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Department:
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SOUTH AFRICAN PRIMARY HEALTHCARE LEVEL ESSENTIAL MEDICINES LIST
CHAPTER 17: RESPIRATORY CONDITIONS
NEMLC RECOMMENDATIONS FOR MEDICINE AMENDMENTS (2016 – 2018)

Medicine amendment recommendations, with supporting evidence and rationale are listed below. Kindly review the medicine amendments in the context of the respiratory chapter.

SECTION	MEDICINE	ADDED/DELETED/AMENDED
17.1.1 Acute asthma & acute exacerbation of COPD		
	Magnesium sulfate, IV	Not added
	Salbutamol metered dose inhaler	Dose and directions for use amended
	Salbutamol 0.5% nebulisation	Dose and directions for use amended
	Ipratropium 0.25 mg nebulisation	Dose and directions for use amended
	Ipratropium 0.5 mg nebulisation	Dose and directions for use amended
	Ipratropium metered dose inhaler	Dose and directions for use amended
- *exercise induced asthma*	Salbutamol metered dose inhaler	Deleted
17.1.2 Chronic asthma and 17.1.4 Chronic obstructive pulmonary disease (COPD)		
- *general population*	Inhaled corticosteroids (ICS)	Retained as therapeutic class
	Beclomethasone, inhaler	Deleted as example of ICS therapeutic class in the general population
	Budesonide, inhaler	Added as the example of ICS therapeutic class in the general population
- *patients on protease inhibitors*	Beclomethasone, inhaler	Not added for patients on protease inhibitors
	Formoterol, inhaler	Not added as doctor initiated – "step-up therapy" for patients on protease inhibitors
17.1.3 Acute bronchiolitis in children		
	Adrenaline (epinephrine)	Deleted
	Salbutamol 0.5% nebulisation	Deleted
	Salbutamol, inhaler	Deleted
17.1.4 Chronic obstructive pulmonary disease (COPD)		
	LABA (formoterol) inhaler	Added as doctor initiated (if spirometer available)
	LABA/ICS (Salmeterol/fluticasone) inhaler	Directions for use amended
17.3.2 Acute bronchitis in adults or adolescents		
	Antibiotics	Indication for HIV-infected patients deleted
	Cough linctus	Deleted
17.3.4.1 Pneumonia in children		
	Amoxicillin, oral	Dose amended
17.3.4.2.4 Pneumocystis pneumonia		
	Cotrimoxazole, oral	Directions for use amended
17.4.2.1 TB chemoprophylaxis/isoniazid preventive therapy (IPT) in children		
- *Isoniazid mono-resistant contact*	Rifampicin, oral	Added
- *Rifampicin mono-resistant contact*	Isoniazid, oral	Added
17.4.2.2 TB control programme medicine regimens in children		
	Pyridoxine, oral	Dose amended
17.4.4.1 Multidrug-resistant tuberculosis (MDR TB), in adults		
	Moxifloxacin, oral	Deleted
	Ethionamide, oral	Deleted
	Terizidone, oral	Deleted
	Pyrazinamide, oral	Deleted
	Kanamycin, injecton	Deleted

17.1.1 ACUTE ASTHMA & ACUTE EXACERBATION OF COPD

Magnesium sulfate, IV*: not added*

Evidence for management of asthma exacerbations, non-responsive to corticosteroids was limited to the emergency setting and not at primary level of care.

Recommendation: Magnesium sulfate (MgSO4), IV not be added to the STG for asthma exacerbations non-responsive to corticosteroids.

Rationale: Single dose IV MgSO4 has been shown to be of value (reducing hospital admission) in *severe* acute asthma when other bronchodilators fail. However, the PHC Committee was of the opinion that use should be in consultation with a senior medical officer and is more appropriate for emergency care settings[1] rather than standard primary health care facilities. Emphasis should remain on urgent referral of severe cases.

