

HISTORICALLY ACCEPTED USE

Tertiary and Quaternary Committee

Executive Summary

<p>Date: March 2023</p> <p>Medicine (INN): Calcium Folate (oral) 15mg tablets</p> <p>Medicine (ATC): V03AF03</p> <p>Indication (ICD10 code): Reduction of the toxicity and counteraction of folic acid antagonists such as methotrexate; used in cytotoxic chemotherapy</p> <p>Patient population: general oncology and haematology [more commonly needed in patients taking high dose (> 500 mg/m²) methotrexate]</p> <p>Prevalence of condition: n/a</p> <p>Level of Care: Tertiary and Quaternary</p> <p>Prescriber Level: Specialist</p> <p>Current standard of Care: calcium folinate oral (<i>this item is currently in use for this indication in the public sector</i>)</p> <p>Efficacy estimates:</p> <ul style="list-style-type: none"> • A 1977 pharmacokinetic study evaluating 78 patients on high-dose methotrexate infusions measured the drug clearance from plasma.¹ Calcium folinate 15 mg per m² was administered 2 hours after completion of methotrexate infusion, and repeated every 6 hours for a total of 8 doses. Patients with 48-hour plasma methotrexate concentrations more than 2 standard deviations received an addition 48 hours of calcium folinate. The study showed that higher doses of calcium folinate was associated with rapid clearance of methotrexate and reduced toxicity. • Calcium folinate rescue has been used with high-dose methotrexate therapy for over 30 years. It has been shown to be effective in preventing myelosuppression, gastrointestinal toxicity and neurotoxicity.²

Historically accepted use Criteria

	Criteria	Comment	
1	The medicine is included in the WHO Model Essential Medicines List, either as a core or complementary item, for the indication requested.	YES <input checked="" type="checkbox"/>	NO <input type="checkbox"/>
		<i>Complementary list</i>	
2	The medicine is currently registered by SAHPRA for the indication.	YES <input checked="" type="checkbox"/>	NO <input type="checkbox"/>
3	There is evidence of long-established (prior to 1996*) safe and effective use of the medicine for the recognised indication in the public health sector.	YES <input checked="" type="checkbox"/>	NO <input type="checkbox"/>
		Comment:	
4	New safety or efficacy concerns.	YES <input type="checkbox"/>	NO <input checked="" type="checkbox"/>
		Comment: No new signals of safety concerns	

		Search: (calcium folinate[MeSH Terms]) AND ((adverse drug event[MeSH Terms]) OR (adverse drug reaction[MeSH Terms])) Filters: Clinical Trial, Meta-Analysis, Observational Study, Randomized Controlled Trial, Systematic Review 48 studies – no signals of new concerning safety issues				
5	Is budget impact expected to have an incremental increase, that a de novo review is justified?	<table border="1"> <tr> <td>YES</td> <td>NO</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> </tr> </table> <p>Calcium Folate; 15mg; Tablet; 10 Tablets: R282.88* *MHPL – February 2023</p>	YES	NO	<input type="checkbox"/>	<input checked="" type="checkbox"/>
YES	NO					
<input type="checkbox"/>	<input checked="" type="checkbox"/>					
6	Equitable access across the country is essential, and is limited only by the availability of adequately trained staff and availability of equipment.	<table border="1"> <tr> <td>YES</td> <td>NO</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table> <p>Comment:</p>	YES	NO	<input checked="" type="checkbox"/>	<input type="checkbox"/>
YES	NO					
<input checked="" type="checkbox"/>	<input type="checkbox"/>					

* The Essential Drugs Programme (EDP) of South Africa was established in terms of the National Drug Policy (NDP), which was implemented in 1996

Recommendation

It is recommended that oral calcium folinate be included on the Tertiary Essential Medicines List for use in patients receiving high-dose methotrexate in cancer chemotherapy regimens to reduce methotrexate toxicity.

REFERENCES

¹ Stroller RG, Hande KR, Jacobs SA, Rosenburg, Chabner BA. Use of Plasma Pharmacokinetics to predict and prevent methotrexate toxicity. NEJM. 1977, 297 (12): 630 – 634.

² Howard SC, McCormick J, Pui CH, Buddington RK, Harvey RD. Preventing and managing toxicities of high-dose methotrexate. The Oncologist. 2016, 21: 1471 – 1482.