High-dose pyridoxine and peripheral neuropathy: Considerations for clinicians, pharmacists and policy-makers

Pyridoxine, the biologically active form of vitamin B6, remains an important adjunct to isoniazid (INH) therapy to prevent peripheral neuropathy, as recommended by the South African (SA) National Department of Health, particularly for people living with HIV (PLWH),[1] malnourished individuals and those with pre-existing neuropathy.[2] However, emerging pharmacovigilance data, particularly those highlighted by the Australian Therapeutic Goods Administration (TGA), show that pyridoxine itself can paradoxically cause neuropathy at doses previously considered safe, even at ≤50 mg/day.[3-5] These findings carry important implications for tuberculosis (TB) programmes and general practice, especially in high-burden settings such as SA.

Growing international safety data indicate that pyridoxine-induced neuropathy is dose-dependent and cumulative, and is being increasingly reported, including in patients taking multiple vitamin B6-containing products without clinician oversight.[6,7] While the association between high-dose pyridoxine and neuropathy is not new,[1,8] the threshold for toxicity appears to be much lower than historically believed.[3,5] The TGA's regulatory actions provide the history of this evolving evidence. TGA safety reviews from 2020 to the present show neuropathy occurring even at modest doses, and have recommended strict controls on products >50 mg daily dosing.[3,5] In November 2025, Australia's medicines regulator instructed the removal of high-dose vitamin B6 supplements from general sale, following hundreds of reports of nerve damage linked to long-term use. This directive will take effect from June 2027, where any product providing >50 mg of vitamin B6 per day will be restricted to 'pharmacist-only access', equivalent to schedule 2 (S2) in SA.[9] This decision follows a TGA safety review and public consultation that identified '250 cases of peripheral neuropathy, since 2023, despite the recommended dietary intake for healthy adults being only 1.3 - 1.7 mg per day'.[4]

At the same time, recent TB research questions the necessity of routine pyridoxine supplementation for all patients receiving INH.[10] Evidence indicates that neuropathy risk is concentrated in specific high-risk groups, while excessive supplementation may itself worsen neuronal damage.[11] Toxicity is thought to occur when high circulating levels of pyridoxine competitively inhibit active co-enzyme pyridoxal-5-phosphate or cause direct dorsal root ganglion injury.[11] Clinically, patients present with symptoms that are indistinguishable from INH-induced neuropathy, such as burning, tingling and numbness in the extremities, leading clinicians to further increase the pyridoxine dose, inadvertently worsening the neuropathy.[8]

For countries with a high TB/HIV burden, wide availability of over-the-counter (OTC) supplements and a culture of nutritional supplementation, these findings raise three concerns:

(*i*) Safety: high-dose vitamin B6 supplements (e.g. 200 mg tablets[12]) or standard 25 mg tablets, which are easily accessible for use without prescription, increase the risk of cumulative toxicity.

(*ii*) Appropriateness: routine dosing for low-risk patients may offer limited benefit while exposing them to unnecessary harm.

(*iii*) Clinical complexity: PLWH, slow acetylators[1,8] and patients with multidrug resistant-TB on cycloserine[13] require tailored dosing, yet uniform regimens remain common practice.

If unaddressed, these issues may undermine TB treatment tolerability, and expose non-TB patients, who may be self-supplementing, to avoidable neurological risk.

The TGA recommendations underscore several actionable steps directly relevant to TB programmes, pharmacy regulation and clinical practice:

1. Adopt a risk-stratified approach to pyridoxine supplementation

Routine prophylaxis should be prioritised for PLWH, malnourished patients, and those with alcohol dependence, diabetes, pregnancy, or pre-existing neuropathy.

2. Limit pyridoxine dosing to established safe thresholds

Clinicians must distinguish between nutritional replacement and therapeutic dosing. Aligning with international safety signals, maintenance doses should generally not exceed 50 mg/day for routine supplementation. Doses >50 mg/day should not be exceeded without clinical oversight.

3. Pharmacist-led vigilance

Pharmacists should review all sources of vitamin B6, including OTC products, multivitamins and B-complex supplements to identify 'hidden' vitamin B6 sources, as patients often combine prescribed pyridoxine with OTC B-complexes. High-dose products containing >50 mg/day dosing should be dispensed with clear warnings, and unsupervised chronic use should be discouraged.

4. Improve labelling and public awareness

The SA Health Products Regulatory Authority (SAHPRA) should consider the TGA's approach: mandatory warning labels, restrictions on high-dose OTC formulations, and potential scheduling reclassification of products >100 mg/day to pharmacist-initiated therapy only (S2).

Currently, SAHPRA classifies oral pyridoxine preparations up to 100 mg (excluding injectables) as S0 (general sale), while doses >100 mg are classified as S1.[14] This creates a significant safety gap, as S1 products containing 200 mg of pyridoxine can be advertised directly to the public and sold OTC.[12] While the Australian TGA restricts 50 - 200 mg doses to 'pharmacist only' advice, simply maintaining a S1 status in SA may be insufficient to mitigate the risk of worsening peripheral neuropathy. A more pragmatic balance between safety oversight and patient access would involve reclassifying doses >100 mg as S2 (pharmacist-initiated therapy), and moving daily doses of ≥200 mg to S3 (prescription only). In this instance, the potential increase in cost and access barriers is a trade-off for ensuring rational use and patient safety.

