doses; outcomes assessed at 6 months	32.2 †	N/A	6 patients With recurrent, corticosteroid dependent ENL of >6 months' duration and poor response toconventional immunosupp ressive therapy
5	Mishra et al., 2022	Comparative clinical study	India	Thalidomide 300 mg/day + prednisolone 40 mg/day Followed by tapering	Clofazimine 300 mg/day + prednisol one 40 mg/day followed by tapering	Initial Treatment for 3 months followed by dose tapering; outcomes followed to 6 months	NR by treatment arm	NR by treatment arm	30 patients With Recurrent ENL who Had Previously received corticosteroids and were considered nonresponders; 15 patients per group
6	Mendes et al., 2022	Case series	Brazil	Anti-TNF-α therapy: etanercept 50 mg/ week (n=3) or Adalimumab 40 mg every 2 weeks (n=1)	N/A	6 months–2 years	44.3†	N/A	4 patients With severe, chronic, refractory ENL who had failed high-dose corticosteroids and thalidomide
7	Bathula et al., 2023	Real-world single-arm study	India	Low-dose Thalidomide 25–150 mg/day with tapering prednisolone	N/A	Individualized; Mean Corticosteroid discontinuation 3.03 Months And Discontinua	NR	N/A	16 patients With ENL, Including 15 with Severe ENL; Both corticosteroid-naïve and

						tion of both drugs in responders by a mean of 5.83 months			corticosteroid dependent patients were included
8	Jaume et al., 2023	Multicentre Retrospective study	France	Methotrexate, Median 20 mg /week, with Concomitant Therapy as clinically indicated	N/A	Median 14 months (range 5–50)	NR‡	N/A	13 patients with corticosteroid-treated leprosy reactions: reversal reaction (n=7) And ENL (n=6)
9	Machado et al., 2023	Case series	Brazil	Cyclophosphamide Pulse therapy 1 g IV Every 4–6 weeks + background prednisone/ thalidomide	N/A	3–6 Cycles Every 4–6 weeks	32.3†	N/A	4 patients With chronic, relapsing, severe, difficult-to-control ENL Despite prolonged prednisone and thalidomide therapy
10	Gomide et al., 2025	Retrospec tive single-centre cohort study	Brazil	Secukinumab 300 mg SC weekly for 4 weeks, followed by 300 mg Every 2–4 weeks	N/A	Follow-up 5–15 months	35.6	N/A	5 male Patients With Refractory Chronic ENL And Inadequate response to systemic corticosteroids plus at least one additional therapy
11	De Barros et al., 2026	International multicentre, double-blind	Ethiopia, India, Indonesia, and Nepal	Methotrexate 15 mg/ week, increased to 20 mg /week	Placebo + Identical Predniso Lone regimen	Methotrexate / Placebo for 48 weeks prednisolone for 20	33.4 ± 9.9	33.9 ± 10.5	137 adults With Severe ENL; 68

		randomized placebo-controlled trial		in patients ≥60 kg, + prednisolone		weeks; follow-up for 60 weeks			received methotrexate + Prednisolone and 69 Received Placebo + prednisolone

Table 2. Study Outcomes

Author, year	Study outcomes	Risk of bias
Lockwood et al., 2017	Addition of azathioprine to prednisolone did not significantly improve the overall clinical reaction severity score compared with prednisolonealone. Approximately 36% of participants required additional corticosteroids because of recurrent skin and/or nerve reactions, and azathioprine did not provide a meaningful corticosteroid-sparing benefit. High treatment withdrawal and missing outcome data were notable limitations.	Moderate risk
Upputuri et al., 2020	Thalidomide was associated with clinical improvement in 68 of 102 patients with ENL who were compliant with therapy. Among responders, recurrence occurred in 11 patients (16.2%). Earlier initiation of thalidomide was associated with faster remission and lower recurrence, supporting its role as a corticosteroid-sparing treatment for ENL.	Moderate risk
Hanumanthu et al., 2021	Minocycline achieved earlier control of chronic or recurrent ENL than clofazimine (2.97 ± 1.90 vs. 4.00 ± 1.96 weeks; p=0.048) and was associated with a longer remission period and fewer adverse events. Recurrence rates and additional prednisolone requirements were not significantly different between groups.	Low risk
Sahani et al., 2022	Etanercept reduced cumulative prednisolone exposure by 42.8%, from 1489.8 mg to 851.5 mg over six months (p=0.03), and reduced the mean number of ENL lesions per episode from 37 to 16 (p=0.019). Corticosteroids were completely discontinued in three patients and successfully tapered in the remaining three.	Moderate risk
Mishra et al., 2022	Both thalidomide plus prednisolone and clofazimine plus prednisolone improved recurrent ENL; however, the thalidomide regimen produced greater reductions in reaction severity and pain. At six months, absence of recurrence with successful steroid withdrawal was observed in 80% of the thalidomide group compared with 66% of the clofazimine group.	Low risk

