South African National Department of Health
HISTORICALLY ACCEPTED USE REVIEW TEMPLATE
ONCOLOGY EVIDENCE WORKING GROUP
of the Expert Review Committee

Executive Summary

Date: November 2025

Medicine(s) (INN): Dactinomycin

Medicine(s) (ATC): L01DA01

Indication/s (ICD10 code/s): Nephroblastoma (Wilms tumour) (C64.9 - Malignant neoplasm of unspecified kidney, except renal pelvis)

Patient population/s: Children, adolescents and young adults presenting with nephroblastoma.

Prevalence of condition/s: Nephroblastoma accounts for 6 – 7 % of all childhood cancers[1] and has an estimated age standardised rate of 87 cases per million children (0 – 14 years) per year.[2]

Level of Care: Tertiary and Quaternary

Prescriber Level: Specialist (Oncologist)

Current Standard(s) of Care: Dactinomycin is historic standard of care

Background:

Nephroblastoma, also known as Wilms tumour, is one of the most common solid tumours in all paediatric cancers, affecting the kidney.[3]

The treatment of nephroblastoma involves multi-agent chemotherapy and surgical resection, with or without radiation therapy – depending on factors such as whether unilateral or bilateral, local stage, presence of metastases, patients age, tumour weight, biological risk factors, histology and clinical response to therapy.[4]

Dactinomycin was previously not registered with the South African Health Products Regulatory Authority (SAHPRA) and was therefore only accessible through a Section 21 authorization, which permits the use of unregistered medicines under specific circumstances. Due to its unregistered status at the time, it could not be included on the National Essential Medicines List. However, in 2022, dactinomycin achieved formal registration with SAHPRA, marking a significant step toward broader and more consistent access within the country.

Thus, since dactinomycin is the historic standard of care it is proposed that this be included on the Essential Medicines List.

Methods: a search was conducted for clinical practice guidelines for Nephroblastoma/Wilms Tumour, as well as Clinical Trials prior to 2007 demonstrating historic use.

Summary of Evidence: Dactinomycin has been used since the 1960's for treatment of nephroblastoma. Following reports of tumour regression, Burgert et.al. 1967[5] investigated whether dactinomycin would decrease the frequency of metastasis, whether it improved survival, and whether the time of administration relative to operation day influence both frequency of metastasis and survival. This study consisted of 122 children from 8 institutions. Conventional therapy was administered to 45 children, 59 children received conventional therapy plus early administration of dactinomycin, and 18 children received conventional therapy plus late administration dactinomycin. In 102 children without metastasis at time of operation, a decreased frequency of metastasis (59% vs 39%, $p < 0.05$) and increased survival (63% alive at 4 years vs 44% alive at 4-years, $p < 0.05$) was seen in those that had dactinomycin therapy. Those patients that received dactinomycin on the day of surgery showed the greatest advantage in survival (89% alive at 4 years). Additionally, patients with metastasis had an improved survival experience even if dactinomycin therapy was started later compared to those that did not receive dactinomycin.

A South African retrospective study[6] in two paediatric oncology units (Bloemfontein and Cape Town) assessed survival rates of childhood cancers from 1987 to 2011. It was found that nephroblastoma had a high survival rate of 62.6% (all-stages), and survival of 81.1% for stage 1 nephroblastoma.

The NCCN (National Comprehensive Cancer Network) Clinical Practice Guidelines for Wilms Tumour 2025[4], include the regimens EE4A (vincristine plus dactinomycin for 18 weeks) or DD4A (vincristine plus dactinomycin plus doxorubicin for 24 weeks) depending on risk group. See table below:

Clinical Practice Guideline (CPG) recommendations:

Guideline	Recommendations	AGREE II assessment
NCCN (National Comprehensive Cancer Network) Clinical Practice Guidelines for Wilms Tumour 2025[4]	Both EE4A (vincristine plus dactinomycin for 18 weeks) and DD4A (vincristine plus dactinomycin plus doxorubicin for 24 weeks) regimens are recommended within the practice guidelines, and treatment guided by presentation, findings and molecular results. *Recommendations in this guideline are Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.*	*5/7* *(good quality, especially in terms of clarity, scope, and clinical applicability, however it lacks transparency in methods used to gather and grade evidence and involves limited patient/public input)*

Historically accepted use Criteria

SECTION A			
	Criteria	**Comment**	
1	The medicine is included in the World Health Organization (WHO) Model Essential Medicines List, either as a core or complementary item, for the indication requested.	YES	NO
		X	
		Listed for the following indications: • **Malignant neoplasms of kidney, except renal pelvis**	

