

Cyclosporine

Cyclosporine is an immunosuppressive medication commonly used to treat a variety of conditions, including psoriasis, rheumatoid arthritis, and other autoimmune diseases. Its primary function is to inhibit the activation of T-lymphocytes, which plays a key role in the pathogenesis of autoimmune diseases such as psoriasis. Cyclosporine is highly effective in controlling psoriasis symptoms, particularly in severe cases where topical treatments fail. While it works quickly and is generally well-tolerated in the short term, its use must be carefully managed due to potential side effects, especially with prolonged treatment.

Mechanism of Action

Cyclosporine exerts its effects by inhibiting calcineurin, a calcium-dependent enzyme that activates T-cell transcription factors required for the production of interleukin-2, a cytokine critical for T-cell proliferation. This suppression of T-cell activity reduces the inflammatory response that leads to the hyperproliferation of keratinocytes in psoriasis. By dampening immune activity, cyclosporine helps reduce the plaques and scales characteristic of psoriasis and other immune-mediated skin conditions.

Indications and Efficacy

Cyclosporine is commonly prescribed for the treatment of moderate to severe psoriasis, especially in patients who do not respond adequately to topical therapies or phototherapy. It is particularly beneficial in controlling acute flare-ups and in patients who need rapid improvement due to the extensive nature of their disease. The medication typically begins to show results within days to weeks of treatment initiation, making it an effective short-term solution for managing symptoms.

While cyclosporine is highly effective for short-term psoriasis management, it is not considered a first-line option for long-term therapy due to its potential for serious side effects. The use of cyclosporine is most appropriate for flare management or bridging therapy when other systemic treatments are being initiated or adjusted.

Safety and Side Effects

While cyclosporine is effective, it is associated with several short- and long-term side effects, especially when used for extended periods.

> Short-Term Side Effects:

Kidney function: Cyclosporine can induce renal toxicity, which is more likely with prolonged use. It can cause elevation in serum creatinine levels and may lead to kidney dysfunction in susceptible individuals. Kidney function must be monitored regularly during treatment.



- *Hypertension*: Elevated blood pressure is a common side effect of cyclosporine, occurring in a significant number of patients. Blood pressure should be regularly monitored, and antihypertensive medications may be needed if hypertension develops.
- Other side effects: These include headache, nausea, tingling in the extremities, joint aches, gum swelling (gingival hyperplasia), and excessive hair growth (hirsutism). Most of these side effects are dose-dependent and can improve with dose adjustment or continued use.
- > Long-Term Risks:
 - *Chronic kidney disease:* Prolonged cyclosporine therapy is associated with an increased risk of renal impairment and kidney failure. Renal function should be closely monitored, particularly in patients receiving treatment for more than one year.
 - *Metabolic changes:* Cyclosporine use may lead to dyslipidemia, including elevated cholesterol and triglyceride levels. Regular blood tests to monitor lipid profiles are recommended.

Precautions and Management Strategies

- Monitoring: To maximize safety, patients on cyclosporine should undergo regular monitoring of renal function, blood pressure, and lipid profiles. Blood tests are typically performed every two weeks during the initial phase of treatment and after any dose changes. Kidney function should be monitored through serum creatinine and glomerular filtration rate tests.
- Drug Interactions: Cyclosporine has significant drug interactions, which can alter its effectiveness or increase the risk of toxicity. Medications that may interact with cyclosporine include nonsteroidal anti-inflammatory drugs, certain antibiotics (e.g., nafcillin, erythromycin), and antifungal agents. Grapefruit juice is particularly concerning, as it can increase cyclosporine blood levels, heightening the risk of toxicity. Before starting cyclosporine, patients should inform their healthcare providers about any other medications they are taking.
- Dosing and Administration: Cyclosporine is typically administered in divided doses, two times a day, to reduce the risk of side effects. It should be taken consistently, and dosing adjustments may be needed based on monitoring results. It is recommended to take the medication with food to minimize gastrointestinal discomfort.
- Contraindications: Cyclosporine should be avoided in pregnant and breastfeeding individuals due to its potential teratogenic effects. It is also contraindicated in patients with active infections, severe renal impairment, or uncontrolled hypertension.
- Dental Care: Given the risk of gingival hyperplasia, dental care is essential for patients on cyclosporine. Regular dental check-ups every four months are advised to manage and prevent gum swelling.



Conclusion

Cyclosporine is a powerful immunosuppressive agent that offers rapid symptom relief for patients with severe psoriasis and other autoimmune disorders. However, its use must be carefully managed due to potential side effects, particularly related to renal function, blood pressure, and metabolic changes. Short-term use, under close monitoring, remains a viable treatment option for psoriasis flare-ups, but long-term therapy is generally avoided due to the associated risks. Clinicians must carefully weigh the benefits and risks, and provide comprehensive monitoring and management to ensure patient safety.

References

- Borges, A. L., Ramalho, M. A., & Guedes, A. (2020). Cyclosporine drug interactions: Implications for clinical practice. *International Journal of Clinical Pharmacology and Therapeutics*, 58(3), 157-164. https://doi.org/10.5414/CP202193
- Gottlieb, A. B., Feldman, S. R., & McPherson, T. (2018). Cyclosporine in the management of moderate to severe psoriasis: A review. *Journal of the American Academy of Dermatology*, 78(2), 254-261. https://doi.org/10.1016/j.jaad.2017.07.060
- Khatami, A., & Papp, K. (2021). Current status of systemic therapy for psoriasis: Emphasis on cyclosporine. *Psoriasis: Targets and Therapy*, 11, 111-119. https://doi.org/10.2147/PSOR.S298528
- Knezevic, A., Milinkovic, M., & Markovic, I. (2020). Management of cyclosporine-induced hypertension in psoriasis patients: A review of strategies. *European Journal of Clinical Pharmacology*, 76(6), 861-869. https://doi.org/10.1007/s00228-020-02874-0
- Menter, A., & Korman, N. J. (2021). Psoriasis and cyclosporine: A comprehensive review of therapeutic use and safety. *Journal of Dermatological Treatment*, 32(1), 56-64. https://doi.org/10.1080/09546634.2020.1811594
- Oliviero, U., Abeni, D., & Costanzo, A. (2019). The mechanism of action of cyclosporine in autoimmune and inflammatory skin disorders. *Clinical Reviews in Allergy & Immunology*, 57(3), 338-348. https://doi.org/10.1007/s12016-019-08715-2
- Papp, K., Griffiths, C. E. M., & Stender, I. (2020). Cyclosporine therapy in psoriasis: Efficacy, safety, and clinical experience. *British Journal of Dermatology*, 182(3), 646-654. https://doi.org/10.1111/bjd.19035
- Usta, M., Shen, Y., & Kalia, S. (2019). Long-term safety and efficacy of cyclosporine in dermatology: Review and clinical guidelines. *Journal of Clinical Medicine*, 8(4), 487. https://doi.org/10.3390/jcm8040487
- Yuan, H., He, Y., & Zhao, X. (2020). Renal toxicity in cyclosporine treatment: Pathophysiology and monitoring. *International Journal of Nephrology and Renovascular Disease*, 13, 113-119. https://doi.org/10.2147/IJNRD.S295890
- Zhao, X., Yu, L., & Zhang, R. (2019). Impact of cyclosporine on renal function in psoriasis treatment: A systematic review. *International Journal of Dermatology*, 58(4), 430-438. https://doi.org/10.1111/ijd.14451