Mendes et al., 2022	Anti-TNF-α therapy with etanercept or adalimumab produced clinical improvement in all four patients with severe refractory ENL. All patients experienced fewer ENL episodes and at least a 50% reduction in conventional immunosuppressive treatment, including corticosteroids, during follow-up. No direct biologic-related adverse events were reported.	Low risk
Bathula et al., 2023	Low-dose thalidomide produced rapid control of severe ENL and a marked corticosteroid-sparing effect. Mean prednisolone dose decreased from 33.16 mg/day to 4.28 mg/day at three months (p<0.05). Corticosteroids were discontinued in 92% of patients by a mean of 3.03 months, and both thalidomide and corticosteroids were discontinued in 80% by a mean of 5.83 months.	Low risk
Jaume et al., 2023	Methotrexate achieved a good clinical response in 8 of 13 patients (61.5%). Among patients receiving corticosteroids at methotrexate initiation, complete corticosteroid withdrawal was achieved in 6 of 11 (54.5%), while the mean corticosteroid dose decreased from 46 mg/day to 4 mg/day. Relapse after methotrexate discontinuation occurred in 42% of responders.	Moderate risk
Machado et al., 2023	Cyclophosphamide pulse therapy improved control of chronic recalcitrant ENL in all four patients and enabled reduction of corticosteroid and/or thalidomide therapy. Prednisone doses decreased by approximately 50–74% in three of four patients, and one patient achieved sustained remission without prednisone, thalidomide, or other immunosuppressive treatment. No adverse events directly related to cyclophosphamide pulse therapy were reported.	Low risk
Gomide et al., 2025	Secukinumab significantly reduced the mean frequency of ENL episodes from 3.0 ± 0.7 to 0.6 ± 0.5 episodes over five months (p=0.0039). Mean cumulative prednisone exposure decreased from 279.0 ± 121.3 mg to 223.0 ± 59.7 mg, although this reduction was not statistically significant (p=0.1764). No secukinumab-related adverse events were reported.	Low risk
de Barros et al., 2026	In the multicentre MaPs in ENL trial, methotrexate added to prednisolone did not reduce the need for additional corticosteroids compared with placebo plus prednisolone. There was no significant difference in time to first ENL flare at 24 weeks (HR 0.98; 95% CI 0.62–1.54) or 48 weeks (HR 0.95; 95% CI 0.62–1.43), and methotrexate did not reduce flare frequency or severity.	Low risk

Note: *Risk of bias was assessed according to study design using RoB 2 for randomized controlled trials, ROBINS-I for non-randomized comparative studies, and the Joanna Briggs Institute Critical Appraisal Tools for observational studies and case series.*