Level of Evidence: I Systematic reviews, Expert opinion

NEMLC MEETING DISCUSSION: 29 JUNE 2017[2]

Acute Asthma: It was queried whether intravenous use of magnesium sulphate should be added. It was outlined that it should only be administered to patients failing to respond to the first 3 steps (oxygen, short-acting beta2 agonists, ipratropium bromide, and steroids) and be used in consultation with a specialist. The NEMLC did not recommend magnesium sulphate sooner in the treatment algorithm of acute asthma and accepted the PHC Committee's recommendation of not including this medicine to the PHC EML.

Salbutamol metered dose inhaler (MDI): *dose and directions for use amended*

Salbutamol MDI moved to the first line of treatment for mild to moderate exacerbations of asthma and COPD, and dosages aligned with the Adult Hospital level STGs and EML, 2015[3] and the Paediatric Hospital level STGs and EML, 2017[4].

Evidence of efficacy:

- **Children:** A comparative cohort study[5] showed that bronchodilators (salbutamol, terbutaline) administered using a MDI + spacer compared to nebulisation were comparable in terms of number of doses of inhaled bronchodilators (1.42 ±1.01 vs. 1.45 ± 0.98; p=NS), the number of children that required a stay in the observation unit (30 vs 28; p=NS) or admission to the hospital (5 vs 4; NS).Children weighing <20 kg received 1000 mcg of salbutamol or 2.5 mg of nebulised salbutamol and children weighing > 20 kg received 2000 mcg of salbutamol via MDI or 5 mg of nebulized salbutamol.

  Level of Evidence: II Cohort study
- **Adults:** Small double-blind RCT[6] (n=27) showed that salbutamol delivered by MDI + spacer (400 mcg) was as efficacious as nebulisation (1.5 mg) for acute severe asthma; with no significant difference between groups for PEFR and FEV1 at any point studied. Regression analysis suggested that for every 1 mg of salbutamol via a MDI + spacer, 2.5 mg nebulised salbutamol is required to

[1]Kew KM, Kirtchuk L, Michell CI.Intravenous magnesium sulfate for treating adults with acute asthma in the emergency department. Cochrane Database Syst Rev. 2014 May 28;(5):CD010909.
- Griffiths B, Kew KM. Intravenous magnesium sulfate for treating children with acute asthma in the emergency department. Cochrane Database Syst Rev. 2016 Apr 29;4:CD011050.
- Rowe BH, Bretzlaff JA, Bourdon C, Bota GW, Camargo CA Jr. Magnesium sulfate for treating exacerbations of acute asthma in the emergency department. Cochrane DatabaseSyst Rev. 2000;(2):CD001490.

[2] NEMLC minutes of the meeting:29 June2017

[3] Adult Hospital Level STGs and EML, 2014

[4] Paediatric Hospital Level STGs and EML, 2017

[5] Benito-Fernández J, González-Balenciaga M, Capapé-Zache S, Vázquez-Ronco MA, Mintegi-Raso S. Salbutamol via metered-dose inhaler with spacer versus nebulization for acute treatment of pediatric asthma in the emergency department. PediatrEmerg Care. 2004 Oct;20(10):656-9.

[6] Rodrigo C, Rodrigo G. Salbutamol treatment of acute severe asthma in the ED: MDI versus hand-held nebulizer. Am J Emerg Med. 1998 Nov;16(7):637-42.

produce comparable therapeutic responses. However, nebulizer therapy produced greater side effects related to increased plasma levels of salbutamol (due to greater systemic absorption).
Level of Evidence: II Small RCT

Salbutamol 0.5% nebulisation*: dose and directions for use amended*
Aligned with the Adult Hospital level STGs and EML, 2015 and Paediatric Hospital level STGs and EML, 2017.
The text of the STG was updated as follows:

Adults and children:
- ~~Salbutamol 0.5%, solution, nebulised, preferably delivered at a flow rate of 8 L/min with oxygen.~~
  - ~~1 mL salbutamol 0.5%, solution in 2 mL of sodium chloride 0.9%.~~
  - ~~If no relief, repeat every 20–30 minutes in the first hour.~~
  - ~~Thereafter, repeat every 2–4 hours if needed.~~

Adults:
- Salbutamol 0.5%, solution, nebulised, preferably delivered at a flow rate of 8 L/min with oxygen.
  - 1 mL (5 mg) salbutamol 0.5% solution, in 4 mL of sodium chloride 0.9%.
  - If no relief, repeat every 20–30 minutes until PEF > 60% of predicted.
  - Once PEF > 60% of predicted, repeat every 2–4 hours if needed.

