

## 17.1 CONDITIONS WITH PREDOMINANT WHEEZE

### 17.1.1 ACUTE ASTHMA & ACUTE EXACERBATION OF COPD, ADULTS

J46/J45.0-1/J45.8-9

#### DESCRIPTION

This is an emergency situation recognised by various combinations of:

- » wheeze » breathlessness
- » tightness of the chest » respiratory distress
- » chest indrawing » cough

In adults, bronchospasm is usually associated with asthma (where the bronchospasm is usually completely reversible) or chronic obstructive pulmonary disease (COPD) (where the bronchospasm is partially reversible).

The clinical picture of pulmonary oedema due to left ventricular heart failure may be similar to that of asthma. If patients >50 years of age present with asthma for the first time, consider pulmonary oedema due to left ventricular heart failure.

All PHC facilities must have peak expiratory flow rate (PEFR) meters, as asthma cannot be correctly managed without measuring PEFR.

#### ASTHMA

##### Recognition and assessment of severity of asthma attacks in adults

	Mild-Moderate	Severe	Life threatening
Oxygen saturation	>90%	<90%	<90%
Talks in	phrases	words	unable to speak
Alertness	normal	Usually agitated	agitated, drowsy or confused
Respiratory rate	20–30 breaths/minute	often >30 breaths/minute	often >30 breaths/minute OR feeble effort
Wheeze	present	present	absent
Heart rate	100–120 beats/minute	>120 beats/minute	bradycardia
PEFR	>60% of predicted	<60% of predicted	<33% of expected or unable to blow

**Note:** PEFR is expressed as a percentage of the predicted normal value for the individual, or of the patient's personal best value obtained previously when on optimal treatment (see nomogram in Appendix I: Asthma monitoring, to predict PEFR).

LoE:IVb<sup>†</sup>

## COPD

### Recognition and assessment of severity of COPD attacks in adults

	Moderate	Severe
<b>Talks in</b>	phrases	words
<b>Alertness</b>	usually agitated	agitated, drowsy or confused
<b>Respiratory rate</b>	20–30 breaths/minute	often >30 breaths/minute
<b>Wheeze</b>	loud	loud or absent
<b>Heart rate</b>	100–120 beats/minute	>120 beats/minute
<b>PEFR after initial nebulisation</b>	±50–75%	<50%; may be too short of breath to blow in PEF meter

**Note:** PEFR is expressed as a percentage of the predicted normal value for the individual, or of the patient's personal best value obtained previously when on optimal treatment (see nomogram in Appendix I: Asthma monitoring, to predict PEFR).

## MEDICINE TREATMENT

See Appendix II: Devices for Respiratory Conditions for guidance on inhaler, spacer and nebuliser device techniques.

### Mild to moderate attacks

- Salbutamol 100 mcg metered-dose inhaler (MDI), LoE:IVb<sup>2</sup>
  - Salbutamol inhaler 400 to 1000 mcg (4 to 10 puffs) using a spacer if required and available. LoE:IVb<sup>3</sup>
  - Shake the inhaler between each puff.
  - If no relief, repeat every 20 to 30 minutes in the first hour.
  - Thereafter, repeat every 2 to 4 hours if needed.

**Note:** Administering salbutamol via a spacer is as effective as, and cheaper than, using a nebuliser.

### OR

- Salbutamol 0.5% (5 mg/mL), solution,
  - 1 mL (5 mg) salbutamol 0.5% solution made up to 4 mL with sodium chloride 0.9%, preferably delivered at a flow rate of 8 L/min with oxygen.
  - If no relief, repeat every 20 to 30 minutes in the first hour.
  - Thereafter, repeat every 2 to 4 hours if needed. LoE:IVb<sup>4</sup>

### PLUS

- Corticosteroids (intermediate-acting), e.g.: LoE:IVb<sup>5</sup>
- Prednisone, oral, 40 mg immediately if patient known to have asthma/COPD.
  - Follow with prednisone, oral, 40 mg daily for 7 days.

**Severe attacks (while awaiting referral)**

- Oxygen to keep oxygen saturation 93–95%.

**Note:** For adults with COPD:

Give oxygen with care (preferably by 24% or 28% facemask, if available). Observe patients closely, as a small number of patients' condition may deteriorate.

**AND**

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

*LoE:IVb<sup>6</sup>***OR**

- Salbutamol, inhalation using a MDI,
  - Salbutamol 400–1000 mcg (4 to 10 puffs), up to 20 puffs, using a spacer.
  - Inhale 1 puff at a time. Allow for 6 breaths through the spacer between puffs.
  - If no relief, repeat every 20 to 30 minutes until PEF >60% of predicted.
  - Once PEF >60% of predicted, repeat every 2 to 4 hours if needed.

*LoE:IVb<sup>7</sup>*

**Note:** Administering salbutamol via a spacer is as effective as, and cheaper than, using a nebuliser.

*LoE:IVb<sup>8</sup>***If poor response after first salbutamol nebulisation/inhalation:**

- Continue salbutamol nebulisation as described in management above and

**ADD**

- Ipratropium bromide 0.5 mg/2mL; nebuliser solution
  - Ipratropium bromide, 2 mL (0.5 mg) added to salbutamol 1 mL (5 mg) solution and made up to 4 mL with sodium chloride 0.9%.
  - Administer every 20 to 30 minutes up to a maximum of 3 doses depending on clinical response.

*LoE:IIb<sup>9</sup>***OR**

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

*LoE:IIb<sup>10</sup>***AND**

- Corticosteroids (intermediate-acting), e.g.:
- Prednisone, oral, 40 mg immediately.
  - Follow with prednisone, oral, 40 mg daily for 7 days.

*LoE:IVb<sup>11</sup>***OR**

If oral prednisone cannot be taken:

- Hydrocortisone IM/slow IV, 100 mg as a single dose.

*LoE:IVb<sup>12</sup>*

Followed with:

- Prednisone, oral, 40 mg daily for 7 days.

**CAUTION**

Avoid sedation of any kind.

**Note:** If poor response to treatment, consider alternate diagnosis and refer urgently.

**Life-threatening attacks**

- Oxygen, to keep oxygen saturation 93 to 95%.

**Note:** For adults with COPD:

- Give oxygen with care (preferably by 24% or 28% facemask, if available). Observe patients closely, as a small number of patients' condition may deteriorate.

**AND**

- Salbutamol 0.5% (5 mg/mL) with ipratropium bromide 0.5 mg/2mL nebuliser solution.
  - Salbutamol 0.5%, 2 mL (10 mg) plus ipratropium bromide, 2 mL (0.5 mg) every 20–30 minutes depending on clinical response for 4 doses over 2 hours.
  - Delivered at a flow rate of 8 L/min with oxygen.
  - If no relief, repeat every 20 to 30 minutes until asthma severity category moves from life-threatening to severe.

**AND**

- Parenteral corticosteroids (intermediate-acting) e.g.:
- Hydrocortisone IM/slow IV, 100 mg as a single dose.

LoE:IVb<sup>13</sup>

Followed with:

- Oral corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg daily for 7 days.

**CAUTION**

Avoid sedation of any kind.

**Note:** If response to treatment is adequate and severity improves to become severe but not life threatening, treat as per severe asthma exacerbation above.

