

SOUTH AFRICAN PRIMARY HEALTHCARE LEVEL ESSENTIAL MEDICINES LIST
CHAPTER 17: RESPIRATORY CONDITIONS
NEMLC RECOMMENDATIONS FOR MEDICINE AMENDMENTS (2020)

Medicine amendment recommendations, with supporting evidence and rationale are listed below.

Kindly review the medicine amendments in the context of the complete chapter for respiratory conditions.

Note: This primary healthcare chapter has been updated to align to previous NEMLC recommendations as well as the recent NEMLC-approved Adult Hospital Level STGs and EML, 2019 edition.

A: NEW STANDARD TREATMENT GUIDELINES

SECTION	CONDITION	MEDICINE MANAGEMENT	MEDICINE ADDED
17.4.2.1	Isoniazid mono-resistant tuberculosis in adults	Rifampicin, oral	Added
		Ethambutol, oral	Added
		Pyrazinamide, oral	Added
		Levofloxacin, oral	Added

17.4.4.1 ISONIAZID MONORESISTANT TUBERCULOSIS

Levofloxacin, oral: added

Rifampicin, oral: added

Ethambutol, oral: added

Pyrazinamide, oral: added

Aligned with the Adult Hospital Level STGs and EML, 2019 edition.

Refer to the medicine review, levofloxacin for INH-resistant TB (September 2019):



Levofloxacin for
INH-resistant TB-Ad

<http://www.health.gov.za/index.php/standard-treatment-guidelines-and-essential-medicines-list/category/286-hospital-level-adults>

Recommendation: Based on this evidence review, the Adult Hospital Committee recommended a levofloxacin-based regimen for treatment of INH-mono-resistant TB, for a duration of 6 months. To assist with adherence, a fixed dose combination (FDC) product is preferred. Rifampicin, pyrazinamide and ethambutol are only available in a fixed dose combination product co-formulated with isoniazid. It is noted that this FDC is routinely prescribed in clinical practice for ease of administration by the patient, and levofloxacin can be added to this.

Rationale: Aligned with WHO conditional recommendation with very low quality evidence³.

Level of Evidence: III Individual patient data meta-analysis (observational data)¹

The following STG was added to the STG:

¹ Fregonese F, Ahuja SD, Akkerman OW, Arakaki-Sanchez D, Ayakaka I, Baghaei P, et al. Comparison of different treatments for isoniazid-resistant tuberculosis: an individual patient data meta-analysis. Lancet Respir Med. 2018;6(4):265-75. <https://www.ncbi.nlm.nih.gov/pubmed/29595509>

MEDICINE TREATMENT

Confirmed INH mono-resistant TB:

- Rifampicin, oral, 10 mg/kg daily.

AND

- Ethambutol, oral, 15 mg/kg daily.

AND

- Pyrazinamide, oral, 25 mg/kg daily.

AND

- Levofloxacin, oral, daily.
 - 30–50 kg: 750 mg
 - >50 kg: 1000 mg

Where single medicines are not available or the pill burden is too high a fixed dose combination of RHZE dosed as per weight may be used, and levofloxacin added to this.

Treatment should be given for at least 6 months.

B: AMENDMENTS TO MEDICINE TREATMENT/ MANAGEMENT

SECTION	MEDICINE/ MANAGEMENT	ADDED/DELETED/AMENDED
17.3.4.2.1 Uncomplicated pneumonia in adults	Chest X-ray	Follow-up chest x-ray after competing therapy added, if possible
17.3.4.2.2 Pneumonia in adults with underlying medical conditions or > 65 years of age	Chest X-ray	Follow-up chest x-ray after competing therapy added, if possible
17.4.1 Pulmonary TB in adults <i>-Diagnosis</i>	Urine LAM	Added
17.4.2.2 TB control programme: medicine regimens in children	Rifampicin/isoniazid/pyrazinamide (75/50/150 mg), oral dispersible formulation	Added
	Rifampicin/isoniazid (75/50 mg), oral dispersible formulation	Added
17.4.4.2 Multidrug-resistant tuberculosis (MDR TB), in adults	MDR-TB management	Guidance added
17.4.4.3 Multidrug-resistant tuberculosis (MDR TB), in children	MDR-TB management	Guidance added
17.1.1 ACUTE ASTHMA & ACUTE EXACERBATION OF COPD	Oral corticosteroids (intermediate-acting)	Added as therapeutic class
	Prednisone, oral	Retained as example of class (listed in the STG)
	Prednisolone, oral	Added as a therapeutic alternative (listed in the interchange database)