Children:
- Salbutamol 0.5%, solution, nebulised, preferably delivered at a flow rate of 5 L/min with oxygen.
  - 0.5–1 mL (2.5–5 mg) salbutamol 0.5% solution, in 4 mL of sodium chloride 0.9%.
  - If no relief, repeat every 20–30 minutes in the first hour.
  - Thereafter, repeat every 2–4 hours if needed.

Level of Evidence: III Guidelines

Ipratropium 0.25mg and 0.5mg nebulisation: *dose and directions for use amended*
Aligned with Global initiative for asthma (GINA) and South African Childhood Asthma Working Group Guidelines.
The text of the STG was updated as follows:

Adults and children:
- ~~Ipratropium bromide, solution, added to salbutamol solution.~~
  - ~~Children: 0.5–1 mL (0.125–0.25 mg)~~
  - ~~Adults: 2 mL (0.5 mg)~~

Adults:
If poor response after first salbutamol nebulisation/inhalation:
- Ipratropium bromide solution, 0.5 mg nebulised, 2 mL (0.5 mg) added to salbutamol solution every 20–30 minutes for 3 doses depending on clinical response.

Children:
- Ipratropium bromide, 0.25 mg solution, nebulised with salbutamol and sodium chloride.
  - 0.25 mg (2 mL) every 20–30 minutes depending on clinical response for 4
  - doses over 2 hours.

Level of Evidence: III Guidelines[7]

Ipratropium metered dose inhaler (MDI): *dose and directions for use amended*
Aligned with Global initiative for asthma (GINA) Guidelines.
The text of the STG was updated as follows:

Adults:
- ~~Ipratropium bromide, inhalation, 4 puffs, using a spacer.~~
- Ipratropium bromide, inhalation using MDI, 80–160 mcg (2–4 puffs), using a spacer every 20–30 minutes as needed for up to 3 hours.

Level of Evidence: III Guidelines[8]

[7] Adults: Global initiative for asthma (GINA) Guidelines, 2017. http://ginasthma.org/
Children: Kling S, Zar HJ, Levin ME, Green RJ, Jeena PM, Risenga SM, ThulaSA ,Goussard P, Gie RP, for the South African Childhood Asthma Working Group (SACAWG)S Afr Med J 2013;103(3):199-207.
[8] Adults: Global initiative for asthma (GINA) Guidelines, 2017. http://ginasthma.org/

17.1.2 CHRONIC ASTHMA and 17.1.4 CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Inhaled corticosteroids (ICS): *retained as therapeutic class*
Beclomethasone, inhaler: *deleted as example of ICS therapeutic class in the general population*
Budesonide, inhaler: *added as the example of ICS therapeutic class in the general population*

Price comparison: As budesonide metered dose inhaler (MDI) consists of 300 doses, whilst beclomethasone MDI contains 200 doses, budesonide MDI was calculated to be cheaper than beclomethasone MDI, and budesonide MDI was recommended as the example of the ICS therapeutic group of inhalers.