**Assessment of response in adults**

	<b>Response</b>	<b>No response</b>
<b>PEFR (if possible)</b>	improvement by >20%	improvement by <20%
<b>Respiratory rate</b>	<20 breaths/ minute	>20 breaths/ minute
<b>Speech</b>	normal	impaired

**Patients responding to treatment:**

- » Routine prescription of antibiotics is not indicated for acute asthma.
- » Review current treatment and possible factors causing acute attack, including poor adherence and poor inhaler technique.
- » Advise patient/caregiver on further care at home, danger signs and that follow up is required.
- » Caution patient on the high chance of further wheezing in the week following an acute attack.
- » Patients with a first attack should be fully assessed for maintenance treatment.
- » Ask about smoking: if yes, urge patient to stop.

**Note:** Patients needing repeated courses of oral corticosteroids (more than twice over 6 months) should be assessed by a doctor for maintenance therapy. (See Section 17.1.3: Chronic asthma.)

**REFERRAL****Urgent (after commencing treatment):**

- » All patients with severe attack.
- » Poor response to initial treatment.
- » PEFR <75% of the predicted normal or of personal best value 15 to 30 minutes after nebulisation.
- » A lower threshold for admission is appropriate in patients when:
  - seen in the afternoon or evening, rather than earlier in the day.
  - recent onset of nocturnal symptoms or aggravation of symptoms.
  - previous severe attacks, especially if the onset was rapid.

**17.1.2 ACUTE ASTHMA, CHILDREN**

J46/J45.0-1/J45.8-9

**DESCRIPTION**

Bronchospasm in children is usually associated with asthma or with infections such as bronchiolitis or bronchopneumonia. Consider foreign bodies or obstruction of airways due to tuberculous nodes or congenital malformation, especially if the wheeze is unilateral.

**Recognition and assessment of severity of attacks in children**

	Mild/Moderate	Severe	Life-threatening
Oxygen saturation	>90%	<90%	<90%
Respiratory rate	<40 breaths/minute	>40 breaths/minute	>60 breaths/minute
Chest indrawing/recession	present	present	present
PEF (if >5 years of age)	>60% of predicted	<60% of predicted	<33% of expected or unable to blow
Speech	normal	difficult	unable to speak
Feeding	normal	difficulty with feeding	unable to feed
Wheeze	present	present	absent
Consciousness	normal	normal	impaired

**MEDICINE TREATMENT**

See Appendix II: Devices for Respiratory Conditions for guidance on inhaler, spacer and nebuliser device techniques.

**Mild to moderate attacks:**

- Salbutamol 100 mcg metered-dose inhaler (MDI).

**Children ≥5 years:**

- Salbutamol inhaler 400 to 1000 mcg (4 to 10 puffs) using a spacer.
  - Shake the inhaler between each puff.
  - If no relief, repeat every 20 to 30 minutes in the first hour.
  - Thereafter, repeat every 2 to 4 hours if needed.

LoE:IVb<sup>14</sup>

**Children <5 years:**

- Salbutamol inhaler 200–600 mcg (2-6 puffs) using a spacer.
  - For children ≥ 3 years, use a spacer with a mouthpiece.
  - If child <3 years of age, use a mask attached to the spacer. Apply the mask to the face to create a seal so that the child breathes through the spacer.
  - Inhale one puff at a time. Use a single breath inhalation technique. If single inhalation technique not possible, allow for 6 breaths through the spacer between puffs.
  - If no relief, repeat every 20 to 30 minutes in the first hour.
  - Thereafter, repeat every 2 to 4 hours if needed.

LoE:IVb<sup>15</sup>

**Note:** Administering salbutamol via a spacer is as effective as, and cheaper than, using a nebuliser.

**OR**

- Salbutamol 0.5% (5 mg/mL), solution,
  - 0.5–1 mL (2.5 to 5 mg) salbutamol 0.5% solution, made up to 4 mL with sodium chloride 0.9%, preferably delivered at a flow rate of 8 L/min with oxygen.
  - If no relief, repeat every 20 to 30 minutes in the first hour.
  - Thereafter, repeat every 2 to 4 hours if needed.

LoE:IVb<sup>16</sup>**PLUS**

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 1 to 2 mg/kg immediately and follow with same dose for 7 days:

LoE:IVb<sup>17</sup>

Weight (kg)	Dose (mg)	Tablet (5 mg)	Age (years)
>11–14 kg	20 mg	4 tablets	>2–3 years
>14–17.5 kg	30 mg	6 tablets	>3–5 years
>17.5 kg	40 mg	8 tablets	>5 years

**Severe attacks (while awaiting referral)**

- Oxygen to keep oxygen saturation 93 to 95%.

**AND**

- Salbutamol 0.5% (5mg/mL) nebuliser solution,
  - 0.5–1 mL (2.5 to 5 mg) salbutamol 0.5% solution, made up to 4 mL with sodium chloride 0.9%, preferably delivered at a flow rate of 8 L/min with oxygen.
  - If no relief, repeat every 20 to 30 minutes depending on clinical response.

**OR**

- Salbutamol, inhalation using an MDI,
  - Salbutamol, 400 to 1000 mcg (4 to 10 puffs), using a spacer.
  - For children ≥3 years, use a spacer with a mouthpiece.
  - If child <3 years of age, use a mask attached to the spacer. Apply the mask to the face to create a seal so that the child breathes through the spacer.
  - Inhale one puff at a time. Use a single breath inhalation technique. If single inhalation technique not possible, allow for 6 breaths through the spacer between puffs.
  - If no relief, repeat every 20 to 30 minutes depending on clinical response.

**Note:** Administering salbutamol via a spacer is as effective as, and cheaper than, using a nebuliser.

If poor response after first salbutamol nebulisation/inhalation:

**ADD**

- Ipratropium bromide 0.25 mg/2ml; nebuliser solution.
  - Ipratropium bromide, 2 mL (0.25 mg) solution, nebulised with salbutamol 0.5 mL (2.5 mg) and made up to 4 mL with sodium chloride 0.9%.
  - Administer every 20 to 30 minutes depending on clinical response for 4 doses over 2 hours.

LoE:IIb<sup>18</sup>

**OR**

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

**AND**

- Corticosteroids (intermediate-acting), e.g.:
- Prednisone, oral, 1 to 2 mg/kg immediately and follow with same dose for 7 days:

LoE:IVb<sup>19</sup>

Weight (kg)	Dose (mg)	Tablet (5 mg)	Age (years)
>11–14 kg	20 mg	4 tablets	>2–3 years
>14–17.5 kg	30 mg	6 tablets	>3–5 years
>17.5 kg	40 mg	8 tablets	>5 years and adult

**OR**

If oral prednisone cannot be taken:

- Hydrocortisone IM/slow IV, 4 mg/kg (maximum 100 mg) immediately. See dosing table: Chapter 23.

Followed with:

- Prednisone 1 to 2 mg/kg daily for 7 days as per dosing table above.

**CAUTION**

Avoid sedation of any kind.

**Note:** If poor response to treatment, consider alternate diagnosis and refer urgently.

**Life-threatening attacks**

- Oxygen, to keep oxygen saturation 93 to 95%.

**AND**

- Salbutamol 0.5% (5 mg/mL) with ipratropium bromide 0.5 mg/2mL nebuliser solution:
  - Salbutamol 0.5%, 2 mL (10 mg) plus ipratropium bromide, 2 mL (0.5 mg) every 20–30 minutes depending on clinical response for 4 doses over 2 hours.
  - Delivered at a flow rate of 8 L/min with oxygen.
  - If no relief, repeat every 20 to 30 minutes until asthma severity category moves from life-threatening to severe.