17.3.4.2.1 UNCOMPLICATED PNEUMONIA (ADULTS)

Chest X-ray: follow-up chest x-ray after competing therapy added, if possible

Aligned with the Adult Hospital Level STGs and EML, 2019 edition (noting that chest X-rays may not be commonly available at all facilities) as follows:

The following text was added to the STG:

A follow-up chest X-ray should ideally be taken to ensure resolution of the pneumonia, in patients > 50 years of age.

Rationale (described in the NEMLC report for the Adult Hospital Level STGs and EML (2017-2019):

- The initial recommendation in the Adult Hospital Level STGs and EML, 2015 edition (to **not** routinely repeat chest x-rays for patients with satisfactory clinical recovery from CAP), is aligned with guidelines.^{2 3}
- Additional guidance added to clarify criteria for reimaging based on limited data that has been cited in these guidelines: *Follow-up chest x-ray recommended in patients with persistent symptoms and who are at risk of malignancy (the elderly);*

² Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, et al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med.* 2019 Oct 1;200(7):e45-e67. <https://www.ncbi.nlm.nih.gov/pubmed/31573350>

³ Lim WS, Baudouin SV, George RC, Hill AT, Jamieson C, Le Jeune I, Macfarlane JT, Read RC, Roberts HJ, Levy ML, Wani M, Woodhead MA; Pneumonia Guidelines Committee of the BTS Standards of Care Committee. BTS guidelines for the management of community acquired pneumonia in adults: update 2009. *Thorax.* 2009 Oct;64 Suppl 3:iii1-55. <https://www.ncbi.nlm.nih.gov/pubmed/19783532>

especially smokers or ex-smokers). Studies of CAP in hospital often exclude patients with lung cancer; but malignancy rates, in patients recovering from CAP has been reported as 1.3% to 4%.^{4 5 6 7} Observational cohort study by Tang et al⁷ showed that risk factors associated with lung cancer (diagnosed after CAP) included age ≥50 years (aHR 19.0; 95% CI, 5.7 to 63.6), male sex (aHR, 1.8; 95% CI, 1.1 to 2.9), and smoking (aHR, 1.7; 95% CI, 1.0 to 3.0). Longer-term study⁸ reported that 9.2% of CAP survivors were newly diagnosed with cancer (predominantly elderly, smokers or ex-smokers and male) with a mean time to diagnosis of 297 days; though only 27% were diagnosed within 90 days of hospital discharge.

Level of Evidence: III Observational studies, Guidelines

17.3.4.2.2 PNEUMONIA IN ADULTS WITH UNDERLYING MEDICAL CONDITIONS OR > 65 YEARS OF AGE

Chest x-ray: *follow-up chest x-ray after competing therapy added, if possible*

See above.

17.4.1 PULMONARY TUBERCULOSIS (TB) IN ADULTS

Diagnosis:

Urine LAM test: *added*

Aligned with the Adult Hospital STGs and EML, 2019, and the following text was added to the STG:

» Urine lipoarabinomannan (LAM) is a good “rule-in” diagnostic test for HIV-infected patients with signs and symptoms of pulmonary and/or extrapulmonary TB and CD4 ≤100 cells/microL.

17.4.2.2 TB CONTROL PROGRAMME: MEDICINE REGIMENS IN CHILDREN

Dispersible fixed dose combinations tablets

Rifampicin/isoniazid/pyrazinamide (75/50/150 mg), oral dispersible formulation: *added*

Rifampicin/isoniazid (75/50 mg), oral dispersible formulation: *added*

Aligned with the Paediatric Hospital Level STGs and EML, 2017 edition.