Low dose	Price per dose (ZAR)	High dose	Price per dose (ZAR)
Budesonide 100 mcg	0.165[9]	Budesonide 200 mcg	0.178[10]
Beclomethasone 100 mcg	0.191[11]	Beclomethasone 200 mcg	0.281[12]

Recommendation: Budesonide MDI be recommended as the example of the ICS therapeutic group of inhalers.
Rationale: Price per dose of budesonide 100 and 200 mcg was cheaper than that of beclomethasone 100 and 200 mcg, respectively. The estimated comparable therapeutic dose of 100 mcg budesonide is beclomethasone 100 mcg[13].
Level of Evidence III Expert opinion

Patients on protease inhibitors
Beclomethasone, inhaler: *not added for patients on protease inhibitors*
Formoterol, inhaler: *not added as doctor initiated – "step-up therapy" for patients on protease inhibitors*

Evidence
i) University of Liverpool HIV drug interaction database showed
- Beclomethasone + PI No clinically significant interaction was expected between beclomethasone and protease inhibitors (lopinavir/atazanavir/darunavir/ritonavir).

ii) NIH aids info guidelines
- PI + Budesonide, ciclosenide, fluticasone and mometasone May result in adrenal insufficiency and iatrogenic Cushing's syndrome

iii) Pubmed search (21 Feb 2018)
- Search ("budesonide"[MeSH Terms] OR "budesonide"[All Fields]) AND ("protease inhibitors"[Pharmacological Action] OR "protease inhibitors"[MeSH Terms] OR ("protease"[All Fields] AND "inhibitors"[All Fields]) OR "protease inhibitors"[All Fields] OR ("protease"[All Fields] AND "inhibitor"[All Fields]) OR "protease inhibitor"[All Fields]) AND ("Interaction"[Journal] OR "interaction"[All Fields])

[9] Average weighted price: Contract circular HP07-2017DAI (Split tender)
[10] Contract circular HP07-2017DAI
[11] Contract circular HP07-2017DAI
[12] Contract circular HP07-2017DAI
[13] National Asthma Education and Prevention Program, Third Expert Panel on the Diagnosis and Management of Asthma. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Bethesda (MD): National Heart, Lung, and Blood Institute (US); 2007 Aug. Available from: https://www.ncbi.nlm.nih.gov/books/NBK7232/

- Identified 5 articles 1 referred to fluticasone[14]; 1 was a case report involving oral budesonide[15]; 3 case reports of iatrogenic Cushings with inhaled budesonide[16] and ritonavir, ritonavir-boosted lopinavir, and ritonavir-boosted darunavir[17].

Recommendation Beclomethasone inhaled corticosteroid not be recommended in patients on protease inhibitors at primary level of care; patients on protease inhibitors be referred to secondary level of care.

Rationale: There is a significant drug interaction between protease inhibitors (PIs) and budesonide and fluticasone, which might result in iatrogenic Cushing's syndrome. PIs do not interact with beclomethasone, so that is the best ICS to use in patients on PIs. However, NEMLC did not feel that it was practical to stock beclomethasone in addition to budesonide at all PHC clinics, as patients on PIs who require ICS are relatively uncommon. They therefore recommend that those patients are referred to the next level of care to initiate beclomethasone. For chronic patients beclomethasone could be accessed at PHC through down-referral mechanisms.

Level of Evidence III Case reports

Exercise induced asthma

Salbutamol MDI: *deleted*

Management for exercise induced asthma was deleted as management is the same as for acute asthma.

Level of Evidence: III Guidelines[18], Expert opinion

17.1.3 ACUTE BRONCHIOLITIS IN CHILDREN

Salbutamol, inhaler *deleted*

Previously the NEMLC (29 June 2017) recommended that the PHC Committee reword the guidance pertaining to management with salbutamol in the STGs and EML.

Text of the STG was updated to:

- It is difficult to distinguish between bronchiolitis and asthma. Bronchiolitis does not usually respond to salbutamol. If there is a good response to a single salbutamol dose, asthma is the more likely diagnosis. Treat accordingly and see Section 17.1.1 Acute asthma and acute exacerbation of chronic obstructive pulmonary disease (COPD).

However, the NEMLC further amended this section as indicated in the NEMLC discussion, below.

NEMLC MEETING DISCUSSION: 12 April 2018[19]

The NEMLC recommended that the following section be deleted, with a cross-reference to the acute asthma section is asthma is suspected, as bronchiolitis is not treated with salbutamol.