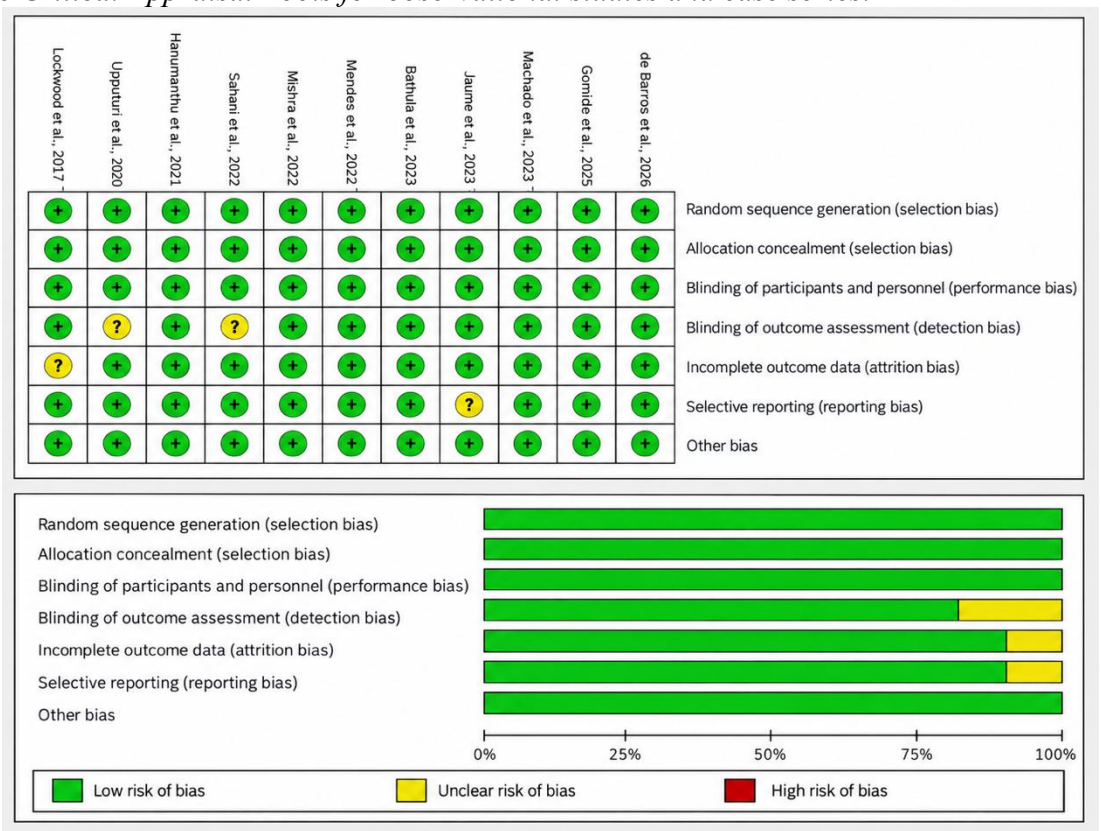


Figure 2. Risk-of-Bias Assessment of the Included Studies

Discussion

This systematic review demonstrates that the evidence supporting corticosteroid-sparing therapy for leprosy reactions remains heterogeneous, with substantial variation in study design, reaction phenotype, therapeutic strategy, and outcome definition. Across the 11 included studies, most investigations focused on chronic, recurrent, severe, or corticosteroid-dependent erythema nodosum leprosum (ENL), whereas evidence for type 1 reactions was considerably more limited. The overall pattern suggests that corticosteroid-sparing efficacy cannot be regarded as a class effect of immunomodulatory therapy. Thalidomide showed the most consistent signal for reducing corticosteroid exposure in ENL, while the effects of methotrexate differed markedly between observational evidence and the recent placebo-controlled trial. Minocycline, anti-TNF-α agents, cyclophosphamide, and secukinumab demonstrated potentially useful clinical activity, but their supporting evidence remains comparatively limited. These findings reinforce the need to distinguish established efficacy from promising signals generated in highly selected refractory populations (Upputuri et al., 2020; Jaume et al., 2023; de Barros et al., 2026).

The clinical importance of corticosteroid-sparing strategies is strengthened by the cumulative toxicity associated with prolonged systemic corticosteroid therapy. Patients with recurrent or chronic leprosy reactions frequently require repeated treatment courses, exposing them to metabolic, infectious, ophthalmological, musculoskeletal, and endocrine complications that may eventually rival the morbidity caused by the reaction itself. A recent systematic review of 111 studies found infections in approximately 15% of corticosteroid-treated individuals and identified tuberculosis as the predominant cause of corticosteroid-associated mortality; cataract and osteoporosis were particularly prominent among patients

with ENL. These observations are especially relevant because the patients represented in the present review were commonly those with prolonged, relapsing disease and previous corticosteroid dependence. A clinically useful corticosteroid-sparing strategy should therefore be judged not only by its ability to suppress visible inflammatory activity, but also by its capacity to reduce cumulative corticosteroid exposure without increasing relapse, neurological deterioration, or treatment-related toxicity (Lun, de Barros and Walker, 2026).