Following text was added to the STG:

Dosing recommendations for dispersible fixed dose combinations tablets:

Weight kg	2 months intensive phase given daily	4 months continuation phase given daily
	RHZ (75/50/150 mg)	RH (75/50 mg)
4–7.9 kg	1 tablet	1 tablet
8–11.9 kg	2 tablets	2 tablets
12–15.9 kg	3 tablets	3 tablets
16–24.9 kg	4 tablets	4 tablets
≥25 kg	Adult dosages recommended	

17.4.4.2 MULTI-DRUG-RESISTANT TUBERCULOSIS (MDR TB), IN ADULTS *and* 17.4.4.3 MULTIDRUG-RESISTANT TUBERCULOSIS (MDR TB), IN CHILDREN

MDR-TB management: *guidance added*

The following was added to the text of the STG, aligned with the Adult Hospital STGs and EML, 2019 edition:

⁴ Macdonald C, Jayathissa S, Leadbetter M. Is post-pneumonia chest X-ray for lung malignancy useful? Results of an audit of current practice. Intern Med J 2015;45:329–334. <https://www.ncbi.nlm.nih.gov/pubmed/25583286>

⁵ Holmberg H, Kraggsbjerg P. Association of pneumonia and lung cancer: the value of convalescent chest radiography and follow-up. Scand J Infect Dis 1993;25:93–100. <https://www.ncbi.nlm.nih.gov/pubmed/8460356>

⁶ Little BP, Gilman MD, Humphrey KL, Alkasab TK, Gibbons FK, Shepard JA, et al. Outcome of recommendations for radiographic follow-up of pneumonia on outpatient chest radiography. AJR Am J Roentgenol 2014;202:54–59. <https://www.ncbi.nlm.nih.gov/pubmed/24370128>

⁷ Tang KL, Eurich DT, Minhas-Sandhu JK, Marrie TJ, Majumdar SR. Incidence, correlates, and chest radiographic yield of new lung cancer diagnosis in 3398 patients with pneumonia. Arch Intern Med 2011;171:1193–1198. <https://www.ncbi.nlm.nih.gov/pubmed/21518934>

⁸ Mortensen EM, Copeland LA, Pugh MJ, Fine MJ, Nakashima B, Restrepo MI, de Molina RM, Anzueto A. Diagnosis of pulmonary malignancy after hospitalization for pneumonia. Am J Med. 2010 Jan;123(1):66-71. <https://www.ncbi.nlm.nih.gov/pubmed/20102994>

**Never treat for MDR TB without laboratory confirmation, either by molecular or phenotypic (culture and sensitivity) results.
All cases should be discussed with a designated specialist centre and MDR TB medicines accessed from the designated centres.**

Refer to the NEMLC report for the Adult Hospital Level STGs and EML (2017-2019), that cites the NEMLC recommendation as follows:

NEMLC MEETING OF 5 DECEMBER 2019:

NEMLC recommended that DR-TB medicines be included on the national EML with a condition – “*all MDR-TB cases should be discussed with a designated specialist centre; and MDR-TB medicines to be accessed from these designated centre(s)*”.
Rationale: Designated MDR-TB facilities are available at all levels of care - where appropriate susceptibility testing, monitoring and management of adverse events is possible; with relevant support from relevant Infectious Disease experts or Advisory Committees.

**17.1.1 ACUTE ASTHMA & ACUTE EXACERBATION OF COPD and 17.2.1 CROUP (LARYNGOTRACHEOBRONCHITIS)
IN CHILDREN and**

Corticosteroids (intermediate acting): *added as therapeutic class*

Prednisone, oral: *retained as example of class (listed in the STG)*

Prednisolone, oral: *added as a therapeutic alternative (listed in the interchange database)*

Aligned with SAMF 2016 and Adult Hospital Level STGs and EML, 2019.

Level of Evidence: III Guidelines