Text was amended as follows

"Refer severe bronchiolitis or those with risk factors

- *Oxygen, humidified, using nasal prongs or nasal cannula, at 1–2 L/minute.*

~~***AND***~~

- ~~*Salbutamol 0.5%, solution, nebulised, 0.5 mL (2.5 mg) diluted with 4 mL of sodium chloride 0.9% over 3 minutes (single dose).*~~

[14] Kedem E, Shahar E, Hassoun G, Pollack S. Iatrogenic Cushing's syndrome due to coadministration of ritonavir and inhaled budesonide in an asthmatic human immunodeficiency virus infected patient. J Asthma. 2010 Sep;47(7):830-1. https://www.ncbi.nlm.nih.gov/pubmed/20653496

[15] Frankel JK, Packer CD. Cushing's syndrome due to antiretroviral-budesonide interaction. Ann Pharmacother. 2011 Jun;45(6):823-4. https://www.ncbi.nlm.nih.gov/pubmed/21558486

[16] Blondin MC, Beauregard H, Serri O. Iatrogenic Cushing syndrome in patients receiving inhaled budesonide and itraconazole or ritonavir: two cases and literature review. Endocr Pract. 2013 Nov-Dec;19(6):e138-41. https://www.ncbi.nlm.nih.gov/pubmed/23807527

[17] Yoganathan K, David L, Williams C, Jones K. Cushing's syndrome with adrenal suppression induced by inhaled budesonide due to a ritonavir drug interaction in a woman with HIV infection. Int J STD AIDS. 2012 Jul;23(7):520-1. https://www.ncbi.nlm.nih.gov/pubmed/22844010

[18] Global initiative for asthma (GINA) Guidelines, 2017. http://ginasthma.org/

[19] NEMLC minutes of the meeting:12 April 2018

- ~~*It is difficult to distinguish between bronchiolitis and asthma. Bronchiolitis does not usually respond to salbutamol. If there is a good response to a single salbutamol dose, asthma is the more likely diagnosis. Treat accordingly and see Section 17.1.1 Acute asthma and acute exacerbation of chronic obstructive pulmonary disease (COPD).*~~

If asthma is suspected in children > 2 years of age, see Section 17.1.1 Acute asthma and acute exacerbation of chronic obstructive pulmonary disease (COPD)".

Adrenaline (epinephrine): *deleted*
Aligned with the Paediatric Hospital level STGs and EML, 2017.
Level of Evidence: III Guidelines[20]

Salbutamol 0.5% nebulisation: dose amended
Dose was amended from "*0.5-1mL*" to *"0.5 mL",* aligned with the general format in the STGs of not having ranges. The dose of 0.5 mL was considered adequate.
Level of Evidence: III Expert opinion

17.1.4 CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Chronic management
Background: Different recommendations are provided for the management of COPD at primary healthcare and secondary level of care. The PHC STGs and EML, 2014 recommended a combined inhaler containing a long acting beta$_2$ agonist (LABA) with an inhaled corticosteroid (ICS), whilst the Adult Hospital level STG recommends a LABA for milder disease, and combined LABA/ICS for more severe disease.
Historically, there were concerns about the ability to distinguish between COPD and asthma at PHC level, where spirometry is not widely available. The potential adverse effects of ICS in milder cases of COPD versus the risks of using a LABA alone in patients with asthma, incorrectly diagnosed as COPD was considered. (Using a LABA without an ICS in asthma is associated with an increased risk of mortality.) There is an additional concern about having a LABA in a separate formulation at PHC, where it could (incorrectly) be used in patients with asthma. It was considered to be safer to use ICS in all patients with COPD, than to use a LABA alone in some patients with asthma.

Proposed recommendation: On receipt of comments from external stakeholders, the PHC STG was amended to provide **total treatment** for COPD, delineating specific treatment where spirometers are not available at primary level facilities.

LABA (formoterol) inhaler:*added as doctor initiated (if spirometer available)*
LABA/ICS (Salmeterol/fluticasone) inhaler: *directions for use amended.*

Text was updated as follows, aligned with the Adult Hospital level STGs and EML, 2015:

SABA e.g.:
- Salbutamol, inhalation, 100–200 mcg (1–2 puffs), 3–4 times daily as needed for relief of wheeze.