**AND**

- Parenteral corticosteroids (intermediate-acting) e.g.:

LoE:IVb<sup>20</sup>

- Hydrocortisone IM/slow IV, 4 mg/kg (maximum 100 mg) immediately. See dosing table: Chapter 23.

Followed with:

- Oral corticosteroids (intermediate-acting) e.g.:
- Prednisone 1 to 2 mg/kg daily for 7 days.

**CAUTION**

Avoid sedation of any kind.

**Note:** If response to treatment is adequate and severity improves to become severe but not life threatening, treat as per severe asthma exacerbation above.

#### Assessment of response in children

	<b>Response</b>	<b>No response</b>
<b>PEFR (if possible)</b>	improvement by >20%	improvement by <20%
<b>Respiratory rate</b>	<40 breaths/minute	>40 breaths/minute
<b>Chest indrawing or recession</b>	absent	present
<b>Speech</b>	normal	impaired
<b>Feeding</b>	normal	impaired

#### Patients responding to treatment:

- Routine prescription of antibiotics is not indicated for acute asthma.
- Review current treatment and possible factors causing acute attack including poor adherence and poor inhaler technique.
- Advise patient/caregiver on further care at home, danger signs and that follow up is required.
- Caution patient/carer on the high chance of further wheezing in the week following an acute attack.
- Patients with a first attack should be fully assessed for maintenance treatment.

**Note:** Patients needing repeated courses of oral corticosteroids (more than twice over 6 months) should be assessed by a doctor for maintenance therapy. (See Section 17.1.3: Chronic asthma.)

#### REFERRAL

##### Urgent (after commencing treatment):

- All patients with severe attack.
- Poor response to initial treatment.
- PEFR <75% of the predicted normal or of personal best value 15 to 30 minutes after nebulisation.
- A lower threshold to admission is appropriate in patients when:
  - seen in the afternoon or evening, rather than earlier in the day.
  - recent onset of nocturnal symptoms or aggravation of symptoms.
  - previous severe attacks, especially if the onset was rapid.

### 17.1.3 CHRONIC ASTHMA

J45.0-1/J45.8-9

#### DESCRIPTION

A chronic inflammatory disorder with reversible airway obstruction. In susceptible patients, exposure to various environmental triggers, allergens or viral infections results in inflammatory changes, bronchospasm, increased bronchial secretions, mucus plug formation and, if not controlled, eventual bronchial muscle hypertrophy of the smooth muscle in the airways. All these factors contribute to airway obstruction.

Asthma varies in intensity and is characterised by recurrent attacks of:

- » wheezing,
- » dyspnoea or shortness of breath,
- » cough, especially nocturnal, and
- » periods of no airway obstruction between attacks.

Acute attacks may be caused by:

- » exposure to allergens,
- » respiratory viral infections,
- » non-specific irritating substances, and
- » exercise.

Asthma must be distinguished from COPD, which is often mistaken for asthma. (See Section 17.1.5: Chronic obstructive pulmonary disease (COPD)). The history is valuable in assessing treatment response.

Asthma	COPD
<ul style="list-style-type: none"> <li>» Young age onset, usually &lt;20 years.</li> <li>» History of hay fever, eczema and/or allergies.</li> <li>» Family history of asthma.</li> <li>» Symptoms are intermittent with periods of normal breathing in between.</li> <li>» Symptoms are usually worse at night or in the early hours of the morning, during an upper respiratory tract infection, when the weather changes, or when upset.</li> <li>» Marked improvement with <math>\beta_2</math>-agonist.</li> </ul>	<ul style="list-style-type: none"> <li>» Older age onset, usually &gt;40 years.</li> <li>» Symptoms slowly worsen over a long period of time.</li> <li>» Long history of daily or frequent cough before the onset of shortness of breath.</li> <li>» Symptoms are persistent rather than only at night or during the early morning.</li> <li>» History of heavy smoking (&gt;20 cigarettes/day for <math>\geq 15</math> years), heavy cannabis use, or previous TB.</li> <li>» Little improvement with <math>\beta_2</math>-agonist.</li> </ul>

Asthma cannot be cured, but it can be controlled with regular treatment.

If symptoms suggest TB (e.g. weight loss, night sweats, etc.), investigate and manage accordingly.

**Note:** The diagnosis of asthma can be difficult in children <6 years of age.

Refer the patient if the diagnosis of asthma is uncertain.

#### ASTHMA DIAGNOSIS AND SEVERITY

##### Peak Expiratory Flow Rate (PEFR)

See PEFR charts in Appendix I: Asthma monitoring.

The PEFR may provide additional information for diagnosis and assessing response to therapy.

- » PEFR is best assessed in the morning and evening.
  - Instruct the patient to blow forcibly into the device after a deep inspiratory effort.

- The patient must perform three blows at each testing point.
  - Take the highest value as the true value.
- » The PEFR can be helpful in confirming a diagnosis of asthma in primary care.
- An improvement of 60 L/min or  $\geq 20\%$  of the pre-bronchodilator PEFR, 10 to 20 minutes after inhalation of a beta<sub>2</sub>-agonist e.g. salbutamol, inhalation, 200 mcg, confirms a diagnosis of asthma.
  - A normal PEFR excludes the possibility of moderate and severe COPD.
- » PEFR may be useful in assessing response to therapy.
- Any value  $>80\%$  of the personal best before the use of a bronchodilator is regarded as confirmation of adequate control. Ensure that pre-bronchodilator values are measured at follow-up visits.

**Note:** Initiating and optimising inhalation corticosteroid therapy for step 1 to 3 asthma therapy should always be done with the use of a peak flow meter to assess asthma control and treatment response of asthma.

### Starting asthma treatment in children aged 6-11, adolescent >12 years of age and in adults

STEP 1	STEP 2	STEP 3
Initial asthma treatment in patients with symptoms less than twice a month, and with no exacerbations within the last 12 months.	Asthma symptoms or need for reliever twice a month or more or any exacerbations within the last 12 months.	Troublesome asthma symptoms most days, or waking up from asthma once a week or more.

**Figure 17.1** Guidance for assessing asthma treatment in children and adolescents (adapted from the GINA 2023)

LoE:IIb<sup>21</sup>

### GENERAL MEASURES

- » Avoid irritant triggers and relevant allergic triggers.
- » Advise patient to stop smoking, and to avoid smoke exposure from others.
- » Avoid exposure to known allergens if avoidance measures are feasible and sensitisation has been proven.
- » Educate patient and caregiver on:
  - early recognition and management of acute attacks,
  - emphasise the diagnosis and explain the nature and natural course of the condition,
  - use a spacer for all children and all adults with step 3 therapy and above,
  - teach and monitor inhaler technique, and
  - reassure parents and patients of the safety and efficacy of continuous regular controller therapy.

## MEDICINE TREATMENT

Medicine treatment is based on severity and control of the asthma and consists of therapy to prevent the inflammation leading to bronchospasm (controller) and to relieve bronchospasm (reliever).

### Reliever medicines in asthma:

- Short acting beta<sub>2</sub>-agonists (SABAs), e.g.:
- Salbutamol:
  - Indicated for the immediate relief of the symptoms of acute attacks, i.e. cough, wheeze and shortness of breath.
  - Can be used as needed.
  - Increasing need for reliever medicine indicates poor asthma control.

