South Africa National Essential Medicine List
Adult Hospital Level Medication Review Process
Component: Oncologic emergencies

MEDICINE REVIEW

1. Executive Summary

Date: 22 November 2019
Medicine (INN): Prednisone, oral
Medicine (ATC): H02AB07
Indication/s (ICD10 code/s): Symptomatic subacute radiation pneumonitis (J70.0)
Patient population/s: Adult cancer patients with a history of thoracic radiation.
Prevalence of condition/s: No local data available. 5 to 15 % of patients irradiated for breast, lung, and mediastinal tumors estimated to develop radiation pneumonitis. Risk is related to the volume of irradiated lung, the amount of radiation and concomitant chemotherapy.[i]
Level of Care: Secondary level – Adult hospital
Prescriber Level: Doctor
Current standard of Care: n/a
Efficacy estimates: Limited evidence in the literature for preventing, mitigating and treating acute and late radiation induced lung injury (See Appendix I). Glucocorticoids are the mainstay of therapy and probably biologically plausible, as suggested in Guidelines and case reports.
Motivators/reviewers*:* Ms TD Leong
PTC affiliation: n/a

2. Name of author(s)/motivator(s)

Reviewers: Ms TD Leong

3. Author affiliation and conflict of interest details

National Department of Health, Essential Drugs Programme, Secretariat to the Adult Hospital Level Committee (2017-2020); No conflicts of interest declared.

4. Introduction/ Background

Radiation pneumonitis is inflammation of the lung caused by radiation therapy to the chest. It mostly develops 1–6 months after treatment. Chronic pneumonitis can lead to called pulmonary fibrosis. Certain chemotherapy agents can also cause induce pneumonitis. Symptoms usually develop approximately 4 to 12 weeks following irradiation and includes a nonproductive cough, dyspnea with exertion, fever, pleuritic and malaise and weight loss may be observed[ii].

Mild cases can be self-limiting and generally, treatment is initiated only when pulmonary function declines or symptoms are troublesome and interfere with daily functions[iii]. Standard of care is oral corticosteroids to reduce inflammation.

This review is to determine the evidence base for oral prednisone for management of radiation pneumonitis.

5. Purpose/Objective

Population: Symptomatic subacute radiation pneumonitis
Intervention: Oral prednisone
Comparison: Placebo

Outcomes: Improvement of symptoms or respiratory function

6. Methods:

a) Data sources and search strategy

i. *Database:* EMBASE
Search strategy: 'adult'/exp AND 'radiation pneumonitis' AND 'glucocorticoid'/exp AND 'placebo'/exp AND 'lung injury'/exp AND 'randomized controlled trial'/exp
Search results: 0 publications retrieved.

ii. *Google scholar:* Guidelines were sourced
Search results: 1 Guideline retrieved and case reports.

b) Evidence synthesis

i. *Guidelines*[iv]*:* Recommends prednisone 50-60 mg daily for 1 week tapering by 10 mg/week if the clinical presentation includes a non-productive cough with a normal white blood cell count and x-ray shows infiltrates in the distribution of the radiotherapy portals. The dose is tapered slowly as some patients experience rebound pneumonitis if tapered too fast. There are cases where maintenance therapy of low dose prednisone may be required for extended periods of time. Management may require require referral to pulmonology medicine, as appropriate.
Differential diagnosis of adult respiratory distress syndrome, infectious pneumonia, pulmonary embolism, and broncholitis obliterans with organizing pneumonia (BOOP) should be considered. Respiratory failure may require intensive care and mechanical ventilation.

ii. *Case reports*[v] [vi] published in the literature shows that radiation-induced lung injury is often misdiagnosed as pneumonia on x-ray, but that promptly resolves on treatment with steroids.

Summary: The recommendation for prednisone use is based upon clinical experience and case reports of prompt response to therapy.

EVIDENCE TO DECISION FRAMEWORK

	JUDGEMENT	SUPPORTING EVIDENCE & ADDITIONAL CONSIDERATIONS
QUALITY OF EVIDENCE	**What is the overall confidence in the evidence of effectiveness?** Confident: [ ] Not confident: [ ] Uncertain: [X]	This is standard practice; and there is a paucity of RCT data.
BENEFITS & HARMS	**Do the desirable effects outweigh the undesirable effects?** Benefits outweigh harms: [ ] Harms outweigh benefits: [ ] Benefits = harms or Uncertain: [X]	This is standard practice; and there is a paucity of RCT data.
VALUES & PREFERENCES / ACCEPTABILITY	**Is there important uncertainty or variability about how much people value the outcomes?** Minor: [ ] Major: [ ] Uncertain: [X] **Is the option acceptable to key stakeholders?** Yes: [ ] No: [ ] Uncertain: [X]	
RESOURCE USE	**How large are the resource requirements?** More intensive: [ ] Less intensive: [ ] Uncertain: [x]	**Cost of medicines/treatment course (70 kg adult):** Medicine: Prednisone 1 mg/kg daily for 2–4 weeks at a maximum daily dose of 40–60 mg, and then taper slowly over 3–12 weeks (for 378 x5mg tablets) — Cost (ZAR)*: R 66.70 * Contract circular RT289-2019: Weighted average price for 5mg prednisone tablet = R0.18
EQUITY	**What would be the impact on health inequity?** Yes: [ ] No: [ ] Uncertain: [X]	
FEASIBILITY	**Is the implementation of this recommendation feasible?** Yes: [x] No: [ ] Uncertain: [ ]	.

Type of recommendation	We recommend against the option or for the alternative	We suggest not to use the option or to use the alternative	We suggest using either the option or the alternative	We suggest using the option	We recommend the option
	☐	☐	☐	☒	☐

Recommendation: Based on this review, the Adult Hospital Level Committee recommends prednisone, oral for management of acute radiation pneumonitis.
Rationale: Limited evidence in the literature for preventing, mitigating and treating acute and late radiation induced lung injury. Mainstay of therapy and probably biologically plausible, as suggested in Guidelines and case reports.
Level of Evidence: III Standard of care as suggested by Guidelines, Case Reports
Review indicator:

Evidence of efficacy	Evidence of harm	Price reduction
	X	

VEN status:

Vital	Essential	Necessary
	X	

NEMLC MEETING OF 5 DECEMBER 2019
NEMLC accepted the proposal as recommended by the Adult Hospital Level Committee, above.

Monitoring and evaluation: n/a

Research priorities : Epidemiology research of radiation and chemotherapy-induced pneumonitis in South Africa.

References:

[i] Berkey FJ. Managing the adverse effects of radiation therapy. Am Fam Physician. 2010 Aug 15;82(4):381-8, 394. https://www.ncbi.nlm.nih.gov/pubmed/20704169
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[vi] Conway JL, Long K, Ploquin N, Olivotto IA. Unexpected Symptomatic Pneumonitis Following Breast Tangent Radiation: A Case Report. Cureus. 2015 Oct 22;7(10):e363. https://www.ncbi.nlm.nih.gov/pubmed/26623218