The marked predominance of ENL studies in the current evidence base also reflects fundamental biological differences between type 1 and type 2 reactions. Type 1 reactions are driven predominantly by an intensification of cell-mediated immunity within existing leprosy lesions and peripheral nerves, whereas ENL involves a more complex systemic inflammatory response incorporating neutrophils, immune complexes, cytokine dysregulation, and several innate and adaptive immune pathways. These differences are therapeutically relevant because an agent capable of suppressing systemic inflammation in ENL cannot automatically be expected to prevent nerve injury in type 1 reactions. The emerging roles of interferon-γ, interleukin pathways, neutrophil activation, regulatory T-cell imbalance, and Th17 responses further suggest that the biological targets responsible for therapeutic benefit may differ across reaction phenotypes. The current literature should therefore be interpreted as two partially distinct therapeutic evidence bases rather than as a single body of evidence for “leprosy reactions” as a uniform clinical entity (Dewi et al., 2023; Serrano-Coll et al., 2024; Mehta et al., 2025).

This distinction is particularly apparent in the evidence for azathioprine. The AZALEP trial remains one of the largest controlled evaluations of corticosteroid-sparing immunosuppression for type 1 reactions and nerve involvement. Addition of azathioprine to prednisolone did not produce a clinically meaningful improvement in reaction severity or demonstrate a convincing reduction in subsequent corticosteroid requirement. Approximately one-third of participants still required additional corticosteroid treatment because of recurrent skin or nerve inflammation. Although methodological limitations, including treatment withdrawal and missing outcome data, complicate interpretation, the absence of a clear therapeutic advantage in a comparatively large randomized study argues against routine addition of azathioprine solely for corticosteroid sparing in type 1 reactions. More importantly, the scarcity of subsequent controlled trials in this phenotype leaves a major therapeutic gap for patients in whom prolonged corticosteroid exposure is unavoidable because of recurrent neuritis or persistent nerve inflammation (Lockwood et al., 2017; Mehta et al., 2025).

In contrast, thalidomide produced the most consistent corticosteroid-sparing signal across the ENL studies included in this review. The five-year retrospective analysis by Upputuri et al. demonstrated clinical improvement among treatment-compliant patients and supported the feasibility of outpatient thalidomide therapy in appropriately selected patients. Mishra et al. subsequently observed greater improvement in reaction severity and pain with a thalidomide-based regimen compared with clofazimine-based treatment, together with a higher proportion of patients achieving steroid withdrawal without recurrence. Particularly striking findings were reported by Bathula et al., in whom mean prednisolone requirement decreased from 33.16 mg/day to 4.28 mg/day within three months, corticosteroids were discontinued in 92% of patients, and both corticosteroid and thalidomide therapy could ultimately be discontinued in 80%. Although these studies differ substantially in design and population, their direction of effect is broadly concordant and supports thalidomide as the best-established corticosteroid-sparing therapy among the interventions examined for recurrent or severe ENL (Upputuri et al., 2020; Mishra et al., 2022; Bathula et al., 2023).

The apparent effectiveness of thalidomide must nevertheless be considered alongside important limitations that restrict its universal application. Teratogenicity remains the

principal barrier to use in individuals with reproductive potential and necessitates stringent pregnancy-prevention programmes, controlled dispensing, and careful counselling. Peripheral neuropathy, sedation, thromboembolic complications, cost, and variable regulatory availability further complicate prolonged therapy, particularly in resource-constrained settings. The low-dose strategy evaluated by Bathula et al. is therefore clinically attractive because it raises the possibility that substantial corticosteroid reduction may be achieved with lower cumulative exposure to thalidomide itself. Clofazimine remains valuable where thalidomide is unavailable or contraindicated, but its delayed anti-inflammatory activity and cumulative pigmentation limit its attractiveness for rapidly active severe disease. The practical value of any corticosteroid-sparing intervention in leprosy must consequently incorporate accessibility, monitoring requirements, reproductive safety, and long-term toxicity rather than therapeutic efficacy alone (Costa et al., 2018; Bathula et al., 2023; Mehta et al., 2025).