### Controller medicines in asthma:

- Inhaled corticosteroids, e.g.:
- Beclomethasone.
  - Must be used twice daily every day, even when the patient feels well.

### Inhalation therapy:

Inhaled therapy is preferable to oral therapy.

See Appendix II: Devices for Respiratory Conditions for guidance on inhaler and spacer device techniques

## STEP 1

Adults and children >6 years

As reliever/rescue therapy:

LoE:IIb<sup>22</sup>

- Short acting beta<sub>2</sub>-agonists, e.g.:
- Salbutamol, MDI, 200 mcg, as needed.

**AND**

- Inhaled corticosteroids, e.g.:
- Budesonide, inhalation, 200 mcg whenever salbutamol is taken.

**Note:** Beclomethasone is the preferred ICS in patients on protease inhibitors due to drug interactions between protease inhibitors and budesonide:

- Beclomethasone, inhalation, 200 mcg whenever salbutamol taken.

## STEP 2

Children <6yrs (wheeze ≥3 times a year):

- Inhaled corticosteroids e.g.:
- Beclomethasone, inhalation, 100 mcg 12 hourly.

**AND**

- Short acting beta<sub>2</sub>-agonists agonist e.g.:
- Salbutamol, inhalation, 100 to 200 mcg (1 to 2 puffs), 6 to 8 hourly as needed (until symptoms are controlled).

**Adults and children ≥ 6yrs****As controller therapy:**

- Inhaled corticosteroids, low dose, e.g.:
- Budesonide, inhalation, 200 mcg 12 hourly.
  - Well and stable after 6 months: can attempt to reduce budesonide dose to 200 mcg daily.
  - Dose adjustments may be required at change of seasons.

LoE:IIIB<sup>23</sup>

**Note:** Beclomethasone is the preferred ICS in patients on protease inhibitors due to drug interactions between protease inhibitors and budesonide.

- Beclomethasone, inhalation, 200 mcg 12 hourly for 6 months; reduced to 200 mcg daily once well and stable.

**AND****As reliever/rescue therapy:**

- Short acting beta<sub>2</sub>-agonists, e.g.:
- Salbutamol, MDI, 200 mcg, 6 hourly as necessary.

Review treatment every 3 months. Adequate control is defined as:

- » ≤ 2 episodes of daytime cough and/or wheeze per week.
- » No night-time cough and/or wheeze.
- » No recent (within the last year) admission to hospital for asthma.
- » PEFR ≥ 80% predicted between attacks.

LoE:IIIB<sup>24</sup>

**If control is inadequate:**

- » Check adherence and inhaler technique, and
- » Exclude ongoing exposure to irritants and allergens.

After excluding those causes, refer to a doctor to confirm the diagnosis of asthma, to exclude other diagnoses.

Once the diagnosis is confirmed, **step-up** treatment to STEP 3 as below:

## **STEP 3**

**Children**

- Inhaled corticosteroids, e.g.:
- Beclomethasone, inhalation, 200 mcg 12 hourly.

**Adults**

- Inhaled corticosteroids, e.g.:
- Budesonide, inhalation, 400 mcg 12 hourly

**Note:** Beclomethasone is the preferred ICS in patients on protease inhibitors due to drug interactions between protease inhibitors and budesonide:

- Beclomethasone, inhalation, 400 mcg 12 hourly.

**If control is still inadequate in adults, re-evaluate inhaler technique (See Appendix II: Devices for Respiratory Conditions for guidance on inhaler and spacer device techniques) and consider treatment with combination of corticosteroid and long-acting beta agonist (LABA):**

Stop corticosteroid inhaler (e.g. budesonide) and replace controller therapy with:

- Inhaled long-acting beta agonist (LABA)/corticosteroid combination, e.g.:
- Salmeterol/fluticasone, inhalation, 50/250 mcg (1 puff) 12 hourly.  
(Doctor initiated.)

LoE:IVb<sup>25</sup>

## AND

As reliever/rescue therapy:

- Short acting beta<sub>2</sub>-agonists, e.g.:
- Salbutamol, MDI, 200 mcg, 6 hourly as necessary.

**Note:** Fluticasone interacts with protease inhibitors. Refer all patients on protease inhibitors requiring inhaled fluticasone for further management.

LoE:IIIb<sup>26</sup>

## Stepping down treatment:

Attempt a reduction in therapy if the patient has not had any acute exacerbation of asthma in the preceding 6 months, and day-time and night-time symptoms are well controlled.

Gradually reduce the dose of inhaled corticosteroid therapy.

If the symptoms are seasonal, corticosteroids may be stopped until the next season.

If symptoms re-appear, increase therapy to the level at which the patient was previously controlled.

## REFERRAL TO DOCTOR

- » All children <6 years of age for assessment and confirmation of diagnosis.
- » Any patient who has received >2 courses of oral prednisone within 6 months.
- » Brittle asthma (very sudden, very severe attacks).
- » All patients without adequate control on step 2 or 3 of treatment.
- » Patients on protease inhibitors, requiring inhaled fluticasone.

## REFERRAL TO HOSPITAL

Uncontrolled asthma.

**Note:** In patients with new onset of exercise-related symptoms, consider other diagnoses, particularly if no response to pre-treatment with SABA is noted.

## 17.1.4 ACUTE BRONCHIOLITIS IN CHILDREN

J20.0-9/J21.0-1/J21.8-9

### DESCRIPTION

Acute bronchiolitis is a common cause of wheezing and cough in the first two years of life. It is caused by viral infections and presents with lower airway obstruction due to inflammation and plugging of the small airways. Recurrent episodes can occur, usually during winter.

It can be difficult to distinguish between bronchiolitis and asthma. Bronchiolitis does not respond to salbutamol. If there is a good response to a single dose of salbutamol, asthma is the likely diagnosis. See Section 17.1.2: Acute asthma, children.

Bronchiolitis is extremely rare in children >2 years of age. Consider other causes of wheeze in children >2 years of age. See Section 17.1.2: Acute asthma, children; and Section 17.3.4.1: Pneumonia in children.

### Child presents with:

- » rapid breathing
- » decreased breath sounds

- » chest indrawing » an audible wheeze or crackles

**Risk factors for severe bronchiolitis:**

- |                            |                            |
|----------------------------|----------------------------|
| » Infants <3 months of age | » Ex-premature babies      |
| » Chronic lung disease     | » Congenital heart disease |

**Signs of severe disease:**

- » Increased respiratory effort: tachypnoea, nasal flaring, severe lower chest wall indrawing, accessory muscle use, grunting.
- » Central cyanosis or hypoxia (oxygen saturation <90% in room air).
- » Apnoea.
- » Inability to feed.
- » Lethargy or decreased level of consciousness.

**DIAGNOSTIC CRITERIA**

- » Prodrome of viral infection: irritability and rhinorrhoea.
- » A wheeze that is slowly responsive or non-responsive to bronchodilators.
- » Tachypnoea: age dependent:

Age	Respiratory rate
Birth to 2 months	≥60 breaths/minute
2 to 12 months	≥50 breaths/minute
1 to 5 years	≥40 breaths/minute

**GENERAL MEASURES**

- » Minimise contact with other children.
- » Avoid routine use of antibiotics and corticosteroids.
- » Do not sedate child.