5. Integrate monitoring and personalised dosing strategies

Patients at highest risk, including those on cycloserine or with HIV-related neuropathy, may require closer clinical monitoring, potential therapeutic drug monitoring, or genotype-informed risk stratification, such as N-acetyltransferase 2 (NAT2) status.[13]

In conclusion, pyridoxine remains essential for preventing INH-induced peripheral neuropathy in high-risk patients, but collective

emerging evidence[15] indicates that high-dose or unmonitored, cumulative and unnecessary supplementation may unintentionally increase the risk of neuropathy, and undermines patient safety. By adjusting SA vitamin and supplement scheduling for pyridoxine to limit the marketing of 200 mg tablets, and ensuring that clinicians prescribe within the safety limits, the risk for inadvertently worsening neuropathies will be mitigated. A shift toward risk-stratified, judicious and pharmacist-initiated therapy of OTC pyridoxine is needed to ensure both efficacy and safety. By adopting the principles of dose limitation, clear labelling and targeted prophylaxis, countries with high vitamin B6 supplementation rates and high TB and HIV burdens can enhance treatment safety while preventing avoidable neurotoxicity.

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1. Van der Watt JJ, Harrison TB, Benatar M, Heckmann JM. Polyneuropathy, anti-tuberculosis treatment and the role of pyridoxine in the HIV/AIDS era: A systematic review. Int J Tuberc Lung Dis 2011;15(6):722-728. https://doi.org/10.5588/ijtld.10.0284
2. National Department of Health, South Africa. National guidelines on the treatment of tuberculosis infection. Pretoria: NDoH, 2023.
3. Therapeutic Goods Administration, Australia. Health supplements containing vitamin B6 can cause peripheral neuropathy. Canberra: Australian Government Department of Health and Aged Care, 2022. https://www.tga.gov.au/news/safety-alerts/health-supplements-containing-vitamin-b6-can-cause-peripheral-neuropathy (accessed 19 May 2026).
4. Therapeutic Goods Administration, Australia. Safety advisory: Peripheral neuropathy from supplemental Vitamin B6 (pyridoxine). Canberra: Australian Department of Health, 2025. https://www.tga.gov.au/resources/publication/scheduling-decisions-interim/notice-interim-decision-proposed-amendments-poisons-standard-relation-pyridoxine-pyridoxal-or-pyridoxamine-vitamin-b6-acms-46-november-2024 (accessed 1 September 2025).
5. Therapeutic Goods Administration, Australia. Vitamin B6 (pyridoxine): Safety advisory – potential for dose-related adverse events. Canberra: Australian Department of Health, 2020. https://www.tga.gov.au/safety/safety-monitoring-and-information/safety-alerts/vitamin-b6-pyridoxine (accessed 19 May 2026).
6. Turck D, Bohn T, Castenmiller J, et al. Scientific opinion on the tolerable upper intake level for vitamin B6. EFSA J 2023;21(5):e08006. https://doi.org/10.2903/j.efsa.2023.8006
7. Van Hunsel F, van de Koppel S, van Puijenbroek E, Kant A. Vitamin B6 in health supplements and neuropathy: Case series assessment of spontaneously reported cases. Drug Saf 2018;41(9):859-869. https://doi.org/10.1007/s40264-018-0664-0
8. Nisar M, Watkin SW, Bucknall RC, Agnew RA. Exacerbation of isoniazid induced peripheral neuropathy by pyridoxine. Thorax 1990;45(5):419-420. https://doi.org/10.1136/thx.45.5.419
9. Therapeutic Goods Administration, Australia. Some dosages to be rescheduled as Pharmacist Only Medicines. Canberra: Australian Department of Health, 2026. https://www.tga.gov.au/news/safety-updates/medicines-containing-vitamin-b6-pyridoxine-pyridoxal-or-pyridoxamine (accessed 19 Feb 2026).
10. Bhargava M, Bhargava A. Pyridoxine for patients suffering from drug-susceptible tuberculosis in India. Pub Health Act 2018;8(2):97. https://doi.org/10.5588/pha.18.0017
11. Hadtstein F, Vrolijk M. Vitamin B-6-induced neuropathy: Exploring the mechanisms of pyridoxine toxicity. Adv Nutr 2021;12(5):1911-1929. https://doi.org/10.1093/advances/nmab033
12. Procter & Gamble Company and affiliates. NEUROBION tablets with Vitamin B1, B6 and B12. The Procter & Gamble Company and affiliates, 2026. https://www.neurobion.com/en-za/neurobion (accessed 19 May 2026).
13. Court R, Centner CM, Chirehwa M, et al. Neuropsychiatric toxicity and cycloserine concentrations during treatment for multidrug-resistant tuberculosis. Int J Infect Dis 2021;105:688-694. https://doi.org/10.1016/j.ijid.2021.03.001
14. National Department of Health, South Africa. Medicines and Related Substances Act, No. 101 of 1965. Consolidated schedules. Pretoria: NDoH, 2025. https://www.sahpra.org.za/wp-content/uploads/2025/08/Consolidated-Schedules_01-August-2025.pdf (accessed 1 September 2025).
15. Muhamad R, Akrivaki A, Papagiannopoulou G, Zavridis P, Zis P. The role of vitamin B6 in peripheral neuropathy: A systematic review. Nutrients 2023;15(13):2823. https://doi.org/10.3390/nu15132823

S Afr Med J 2026;116(5):e4610. https://doi.org/10.7196/SAMJ.2026.v116i5.4610