The randomized comparison between minocycline and clofazimine provides a different perspective on corticosteroid-sparing management. Minocycline achieved more rapid initial control of chronic or recurrent ENL and prolonged remission after initial response, with fewer adverse events than high-dose clofazimine. Nevertheless, recurrence remained common in both groups, and the additional prednisolone requirement did not differ significantly. This distinction is clinically important because faster control of inflammatory activity should not automatically be interpreted as a corticosteroid-sparing effect. An agent may reduce lesion burden or improve time to remission without meaningfully reducing cumulative corticosteroid exposure or preventing subsequent flares. The findings therefore support minocycline as a potentially useful adjunct in chronic or recurrent ENL, particularly when clofazimine-related adverse effects are problematic, while providing insufficient evidence that it substantially reduces long-term corticosteroid dependence (Hanumanthu et al., 2021).

Methotrexate provides perhaps the clearest example of why corticosteroid-sparing efficacy requires confirmation in adequately controlled trials. In the French multicentre retrospective study by Jaume et al., 61.5% of patients achieved a good clinical response, complete corticosteroid withdrawal was possible in 54.5% of patients receiving corticosteroids at methotrexate initiation, and no severe methotrexate-related adverse events were reported. These findings provided a compelling rationale for considering methotrexate as an affordable and widely available alternative for both reversal reactions and ENL. However, relapse following methotrexate discontinuation occurred in 42% of responders, already indicating that suppression of disease activity might depend on continued treatment. The subsequent MaPs in ENL trial fundamentally altered this interpretation by demonstrating no reduction in the requirement for additional prednisolone, no delay in time to first ENL flare, and no meaningful reduction in flare frequency or severity when methotrexate was added to standard prednisolone therapy (Jaume et al., 2023; de Barros et al., 2026).

The discrepancy between the observational methotrexate data and the MaPs trial illustrates several recurrent methodological challenges within the leprosy-reaction literature. Patients selected for retrospective treatment series frequently have highly refractory disease but also receive individualized concomitant therapies, prolonged follow-up, and clinician-guided tapering, making it difficult to separate treatment effect from regression to the mean, background corticosteroid exposure, or the fluctuating natural history of reactional episodes. In contrast, randomized placebo-controlled trials impose standardized corticosteroid schedules and prospectively defined outcome measures, providing a more reliable estimate of incremental treatment benefit. In MaPs, nearly two-thirds of participants experienced a flare requiring additional prednisolone by 24 weeks and approximately three-quarters by 48

weeks, irrespective of methotrexate allocation, emphasizing the intrinsic relapsing nature of severe ENL. The negative trial should not be interpreted as evidence that methotrexate has no anti-inflammatory activity, but it substantially weakens the rationale for its routine use specifically as a corticosteroid-sparing agent in severe ENL (Jaume et al., 2023; de Barros et al., 2026).

Biological inhibition of TNF-α represents a more targeted strategy supported by strong pathophysiological rationale but limited clinical evidence. Sahani et al. reported a 42.8% reduction in cumulative prednisolone exposure following etanercept treatment in six patients with recurrent steroid-dependent ENL, with complete corticosteroid discontinuation in half of the cohort. Similarly, Mendes et al. described four patients with chronic severe ENL treated with etanercept or adalimumab after failure of high-dose corticosteroids and thalidomide; all experienced fewer reaction episodes and at least a 50% reduction in conventional immunosuppressive treatment. These responses are noteworthy because the study populations represented particularly treatment-refractory disease, in which therapeutic options are otherwise extremely limited. Nevertheless, the very small samples, absence of contemporaneous controls, and individualized concomitant treatment prevent reliable estimation of treatment effect. TNF inhibition also requires rigorous infection screening and specialist monitoring, considerations that may substantially constrain scalability in settings where leprosy remains endemic (Sahani et al., 2022; Mendes et al., 2022; Mehta et al., 2025).