**MEDICINE TREATMENT**

Mild cases, without risk factors may be managed as an outpatient.

**Refer severe bronchiolitis or those with risk factors:**

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

**REFERRAL**

- » Signs of severe bronchiolitis (respiratory distress, hypoxia, apnoea, inability to feed, lethargy/decreased level of consciousness).
- » Bronchiolitis with risk factors for severe disease.
- » Previous admission for same problem.

## 17.1.5 CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

J43.0-2/J43.8-9/J44.0-1/J44.8-9

### DESCRIPTION

Also referred to as chronic obstructive airways disease (COAD), and comprises chronic bronchitis and emphysema which are characterised by:

- » chronic cough with/without sputum production on most days of  $\geq 3$  months for  $\geq 2$  consecutive years;
- » dyspnoea or shortness of breath; and
- » wheezing.

The onset is very gradual with progressively worsening symptoms. Due to the large reserve capacity of the lungs, patients often present when there is considerable permanent damage to the lungs. In addition to the symptoms listed above, patients may present with symptoms or signs of right heart failure. The airways obstruction is not fully reversible (in contrast to asthma).

The main causes of COPD are chronic irritation of the airways caused by smoking, air pollution, previous TB, and previous cannabis (dagga) smoking, although there are many other causes.

If symptoms suggest TB (e.g. weight loss, night sweats, etc.), investigate and manage accordingly. (See Section 17.4: Pulmonary Tuberculosis (TB).)

### GENERAL MEASURES

- » Smoking cessation, including cannabis (dagga), is the mainstay of therapy.
- » Chest physiotherapy where available.
- » Exercise.

### MEDICINE TREATMENT

See Appendix II: Devices for Respiratory Conditions for guidance on inhaler, spacer and nebuliser device techniques.

#### Acute lower airways obstruction:

Treat as for acute asthma but in addition, add antibiotics if patients have increased sputum purulence AND either increased sputum volume or increased dyspnoea.

- Amoxicillin, oral, 500 mg 8 hourly for 5 days. A

LoE:IIb<sup>27</sup>

#### Severe penicillin allergy:

Z88.0

Azithromycin, oral, 500 mg daily for 3 days. W

#### Chronic management:

- » In a stable patient, check PEFR.
- » Then give a test dose of salbutamol, i.e. 2 puffs.
- » Repeat PEFR 15 minutes later.
- » If there is  $\geq 20\%$  improvement in peak flow, diagnose asthma and manage patient accordingly. See Section 17.1.3: Chronic asthma.
- » Perform spirometry if available. Diagnose COPD if post-bronchodilator FEV<sub>1</sub>/FVC <70%.
- Short acting beta<sub>2</sub> agonist, e.g.:

- Salbutamol, inhalation, 100 to 200 mcg (1 to 2 puffs), 3 to 4 times daily via a spacer 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 beta<sub>2</sub> agonist (LABA), e.g.:
- Formoterol, inhaled 12 mcg (1 puff) 12 hourly. (Doctor initiated.)

LoE:IVb<sup>28</sup>

**If not controlled on SABA alone and spirometry not available:**

- Inhaled LABA/corticosteroid combination e.g.:
- Salmeterol/fluticasone, inhalation, 50/250 mcg (1 puff) 12 hourly. (Doctor initiated.)

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

Measure blood eosinophil levels.

If eosinophils  $>0.1 \times 10^9$  cells/L, replace with:

- Inhaled LABA/corticosteroid combination e.g.:
- Salmeterol/fluticasone, inhalation, 50/250 mcg (1 puff) 12 hourly. (Doctor initiated.)

LoE:IVb<sup>29</sup>

#### Note:

- » Fluticasone and budesonide interact with protease inhibitors. Refer all patients on protease inhibitors requiring inhaled corticosteroids for further management.
- » Oral corticosteroids may be required for acute exacerbations, but these have severe long-term complications and should only be used long-term if advised by a specialist.
- » Do not measure blood eosinophil levels while taking oral corticosteroids, as this may temporarily lower the eosinophil count.

LoE:IIIb<sup>30</sup>

#### Prophylaxis against respiratory tract infections:

Z25.1

- Influenza vaccination, annually.

#### REFERRAL

- » Poor response to above therapy, for further investigations and adjustment of treatment.
- » Patients on protease inhibitors, requiring inhaled corticosteroids.

## 17.2 STRIDOR (UPPER AIRWAYS OBSTRUCTION)

### 17.2.1 CROUP (LARYNGOTRACHEO BRONCHITIS) IN CHILDREN

J05.0-1

#### DESCRIPTION

Croup is a common cause of potentially life-threatening airway obstruction in childhood. It is characterised by inflammation of the larynx, trachea and bronchi. Most common causative pathogens are viruses, including measles.

A clinical diagnosis of viral croup can be made if a previously healthy child develops progressive, inspiratory airway obstruction with stridor and a barking cough, 1 to 2 days after the onset of an upper respiratory tract infection. A mild fever may be present. Suspect foreign body aspiration if there is a sudden onset of stridor in an otherwise healthy child.

Suspect epiglottitis if the following are present in addition to stridor:

- » very ill child
  - » high fever
  - » sitting upright with head held erect
  - » drooling saliva
  - » unable to swallow

## **Assessment of the severity of airway obstruction and management in croup**

<b>Grade 1</b> Inspiratory stridor only	<ul style="list-style-type: none"> <li>▪ Corticosteroids (intermediate-acting) e.g.:</li> <li>▪ Prednisone, oral, 1 to 2 mg/kg, single dose.           <ul style="list-style-type: none"> <li>○ Do not give if measles or herpes infection present.</li> </ul> </li> <li>» Refer.</li> </ul>
<b>Grade 2</b> Inspiratory and expiratory stridor	<ul style="list-style-type: none"> <li>▪ Corticosteroids (intermediate-acting) e.g.:</li> <li>▪ Prednisone, oral, 1 to 2 mg/kg, immediately as a single dose.</li> <li>▪ Adrenaline (epinephrine), 1:1000 diluted in sodium chloride 0.9%, nebulised, immediately.           <ul style="list-style-type: none"> <li>○ Dilute 1 mL of 1:1000 adrenaline with 1 mL sodium chloride 0.9%.</li> <li>○ Repeat every 15 to 30 minutes until expiratory stridor disappears.</li> </ul> </li> <li>» Refer.</li> </ul>
<b>Grade 3</b> Inspiratory and expiratory stridor with active expiration, using abdominal muscles	<ul style="list-style-type: none"> <li>» Treat as above.</li> <li>» If no improvement within one hour, refer <b>urgently</b> (intubate before referral if possible).</li> </ul>
<b>Grade 4</b> Cyanosis, apathy, marked retractions, impending apnoea	<ul style="list-style-type: none"> <li>» Intubate (if not possible give treatment as above).</li> <li>» Refer <b>urgently</b>.</li> </ul>

## GENERAL MEASURES

- » Keep child comfortable.
  - » Continue oral fluids provided that patient is able to swallow.
  - » Encourage parent or caregiver to remain with the child.

## MEDICINE TREATMENT

- Paracetamol, oral, 10 to 15 mg/kg/dose 6 hourly when required. See dosing table: Chapter 23.