		• Malignant trophoblastic neoplasms of placenta • Rhabdomyosarcoma primary site • Ewing sarcoma of bone and articular cartilage of unspecified sites.
2	The medicine is currently registered by South African Health Products Regulatory Authority (SAHPRA).	YES: X / NO: Registered with SAHPRA in 2022
3	A documented rapid literature review identified no new safety concerns or new evidence of lack of efficacy.	YES: X / NO: *See above: Summary of Evidence*
4	The anticipated costs and usage are not likely to result in a substantial impact on the budget.	YES: X / NO: *Comment:* *SEP: R2611.46 (dactinomycin 0.5mg injection) – July 2025.*
SECTION B		
1	There is evidence prior to 2007* of safety and efficacy for the recognised indication (a systematic review/meta-analysis, or at least one critically appraised controlled trial.) *Information after 2007 would need to be subject to standard review processes for a new inclusion.*	YES: X / NO: *See above: Summary of Evidence*
OR		
2	It is included as part of standard of care in a critically appraised clinical practice guideline (CPGs) of adequate quality, for the particular indication.	YES: X / NO: *See above: CPG recommendations*
AND		
3	It is currently use in practice for this indication.	YES: X / NO: *Comment: Current standard of care*

Modified Evidence to Decision Framework

	JUDGEMENT	EVIDENCE & ADDITIONAL CONSIDERATIONS
EVIDENCE OF BENEFIT	**What is the size of the effect for beneficial outcomes?** Large: X / Moderate: / Small: / None:	*Survival Benefit.*

	JUDGEMENT	EVIDENCE & ADDITIONAL CONSIDERATIONS
EVIDENCE OF HARMS	**What is the size of the effect for harmful outcomes?** Large [ ] Moderate [ ] Small [X] None [ ]	
QUALITY OF EVIDENCE	**What is the certainty/quality of evidence?** High [ ] Moderate [X] Low [ ] Very low [ ] *High quality:* confident in the evidence *Moderate quality:* mostly confident, but further research may change the effect *Low quality:* some confidence, further research likely to change the effect *Very low quality:* findings indicate uncertain effect	
BENEFITS & HARMS	**Do the desirable effects outweigh the undesirable harms?** Favours intervention [X] Favours control [ ] Intervention = Control *or* Uncertain [ ]	*Survival benefit*
THERAPEUTIC INTERCHANGE	Therapeutic alternatives available: Yes [ ] No [X]	
FEASIBILITY	**Is implementation of this recommendation feasible?** Yes [X] No [ ] Uncertain [ ]	
RESOURCE USE	**How large are the resource requirements?** More intensive [ ] Less intensive [X] Uncertain [ ]	Potentially less intensive, as if allocated as an EML agent, a national tender with combined volumes can be undertaken with potentially better pricing.
VALUES, PREFERENCES, ACCEPTABILITY	**Is there important uncertainty or variability about how much people value the options?** Minor [ ] Major [ ] Uncertain [X] **Is the option acceptable to key stakeholders?** Yes [X] No [ ] Uncertain [ ]	
EQUITY	**Would there be an impact on health inequity?** Yes [ ] No [ ] Uncertain [X]	

RECOMMENDATION:					
Type of recommendation	We recommend against the option and for the alternative **(strong)**	We suggest not to use the option **(conditional)**	We suggest using either the option or the alternative **(conditional)**	We suggest using the option **(conditional)**	We recommend the option **(strong)**
					X
Recommendation: It is recommended that dactinomycin be included on the Essential Medicine List for use in regimens to manage nephroblastoma. *Rationale: Dactinomycin has historically been used as part of regimens for the management of Nephroblastoma since the 1960s and is part of regimens in established frontline treatment guidelines.* **Level of Evidence:** *Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.*[4] **Review indicator:** Change in evidence or safety/efficacy.					
NEMLC RECOMMENDATION: NEMLC ratified recommendation 27 November 2025.					
Monitoring and evaluation considerations: n/a					
Research priorities: n/a					

References

[1] Poole JE. Wilms' tumour (nephroblastoma). CME. 2010, 28 (7): 324-326.

[2] Stefan DC, Stones DK, Wainwright RD, Kruger M, Davidson A, Poole J, et.al. Childhood cancer incidence in South Africa, 1987 – 2007. SAMJ. 2015, 105(11): 939 – 947.

[3] Brits E, Gerber E, Iroka I, Mgidlana L, Willoughby J, Dhlamini S, et.al. Paediatric nephroblastoma at a South African tertiary hospital: A 21-year retrospective analysis. SAMJ. 2024, 114(12): 56 – 64.

[4] Balis F, Green DM, Armstrong A, Aye J, Benedetti D, Brown B, et.al. Wilms Tumor, Version 2.2025. NCCN (National Comprehensive Cancer Network) Clinical Practice Guidelines in Oncology. JNCCN. 2025, 23 (8): 319-342.

[5] Burgert EO, Gildewell O. Dactinomycin in Wilms' Tumor. JAMA. 1967, 199(7): 464-467.

[6] Stones DK, de Bruin GP, Esterhuizen TM, Stefan DC. Childhood Cancer Survival Rates in two South African units. SAMJ, 2014, 104 (7): 501 - 504