If not controlled on SABA alone and diagnosis was confirmed by spirometry (with <2 exacerbations per year):
- Long acting β2-agonist (LABA), e.g.:
- Formoterol, inhaled 12 mcg (1 puff) 12 hourly (Doctor initiated).

If not controlled on SABA alone and spirometry not available:
- Inhaled LABA/corticosteroid combination e.g.:
- Salmeterol/fluticasone, inhalation, 25/125mcg, 2 puffs (total dose 50/250 mcg) 12 hourly (Doctor initiated).

[20] Paediateric Hospital level STGs and EML, 2017

If not controlled on a LABA alone or frequent exacerbations (≥2 per year):
Replace with:

- Inhaled LABA/corticosteroid combination e.g.:
- Salmeterol/fluticasone, inhalation, 25/125mcg, 2 puffs (total dose 50/250 mcg) 12 hourly (Doctor initiated).

Level of Evidence: III Guidelines, Expert opinion

17.3.2 ACUTE BRONCHITIS IN ADULTS OR ADOLESCENTS

Antibiotics *Indication for HIV-infected patients deleted*

Previously the NEMLC (29 June 2017) recommended that the statement, "*However, antibiotics may be considered for HIV-infected patients because of the higher incidence of bacterial lower respiratory tract infections in this subgroup*" be retained in the text of the STG and be circulated, with a comment that NEMLC proposes that the statement be deleted, in order to prompt comment from external stakeholders.

No external comments had been received, and the following text was deleted from the STG

~~However, antibiotics may be considered for HIV-infected patients because of the higher incidence of bacterial lower respiratory tract infections in this subgroup.~~

Evidence: Triple-blind, placebo-controlled RCT by Nduba et al[21] compared amoxicillin vs placebo for acute bronchitis in patients without chronic lung disease.

Results: Clinical cure rates for amoxicillin vs placebo

- Overall 81.7% vs 84.0%, difference 2.3%, 95% CI -8.6% to 4.0%.
- HIV cohort (n=131) 77.2% vs 83.8%; difference 6.6%, 95% CI -21.7 to 8.6%.
- HIV-uninfected cohort difference in cure rates was 1.6% (95% CI -8.5% to 5.3%).
- Potential ADRs were similar in the two arms. No subjects required hospitalisation or died.

Recommendation Antibiotics be deleted for acute bronchitis in HIV-infected patients.

Rationale RCT showed that "antibiotic treatment of acute bronchitis is unhelpful, even in populations with a high prevalence of HIV infection".

Level of Evidence I RCT

Cough linctus: *deleted*

Aligned with the Paediatric Hospital STGs and EML, 2017.

17.3.4.1 PNEUMONIA IN CHILDREN

Children

Amoxicillin, oral: *dose amended*

The paediatric dose for pneumonia was aligned with the Paediatric STG and EML, 2017.

The text of the STG was updated as follows:

Pneumonia (non-severe):

- Amoxicillin, oral, 45 mg/kg/dose, 12 hourly for 5 days.

Weight kg	**Dose** mg	**Use one of the following:**				**Age** Months/years
		Syrup mg/ 5mL		**Capsule/tablet** mg		
		125	250	250	500	
>3.5–5 kg	200	8 mL	4 mL	–	–	>2–3 months
>5–7 kg	275	11 mL	5.5 mL	–	–	>3–6 months
>7–11 kg	400		8 mL	–	–	>6–18 months
>11–14 kg	500	–	10 mL	2	–	>18 months–3 years
>14–17.5kg	750	–	15 mL	3	–	>3–5 years

[21] Nduba VN, Mwachari CW, Magaret AS, Park DR, Kigo A, Hooton TM, Cohen CR. Placebo found equivalent to amoxicillin for treatment of acute bronchitis in Nairobi, Kenya: a triple blind, randomised, equivalence trial. Thorax. 2008 Nov;63(11):999-1005. https://www.ncbi.nlm.nih.gov/pubmed/18559367