**Children grade 2 or more stridor- while awaiting transfer:**

- Corticosteroids (intermediate-acting) e.g.:
    - Prednisone, oral, 1 to 2 mg/kg immediately as a single dose.
    - Adrenaline (epinephrine), 1:1000, nebulised, immediately using a nebuliser.
      - If there is no improvement, repeat every 15 minutes until the child is transferred.
      - Dilute 2 mL of 1:1000 adrenaline with 2 mL sodium chloride 0.9%.
      - Nebulise the entire volume with oxygen at a flow rate of 6 to 8 L/minute.

**Weight-based prednisone dosing for children <18 kg:**

Weight (kg)	Dose (mg)	Tablet (5 mg)	Age (years)
>11–14 kg	20 mg	4 tablets	>2–3 years
>14–17.5 kg	30 mg	6 tablets	>3–5 years

If epiglottitis suspected:

- Ceftriaxone, IM, 80 mg/kg/dose immediately as a single dose and refer.  See dosing table: Chapter 23.
  - Do not inject more than 1 g at one injection site.

**CAUTION: USE OF CEFTRIAXONE IN NEONATES AND CHILDREN**

- » If SUSPECTING SERIOUS BACTERIAL INFECTION in neonate, give ceftriaxone, even if jaundiced.
- » Always include the dose and route of administration of ceftriaxone in the referral letter.

Management during transfer:

- » Give the child oxygen to keep oxygen saturation levels at 93 to 95%.
- » Continue nebulisations with adrenaline (epinephrine).
- » If grade 2 to 3, contact ambulance or nearest doctor.
- » If grade 4, intubate and transfer.

**REFERRAL****Urgent**

- » Children with:
  - Grade 2-4 stridor,
  - chest indrawing,
  - rapid breathing,
  - altered consciousness,
  - inability to drink or feed.
- » For confirmation of diagnosis.
- » Suspected foreign body.
- » Suspected epiglottitis.

**Non Urgent**

- » All children with grade 1 stridor.

**17.3 RESPIRATORY INFECTIONS****17.3.1 INFLUENZA**

J09/J10.0-1/J10.8/J11.0-1/J11.8

**DESCRIPTION**

Influenza is a self-limiting viral condition that presents with headache, muscular pain and fever. It usually begins to clear within 7 days but may last up to 14 days. Malnourished children, the elderly and debilitated patients are at greater risk of developing complications.

**CAUTION**

Malaria, measles, and HIV seroconversion may present with flu-like symptoms.

**Complications:**

Secondary bacterial infections, including:

- » pneumonia secondary to influenza
- » sinusitis
- » otitis media

**GENERAL MEASURES**

- » Bed rest, if feverish.
- » Ensure adequate hydration.
- » Advise patient to return to clinic if earache, tenderness or pain over sinuses develops and/or cough or fever persists for longer than a week.

**MEDICINE TREATMENT**

**Note:** Antibiotics are of no value in the treatment of influenza.

Infants

- Sodium chloride 0.9%, instilled into each nostril as required.

**Pain and fever with distress:**Children

- Paracetamol, oral, 10 to 15 mg/kg/dose 4 to 6 hourly when required. See dosing table: Chapter 23.

Adults

- Paracetamol, oral, 500 mg to 1 g, 4 to 6 hourly as required (to a maximum of 4 g in 24 hours).
  - Maximum dose: 15 mg/kg/dose.

**17.1.4 REFERRAL**

Severe complications.

**17.3.2 ACUTE BRONCHITIS IN ADULTS OR ADOLESCENTS**

J20.0-9

**DESCRIPTION**

Acute airway infections, mostly of viral origin, accompanied by cough, sputum production, and sometimes a burning retrosternal chest pain in patients with otherwise healthy lungs.

Clinical features:

- » initially: non-productive cough.
- » later: productive cough with yellow or greenish sputum.

Viral bronchitis is usually part of an upper respiratory viral infection. It may be accompanied by other manifestations of viral infections. It is important to exclude underlying bronchiectasis or an acute exacerbation of chronic bronchitis in adults.

Antibiotics are not indicated in acute bronchitis in the absence of underlying COPD.

### 17.3.3 ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

See Sections 17.1.1: Acute asthma and acute exacerbation of COPD, adults, and 17.1.5: Chronic Obstructive Pulmonary Disease.

### 17.3.4 PNEUMONIA

#### DESCRIPTION

Acute infection of the lung parenchyma, usually caused by bacteria, especially *Streptococcus pneumoniae* (pneumococcus).

Management is guided by:

- » age
- » co-morbidity
- » severity of the pneumonia

Manifestations include:

- » malaise;
- » fever, often with sudden onset and with rigors;
- » cough, which becomes productive of rusty brown or yellow-green sputum;
- » pleuritic type chest pain;
- » shortness of breath;
- » and in severe cases, shock and respiratory failure.

On examination there is:

- » fever
- » crackles or crepitations
- » tachypnoea
- » bronchial breath sounds

A pleural rubbing sound, or signs of a pleural effusion may be present.

Predisposing conditions include:

- » very young or old age
- » other concomitant diseases
- » malnutrition
- » HIV infection

Pneumococcal pneumonia often occurs in previously healthy adults.

Adults with mild to moderately severe pneumonia may be managed at PHC level, depending on the response to initial treatment (see below).

#### 17.3.4.1 PNEUMONIA IN CHILDREN

J18.0-2/J18.8-9

#### DESCRIPTION

Pneumonia should be distinguished from viral upper respiratory infections. With viral URTIs' the respiratory rate will be normal. A raised respiratory rate indicates an alternate diagnosis such as bronchiolitis or pneumonia.

**Assess the child for the severity of the pneumonia**

Classify children according to the severity of the illness:

- » Pneumonia: fever, cough and rapid breathing, but no chest indrawing (of the lower chest wall) and no flaring of nostrils.
- » Severe pneumonia: fever, cough, rapid breathing, chest indrawing and flaring nostrils, or grunting.

**Note:** Children <2 months of age with rapid breathing should be classified as having severe pneumonia.

Rapid breathing is defined according to age:

Age	Respiratory rate
Birth – 2 months	≥ 60 breaths/minute
2–12 months	≥ 50 breaths/minute
1–5 years	≥ 40 breaths/minute

Danger signs indicating urgent and immediate referral include:

- » oxygen saturation of <90% in room air      » cyanosis
- » inability to drink                                  » <2 months of age
- » impaired consciousness                            » grunting

**GENERAL MEASURES**

- » Ensure adequate hydration.
- » Continue feeding.

**MEDICINE TREATMENT**

Pneumonia (non-severe):

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

LoE:IVb<sup>34</sup>

Weight (kg)	Dose mg	Use one of the following:				Age (Months/years)	
		Syrup (mg/5mL)		Capsule (mg)			
		125	250	250	500		
>3.5–5 kg	175 mg	7 mL	3.5 mL	–	–	>1–3 months	
>5–7 kg	250 mg	10 mL	5 mL	–	–	>3–6 months	
>7–11 kg	375 mg	15 mL	7.5 mL	–	–	>6–18 months	
>11–14 kg	500 mg	–	10 mL	2	1	>18 months–3 years	
>14–17.5 kg	750 mg	–	15 mL	3	–	>3–5 years	
>17.5–25 kg	1000 mg	–	20 mL*	4	2	>5–7 years	
>25–30 kg	1250 mg	–	25 mL*	5	–	>7–10 years	
>30 kg	1500 mg	–	–	6	3	>10 years	

\*capsule/tablet preferred

**Severe penicillin allergy:**

Z88.0

Children

- Macrolide, e.g.:
- Azithromycin, oral, 10 mg/kg/dose daily for 3 days. W See dosing table: Chapter 23.