Other emerging immunomodulatory strategies should currently be regarded primarily as rescue approaches rather than established alternatives. Cyclophosphamide pulse therapy was associated with improvement in all four patients with chronic recalcitrant ENL described by Machado et al., allowing substantial reductions in prednisone and/or thalidomide exposure, with one patient maintaining remission without either agent. The response is clinically meaningful in the context of exceptionally refractory disease, but the small uncontrolled series and the recognised intensity of cyclophosphamide immunosuppression make routine application difficult to justify without comparative evidence. Secukinumab provides an even more targeted biological approach through IL-17A inhibition. In five refractory patients, ENL episode frequency decreased significantly from 3.0 to 0.6 episodes over five months, whereas the reduction in cumulative prednisone exposure was numerically favourable but not statistically significant. These observations support further investigation of IL-17-mediated pathways, but they remain hypothesis-generating rather than sufficient to define a new standard of care (Machado et al., 2023; Gomide et al., 2025; Serrano-Coll et al., 2024).

A central limitation of the existing evidence is the absence of a uniform definition of corticosteroid-sparing success. Included studies variously reported daily dose reduction, cumulative dose reduction, time to corticosteroid withdrawal, proportion achieving complete withdrawal, need for additional rescue prednisolone, recurrence after tapering, or clinical remission while corticosteroids were being reduced. These endpoints capture different dimensions of treatment benefit and cannot be considered interchangeable. A reduction in mean daily dose may coexist with frequent relapses, while complete withdrawal achieved over a short observation period may not represent durable control. The use of standardized reaction-severity measures in the MaPs trial illustrates an important methodological advance, but future studies should combine disease activity with prespecified cumulative corticosteroid exposure, time to successful discontinuation, relapse-free survival, neurological outcomes, and patient-reported quality of life. Such standardization would substantially improve comparability between future trials and facilitate quantitative synthesis (Hanumanthu et al., 2021; Jaume et al., 2023; de Barros et al., 2026).

The methodological profile of the literature also warrants caution when translating therapeutic signals into clinical recommendations. Only a minority of the included studies

were randomized, while much of the evidence for biologic agents and intensive immunosuppression arose from small retrospective series or case series. Such designs are valuable in rare, treatment-refractory conditions, particularly for identifying potential therapeutic signals, but are inherently vulnerable to selection bias, confounding by indication, heterogeneous background therapy, and preferential publication of successful outcomes. Geographic concentration is another consideration: a substantial proportion of the available evidence originated from specialist centres in India and Brazil, where clinical experience with severe leprosy reactions is substantial but treatment access, comorbidity profiles, and monitoring infrastructure may differ from other endemic settings. The international multicentre design of MaPs therefore represents an important progression toward more generalisable evidence and highlights the value of collaborative trials across leprosy referral networks (Mendes et al., 2022; Machado et al., 2023; de Barros et al., 2026).

From a clinical perspective, the current evidence supports a differentiated rather than uniform approach to corticosteroid-sparing therapy. For ENL, thalidomide remains the intervention with the most consistent evidence of clinically meaningful corticosteroid reduction, provided that reproductive risk, neurological toxicity, and access can be adequately managed. Clofazimine and minocycline may provide useful alternatives or adjuncts, although direct evidence for substantial corticosteroid reduction is less convincing. Methotrexate should be interpreted cautiously following the negative MaPs trial and cannot currently be considered an evidence-based routine corticosteroid-sparing intervention for severe ENL. TNF-α inhibitors, cyclophosphamide, and secukinumab may be considered investigational or highly selected rescue options in refractory disease within specialist settings, rather than therapies supported for widespread use. For type 1 reactions, the evidence remains considerably weaker, and the negative AZALEP findings underline the continued absence of a well-established corticosteroid-sparing alternative capable of reliably protecting nerve function (Lockwood et al., 2017; Hanumanthu et al., 2021; Bathula et al., 2023; de Barros et al., 2026).

Several limitations of this systematic review arise from the underlying literature. The small number of eligible studies, heterogeneity in reaction phenotype and disease severity, variable corticosteroid regimens, inconsistent definitions of response, and predominance of uncontrolled studies precluded meaningful quantitative pooling. Long-term neurological outcomes were also insufficiently reported, despite prevention of irreversible nerve damage being one of the most clinically important objectives in reaction management. Future trials should stratify participants by acute, recurrent, and chronic reaction phenotypes; distinguish type 1 reactions from ENL; apply validated reaction-severity measures; and prospectively define clinically meaningful corticosteroid-sparing endpoints. Multicentre studies conducted in endemic regions should additionally incorporate infection surveillance, reproductive safety, cost, treatment accessibility, and quality-of-life outcomes so that efficacy can be interpreted alongside real-world feasibility. The present evidence indicates that reducing corticosteroid dependence in leprosy reactions is achievable in selected settings, but only a small proportion of candidate therapies have yet been tested with sufficient methodological rigour to support routine clinical adoption (Lun, de Barros and Walker, 2026; Mehta et al., 2025; de Barros et al., 2026).