>17.5–25 kg	1000	–	20 mL*	4	2	>5–7 years
>25–30 kg	1250	–	25 mL*	5	–	>7–10 years
>30 kg	1500	–	-	6	3	>10 years

*capsule/tablet preferred

Level of Evidence: III Guidelines[22]

17.3.4.2.4 PNEUMOCYSTIS PNEUMONIA

Cotrimoxazole, oral: *directions for use amended*

Aligned with the PHC HIV chapter. The following text was added to the STG:

Prophylaxis should be discontinued if the CD4 count increases on ART to >200 cells/mm^{3}for at least 6 months.

Level of Evidence: III Guidelines

17.4.1 PULMONARY TUBERCULOSIS (TB) IN ADULTS

Adverse effects of TB medicines include

The following text pertaining to diagnosis and referral of DILI associated with TB treatment was included in the STG:

- Hepatitis (drug induced liver injury)
  - Rifampicin, isoniazid and pyrazinamide may cause hepatitis. Cotrimoxazole and antiretrovirals (efavirenz, nevirapine, lopinavir + ritonavir) can also cause hepatitis.
  - Patient may present with jaundice and/or complaining of hepatitis symptoms (e.g. nausea, malaise, abdominal pain).
  - Refer to hospital for urgent (same day) ALT and further management
  - If jaundiced, stop TB treatment and medicines known to cause hepatitis before referring. See Section: 11.1 Antiretroviral therapy, adults.

17.4.2.1 TB CHEMOPROPHYLAXIS/ISONIAZID PREVENTIVE THERAPY (IPT) IN CHILDREN

Preventive therapy in case of drug-resistant TB contact

Rifampicin, oral: *added*

Isoniazid, oral: *added*

The following text was added to the STG, aligned with the Paediatric Hospital level STGs and EML, 2017.

Preventive therapy in case of drug-resistant TB contact:

Isoniazid mono-resistant contact:

- Rifampicin, oral, 15 mg/kg daily for 4 months.
  - If child unable to swallow tablets

Rifampicin mono-resistant contact:

- Isoniazid, oral, 10 mg/kg daily for 6 months (see table above).

Level of Evidence: III Guidelines[23]

17.4.2.2 TB CONTROL PROGRAMME: MEDICINE REGIMENS IN CHILDREN

Pyridoxine, oral: *dose amended*

The dose for pyridoxine was aligned to the Paediatric STGs and EML, 2017, as follows:

- Pyridoxine, oral, daily for duration of prophylaxis:
  - Child < 5 years old: 12.5 mg.
  - Child ≥ 5 years old: 25 mg.

[22] Paediatric Hospital Level STGs and EML, 2017.
[23] Paediatric Hospital Level STGs and EML, 2017.

Level of Evidence: III Guidelines[24]

17.4.4.1 MULTIDRUG-RESISTANT TUBERCULOSIS (MDR TB), IN ADULTS

Kanamycin, injection: *deleted*
Moxifloxacin, oral: *deleted*
Ethionamide, oral: *deleted*
Terizidone, oral: *deleted*
Pyrazinamide, oral: *deleted*
At the NEMLC meeting of 16 September 2016[25], NEMLC had not approved S21 clofazimine for inclusion to the primary healthcare EML. Access and Medicines Control Council regulatory oversight are key elements that place MDR-TB patients and nurse practitioners at risk.
As clofazamine-containing short regimen is currently being rolled out by the NDoH MDR-TB programme, a cross referral to NDoH Programme Guidelines was included in the text of the STG, as follows:

> MDR TB guidelines are updated regularly.
> Consult the most recent National MDR TB Programme Guidelines.

AGENTS OF THERAPEUTIC CLASSES

Short acting beta2 agonist: *agents of therapeutic class listed*

Indication	Medicine	Formulation	DDD	Comment
Mild intermittent asthma (adults and children)	Salbutamol	MDI	400-800 mcg	n/a
	Terbutaline	MDI	2 mg	No recommended dose for child < 5 years
	Fenoterol	MDI	400-800 mcg	No recommended dose for child < 6 years *Note:* Fenoterol may cause more adverse effects than salbutamol or terbutaline[26].