**Severe pneumonia:**

- Oxygen, using nasal cannula at 1–2 L/minute before and during transfer.

- Ceftriaxone, IM, 80 mg/kg/dose immediately as a single dose.  See dosing table: Chapter 23.
  - Do not inject more than 1 g per injection site.

**CAUTION: USE OF CEFTRIAXONE IN NEONATES AND CHILDREN**

- » If SUSPECTING SERIOUS BACTERIAL INFECTION in neonate, give ceftriaxone, even if jaundiced.
- » Always include the dose and route of administration of ceftriaxone in the referral letter.

## REFERRAL

### Urgent

- » All children with severe pneumonia, i.e. chest indrawing (of the lower chest wall), flaring nostrils or cyanosis.
- » All children <2 months of age.

### Non urgent

- » Inadequate response to treatment.
- » Children coughing for >3 weeks to exclude other causes such as TB, foreign body aspiration or pertussis.

## 17.3.4.2 PNEUMONIA IN ADULTS

### 17.3.4.2.1 UNCOMPLICATED PNEUMONIA

J18.0-2/J18.8-9

## DIAGNOSIS

A chest X-ray should ideally be taken in all patients to confirm the diagnosis. Send one sputum specimen for TB DNA PCR (Xpert<sup>®</sup> MTB/RIF) to exclude pulmonary tuberculosis.

## MEDICINE TREATMENT

### If not severely ill (see referral criteria below):

- Amoxicillin, oral, 1 g 8 hourly for 5 days.

### Severe Penicillin allergy:

Z88.0

- Moxifloxacin, oral, 400 mg daily for 5 days.

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

 LoE:IIIb<sup>35</sup>

## REFERRAL

Any of the following:

- » Confusion or decreased level of consciousness.
- » Cyanosis.
- » Respiratory rate of ≥30 breaths/minute.
- » Systolic BP <90 mmHg.
- » Diastolic BP <60 mmHg.
- » Deterioration at any point.
- » No response to treatment after 48 hours.
- » Patients with pneumonia:

- from a poor socio-economic background,
- who are unlikely to comply with treatment,
- who live a considerable distance from health centres,
- who have no access to immediate transport.

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

J18.0-2/J18.8-9

A chest X-ray should ideally be taken in all patients to confirm the diagnosis. Send one sputum specimen for TB DNA PCR (Xpert® MTB/RIF) to exclude pulmonary tuberculosis.

Common underlying conditions include:

- |                      |                           |
|----------------------|---------------------------|
| » Diabetes mellitus. | » Alcoholism.             |
| » HIV infection.     | » Chronic liver disease.  |
| » Cardiac failure.   | » Chronic kidney disease. |
| » COPD.              |                           |

Most of these patients will require referral to a doctor.

#### MEDICINE TREATMENT

##### Mild pneumonia:

- Amoxicillin/clavulanic acid 875/125 mg, oral, 12 hourly for 5 days. A

##### Severe Penicillin allergy:

Z88.0

- Moxifloxacin, oral, 400 mg daily for 5 days. W

LoE: IIb<sup>36</sup>

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

### 17.3.4.2.3 SEVERE PNEUMONIA

J18.0-2/J18.8-9

#### DESCRIPTION

Severe pneumonia is defined as ≥ 2 of the following:

- |   |                         |
|---|-------------------------|
| » confusion/ decreased level of consciousness | » systolic BP <90 mmHg  |
| » respiratory rate of ≥ 30 breaths/minute     | » diastolic BP <60 mmHg |
| » >65 years of age                            |                         |

#### MEDICINE TREATMENT

##### While awaiting transfer:

- Oxygen, to achieve a saturation of 92%.
- Ceftriaxone, IV/IM, 1 g, as a single dose before referral.

#### CAUTION

Do not administer calcium containing intravenous fluids, e.g.  
Ringer Lactate, concurrently with IV ceftriaxone.

**REFERRAL****Urgent**

All patients.

**17.3.4.2.4 PNEUMOCYSTIS PNEUMONIA**

B20.6

**DESCRIPTION**

Interstitial pneumonia occurring with advanced HIV infection due to *Pneumocystis jiroveci* (formerly *carinii*). Patients usually present with shortness of breath or dry cough. Chest X-ray may be normal in the early stages, but typically shows bilateral interstitial or ground glass pattern.

**GENERAL MEASURES**

Ensure adequate hydration.

**MEDICINE TREATMENT****Adults**

- Cotrimoxazole, oral, 6 hourly for 3 weeks. A

Approx. weight kg	Use one of the following tablet formulations	
	80/400 mg	160/800 mg
<40 kg	2 tablets	1 tablet
>40–56 kg	3 tablets	1½ tablets
>56 kg	4 tablets	2 tablets

**For secondary prophylaxis**

- Cotrimoxazole, oral, daily. A

Use one of the following tablet formulations	
80/400 mg	160/800 mg
2 tablets	1 tablet

**Note:** Discontinue cotrimoxazole prophylaxis once the CD4 count increases on ART to >200 cells/mm<sup>3</sup> for at least 6 months.

**REFERRAL**

- All children.
- Breathing rate >24 breaths/minute.
- Shortness of breath with mild effort.
- Cyanosed patients.

**17.4 PULMONARY TUBERCULOSIS (TB)**

Note: TB is a notifiable disease.

TB guidelines are updated regularly.

Consult the most recent National Tuberculosis Control Programme Guidelines.

**DESCRIPTION**

Tuberculosis is an infection caused by *Mycobacterium tuberculosis*. The risk of developing TB disease is higher among people living with HIV.

**17.4.1 PULMONARY TUBERCULOSIS (TB) IN ADULTS**

A15.0-3/A15.7-8/A16.0-2/A16.4/A16.7-9 + (B20.0)

**DIAGNOSIS**

Pulmonary TB is diagnosed on sputum by TB nucleic acid amplification tests (TB-NAAT) such as Xpert® MTB/RIF Ultra, sputum smear, or culture.

- » Send 1 sputum specimen for TB-NAAT.
  - If TB-NAAT is unsuccessful: collect another sample and repeat TB-NAAT.
  - If TB-NAAT is trace (only applies to Xpert® MTB/RIFUltra): If the clinical presentation and chest X-ray are suggestive of TB, treat for drug-sensitive TB (DS-TB), and collect sputum specimen for TB culture and drug sensitivity testing (DST). If the patient is asymptomatic, with no abnormalities on chest X-ray, continue routine care with close follow-up for features of TB.
  - If TB-NAAT is positive and susceptible to rifampicin: treat for DS-TB and send a sputum specimen for baseline smear microscopy (the smear is used for reporting, not for diagnosis).
  - If TB-NAAT is positive, susceptible to rifampicin and resistant to isoniazid: treat for isoniazid monoresistant TB (See Section 17.4.4.1: Isoniazid mono-resistant tuberculosis in adults). Collect sputum sample for reflex testing of fluoroquinolone susceptibility.
  - If TB-NAAT is positive and rifampicin unsuccessful: start DS-TB treatment and collect another sputum sample for smear, culture and drug sensitivity testing (DST). Follow-up culture and DST results.
  - If TB-NAAT is positive and resistant to rifampicin (with or without isoniazid resistance): treat for rifampicin resistant TB and send sputum sample for further reflex testing and DST.
  - If TB-NAAT is negative and patient is living with HIV: send sputum for TB culture and perform chest X-ray. If CD4 <200 within the last 6 months and they have signs and symptoms of TB (pulmonary or extrapulmonary), the patient has advanced HIV disease or the patient is currently seriously ill and requiring hospitalization, perform urine LAM (U-LAM) test. LoE: I<sup>87</sup>
  - If TB-NAAT is negative and patient is HIV negative: treat with antibiotics and consider further investigation only if symptoms persist.