CONCLUSION

This systematic review indicates that corticosteroid-sparing therapy for leprosy reactions remains an evolving field with markedly stronger evidence for erythema nodosum leprosum than for type 1 reactions. Thalidomide showed the most consistent corticosteroid-sparing benefit, with several studies demonstrating substantial reductions in prednisolone exposure and successful corticosteroid withdrawal, although its use remains constrained by teratogenicity, neurotoxicity, and access-related limitations. Clofazimine and minocycline may provide useful adjunctive options, while azathioprine did not demonstrate a meaningful corticosteroid-sparing advantage in type 1 reactions. Methotrexate appeared promising in observational studies but failed to reduce corticosteroid requirement or ENL flares in the recent multicentre randomized MaPs in ENL trial, highlighting the importance of controlled evidence before routine adoption. Emerging approaches, including TNF-α inhibitors, cyclophosphamide, and secukinumab, showed encouraging activity in refractory disease but are currently supported mainly by small observational studies and case series. Overall, corticosteroid-sparing strategies should be individualized according to reaction phenotype, disease severity, treatment toxicity, comorbidities, and drug accessibility, while future multicentre trials using standardized corticosteroid-sparing endpoints, neurological outcomes, relapse measures, and long-term safety assessments are required to establish more definitive treatment pathways.

REFERENCES

Bathula, S., Sardana, K., Mathachan, S.R., Khurana, A., Ahuja, A. and Paliwal, P. (2023) 'A real-world study of low-dose thalidomide in severe erythema nodosum leprosum highlighting its mechanistic rationale in a resource-constrained target population', *International Journal of Dermatology*, 62(1), pp. 48–55. doi:10.1111/ijd.16315.

Costa, P.S.S., Fraga, L.R., Kowalski, T.W., Daxbacher, E.L.R., Schuler-Faccini, L. and Vianna, F.S.L. (2018) 'Erythema nodosum leprosum: Update and challenges on the treatment of a neglected condition', *Acta Tropica*, 183, pp. 134– 141. doi:10.1016/j.actatropica.2018.02.026.

de Barros, B., Sultana, F., Maximus, N., Pai, V.V., Wakade, A., Bhame, B. *et al*. (2026) 'Methotrexate and prednisolone compared to placebo and prednisolone in the treatment of severe erythema nodosum leprosum: An international multicentre, double-blind randomised controlled clinical trial—MaPs in ENL', *PLOS Neglected Tropical Diseases*, 20(9), e0014739. doi:10.1371/journal.pntd.0014739.

Dewi, D.A.R., Djatmiko, C.B.P., Rachmawati, I., Arkania, N., Wiliantari, N.M. and Nadhira, F. (2023) 'Immunopathogenesis of type 1 and type 2 leprosy reaction: An update review', *Cureus*, 15(11), e49155. doi:10.7759/cureus.49155.

Gomide, L.V., Brufatto, J.P.T., Kucarz, T.J., Velho, P.E.N.F. and França, A.F.E.C. (2025) 'Managing leprosy reactions with secukinumab: Insights from a case series', *Revista da Sociedade Brasileira de Medicina Tropical*, 58, e0118-2025. doi: 10.1590/0037-8682-0118-2025.

Hanumanthu, V., Thakur, V., Narang, T. and Dogra, S. (2021) 'Comparison of the efficacy and safety of minocycline and clofazimine in chronic and recurrent erythema nodosum leprosum: A randomized clinical trial', *Dermatologic Therapy*, 34(6), e15125. doi: 10.1111/dth.15125.

Jaume, L., Hau, E., Monsel, G., Mahé, A., Bertolotti, A., Petit, A. *et al*. (2023) 'Methotrexate as a corticosteroid-sparing agent in leprosy reactions: A French multicenter

retrospective
study', *PLOS Neglected Tropical Diseases*, 17(4), e0011238. doi:10.1371/journal.pntd.0011238.