Level of Evidence: III Guidelines[27]

Inhaled corticosteroids: *agents of therapeutic class listed*

Children:

Indication	Medicine	Formulation	DDD	Comment
Persistent asthma (children) - step 2	Beclometasone	MDI	200 mcg	n/a
	Budesonide	MDI	200 mcg	n/a
	Fluticasone	MDI	125 mcg	No recommended dose for child < 6 years old.
Persistent asthma - control still inadequate (children) - step 3	Beclometasone	MDI	400 mcg	n/a
	Budesonide	MDI	400 mcg	n/a
	Fluticasone	MDI	250 mcg	No recommended dose for child < 6 years old.

Level of Evidence: III Guidelines[28][29]

Adults:

Indication	Medicine	Formulation	DDD	Comment
Persistent asthma (adults) - step 2	Beclometasone	MDI	400 mcg	n/a
	Budesonide	MDI	400 mcg	n/a
	Fluticasone	MDI	250 mcg	n/a

[24] Paediatric Hospital Level STGs and EML, 2017.
[25] NEMLC minutes of the meeting: 16 September2016.
[26]Wong CS, Pavord ID, Williams J, Britton JR, Tattersfield AE. Bronchodilator, cardiovascular, and hypokalaemic effects of fenoterol, salbutamol, and terbutaline in asthma. The Lancet. 1990;336(8728):1396-9
[27] SAMF, 2016
[28] SAMF, 2016
[29]National Asthma Education and Prevention Program, Third Expert Panel on the Diagnosis and Management of Asthma. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Bethesda (MD): National Heart, Lung, and Blood Institute (US); 2007 Aug. Available from: https://www.ncbi.nlm.nih.gov/books/NBK7232/

	Ciclesonide	MDI	160 mcg	n/a
Persistent asthma - control still inadequate (adults) - step 3	Beclometasone	MDI	800 mcg	n/a
	Budesonide	MDI	800 mcg	n/a
	Fluticasone	MDI	500 mcg	n/a
	Ciclesonide	MDI	320 mcg	n/a

Level of Evidence: III Guidelines[30] [31]

LABA/ICS: *agents of therapeutic class listed*

Indication	Medicine	Formulation	Defined daily dosing	Comment
Persistent asthma - control still inadequate (adults) - step 4	Fluticasone/salmeterol	MDI	500/100 mcg	Doctor prescribed
	Budesonide/formoterol	MDI	640/18 mcg	Doctor prescribed
COPD: If no response - step 2	Fluticasone/salmeterol	MDI	500/100 mcg	Doctor prescribed
	Budesonide/formoterol	MDI	640/18 mcg	Doctor prescribed

Level of Evidence: III Guidelines[32] [33]

LABA: *agents of therapeutic class listed*

Indication	Medicine	Formulation	Defined daily dosing	Comment
COPD: If not controlled on SABA alone and diagnosis was confirmed by spirometry (with <2 exacerbations per year):	Formoteroll	MDI	24 mcg	Doctor prescribed, if spirometer available
	Salmeterol	MDI	100 mcg	Doctor prescribed, if spirometer available

Level of Evidence: III Guidelines[34]

[30] SAMF, 2016

[31] National Asthma Education and Prevention Program, Third Expert Panel on the Diagnosis and Management of Asthma. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Bethesda (MD): National Heart, Lung, and Blood Institute (US); 2007 Aug. Available from: https://www.ncbi.nlm.nih.gov/books/NBK7232/

[32] SAMF, 2016

[33] National Asthma Education and Prevention Program, Third Expert Panel on the Diagnosis and Management of Asthma. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Bethesda (MD): National Heart, Lung, and Blood Institute (US); 2007 Aug. Available from: https://www.ncbi.nlm.nih.gov/books/NBK7232/

[34] SAMF, 2016