Lockwood, D.N.J., Darlong, J., Govindharaj, P., Kurian, R., Sundarrao, P. and John, A.S. (2017) 'AZALEP a randomized controlled trial of azathioprine to treat leprosy nerve damage and type 1 reactions in India: Main findings', *PLOS Neglected Tropical Diseases*, 11(3), e0005348. doi:10.1371/journal.pntd.0005348.

Lun, A.I., de Barros, B. and Walker, S.L. (2026) 'A systematic review of adverse effects associated with systemic corticosteroids in the management of leprosy', *PLOS Neglected Tropical Diseases*, 20(3), e0014152. doi:10.1371/journal.pntd.0014152.

Machado, G.U., Amparo, T., Bulhões, F. and Machado, P.R.L. (2023) 'Case report: Cyclophosphamide pulse therapy for chronic recalcitrant erythema nodosum leprosum', *Frontiers in Medicine*, 10, 1272404. doi: 10.3389/fmed.2023.1272404.

Mehta, H., Jain, S., Narang, T., Chhabra, S. and Dogra, S. (2025) 'Leprosy reactions: New knowledge on pathophysiology, diagnosis, treatment and prevention', *Indian Journal of*
Dermatology, Venereology and Leprology, 91(4), pp. 470– 481. doi:10.25259/IJDVL_915_2024.

Mendes, A.F.M., Gomes, C.M., Kurizky, P.S. and Ianhez, M. (2022) 'Case report: A case series of immunobiological therapy (anti-TNF-α) for patients with erythema nodosum leprosum', *Frontiers in Medicine*, 9, 879527. doi:10.3389/fmed.2022.879527.

Mishra, S.R.P.K., Samal, R. and Behera, B. (2022) 'Thalidomide and steroid in the management of erythema nodosum leprosum', *Indian Journal of Pharmacology*, 54(3), pp. 177–182. doi: 10.4103/ijp.ijp_946_21.

Narang, T., Ashraf, R., Kaushik, A. and Dogra, S. (2021) 'Apremilast in multibacillary leprosy patients with chronic and recurrent erythema nodosum leprosum: A prospective single-centre pilot study', *Journal of the European Academy of Dermatology and Venereology*, 35(12), pp. e917–e919. doi:10.1111/jdv.17585.

Pérez-Molina, J.A., Arce-García, O., Chamorro-Tojeiro, S., Norman, F., Monge-Maillo, B., Comeche, B. and López-Vélez, R. (2020) 'Use of methotrexate for leprosy reactions. Experience of a referral center and systematic review of the literature', *Travel Medicine and Infectious Disease*, 37, 101670. doi:10.1016/j.tmaid.2020.101670.

Putri, A.I., de Sabbata, K., Agusni, R.I., Alinda, M.D., Darlong, J., de Barros, B. *et al*. (2022) 'Understanding leprosy reactions and the impact on the lives of people affected: An exploration in two leprosy endemic countries', *PLOS Neglected Tropical Diseases*, 16(6), e0010476. doi:10.1371/journal.pntd.0010476.

Sahani, M.K., Asati, D.P., Kaur, M. and Patra, S. (2022) 'Can etanercept be an option in management of recurrent steroid-dependent erythema nodosum leprosum? A retrospective study of six patients', *Indian Journal of Dermatology, Venereology and Leprology*, 88(2), pp. 243–246. doi: 10.25259/IJDVL_726_20.

Serrano-Coll, H., Wan, E.L., Restrepo-Rivera, L. and Cardona-Castro, N. (2024) 'Leprosy reactions: Unraveling immunological mechanisms underlying tissue damage in leprosy patients', *Pathogens and Disease*, 82, ftae013. doi:10.1093/femspd/ftae013.

Upputuri, B., Pallapati, M.S., Tarwater, P. and Srikantam, A. (2020) 'Thalidomide in the treatment of erythema nodosum leprosum (ENL) in an outpatient setting: A five-year retrospective analysis from a leprosy referral centre in India', *PLOS Neglected Tropical Diseases*, 14(10), e0008678. doi:10.1371/journal.pntd.0008678.