**Note:** Patients with a history of TB can remain TB-NAAT positive for several years after completion of appropriate anti-TB treatment. To diagnose a new episode of TB in previously treated patients, send sputum for smear microscopy and culture instead.

## GENERAL MEASURES

- » Counsel patients about the disease and infection control in the home. Explain the importance of completing treatment.
- » Advise against the use of tobacco and excessive alcohol.
- » If more than two doses of treatment are missed, extra effort should be made to identify and manage any problems the patient might have.

## MEDICINE TREATMENT

Administer total daily amount of each medicine in one dose and not as divided doses.

### Important medicine interactions

Rifampicin may reduce the efficacy of low dose combined oral contraceptives and progestin-only implants, resulting in possible unplanned pregnancies. (See Chapter 7: Family planning.)

- » Use of alternative contraceptive methods, such as IUD or DMPA, should be advised.
- OR**
- » Women choosing to use a progestin-only subdermal implant should be advised to use additional contraception for the duration of TB therapy. See Section 11.1: Antiretroviral therapy, adults and adolescents.

### CAUTION

Antiretroviral medicines frequently interact with TB medicines.  
Consult the National Department of Health antiretroviral treatment guidelines.

### Dose adjustment in renal impairment (eGFR <30 mL/min).

- Ethambutol 15 – 25mg/kg three times weekly.
- Pyrazinamide 20 – 30 mg/kg three times weekly.
- Rifampicin and isoniazid do not require dose adjustment.

### Intensive phase of treatment:

- Alternate day dosing of RH and RHZE.
  - Administer standard weight-based dosing of RH on Tuesday, Thursday, Saturday, Sunday.

### AND

- Administer standard weight-based dosing with RHZE on Monday, Wednesday, Friday.

### Continuation phase of treatment:

- Rifampicin and isoniazid
  - Do not require dose adjustment. Continue daily weight-based dosing of RH.

LoE:IVb

### Adverse effects of TB medicines include:

- » Nausea:
  - Taking medicines with meals can minimise nausea.
  - Hepatitis must be excluded, if there is new onset nausea. Request serum alanine aminotransferase test urgently in these patients.
- » 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 and adolescents (Rifampicin-based TB treatment).
- » New onset skin rash:
- Refer if suspected drug rash.
- » Neuropathy:
- Can be prevented by taking pyridoxine.
- » Arthralgia:
- Exclude gout, and treat symptomatically.

#### **17.4.1.1 TB CHEMOPROPHYLAXIS/ISONIAZID PREVENTIVE THERAPY (IPT) IN ADULTS**

See Section 11.2.2: Tuberculosis preventive therapy (TPT).

#### **17.4.1.2 TB CONTROL PROGRAMME: MEDICINE REGIMENS IN ADULTS**

A15.0-3/A15.7-8/A16.0-2/ A16.4/A16.7-8 + (B20.0)

Treatment should be given once daily, **seven days per week**, in both the intensive and continuation phases.

R – Rifampicin

H – Isoniazid

Z or PZA – Pyrazinamide

E or EMB – Ethambutol

Pre-treatment body weight kg	Two months initial phase	Four months continuation phase	
	RHZE (150/75/400/275)	RH (150/75)	RH (300/150)
30–37 kg	2 tablets	2 tablets	
38–54 kg	3 tablets	3 tablets	
55–70 kg	4 tablets		2 tablets
≥71kg	5 tablets		2 tablets

» Adhere to the correct dose and the duration of treatment.

» Weigh patient frequently and adjust the dose according to current weight.

#### **17.4.2 PULMONARY TUBERCULOSIS (TB) IN CHILDREN**

A15.0-3/A15.7-8/A16.0-2/A16.4/A16.7-8 + B20.0

Most children acquire tuberculosis from infected adults by inhalation. Malnourished, immunosuppressed (HIV and AIDS) children, and children <5 years of age, are at increased risk for pulmonary tuberculosis.

## DIAGNOSIS

Any child presenting with symptoms and signs suggestive of pulmonary TB is regarded as a case of TB if there is:

- » A chest X-ray suggestive of TB,

### AND/OR

- » History of exposure to an infectious TB case and/or positive tuberculin skin test (TST) e.g. Mantoux.

A positive TB-NAAT and/or smear microscopy and/or culture, on early morning gastric aspirate or induced sputum, confirms TB disease.

### Signs and symptoms include:

- » unexplained weight loss or failure to thrive,
- » unexplained fever for  $\geq 2$  weeks,
- » chronic unremitting cough for  $>14$  days,
- » lymphadenopathy (especially cervical, often matted),
- » hepatosplenomegaly,
- » consolidation and pleural effusion.

### Tuberculin skin test (TST), e.g. Mantoux:

- » A positive test: TST induration  $\geq 10$  mm.
- » A TST may be falsely negative in the presence of:
  - malnutrition,
  - immunodeficiency, e.g. HIV and AIDS,
  - immunosuppression, e.g. steroid therapy, cancer chemotherapy,
  - following overwhelming viral infection, e.g. measles or post vaccination.

In these circumstances a TST induration  $\geq 5$  mm may be regarded as positive.

Frequently, the TST will be non-reactive in these cases. TB treatment should be considered, despite a negative TST.

### The following may be evident on chest X-ray:

- » Direct or indirect evidence of hilar or mediastinal adenopathy, with or without parenchymal opacification, and/or bronchopneumonia.

## GENERAL MEASURES

- » Identify and treat the source case.
- » Screen all contacts for TB infection.
- » Monitor the nutritional status of the child to assess response to treatment.

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

Z20.1

Consider TB chemoprophylaxis/isoniazid preventive therapy (IPT) in all children younger than 5 years, or who are living with HIV, and exposed to a pulmonary TB contact.

### Exclude active TB (i.e. no signs or symptoms suggestive of TB):

- » Refer to Section 17.4.2: Pulmonary tuberculosis (TB) in children.
- » If any signs or symptoms of pulmonary TB are present, refer for chest X-ray.

- » Never give TPT to children with active TB.

TB chemoprophylaxis/ IPT is only used in:

- » Children <5 years of age.

**OR**

- » Children of any age, who are living with HIV.

**WITH EITHER**

- Close contact with an infectious pulmonary TB case. If child is re-exposed to a close contact, TB chemoprophylaxis must be repeated (Previous IPT does not protect the child against subsequent TB exposure/ infection).
- Positive TST (only applicable on the first occasion of a positive TST).

## MEDICINE TREATMENT

### Preventive therapy in case of drug-sensitive TB contact:

- Isoniazid, oral, 10 mg/kg daily for 6 months.
  - Maximum dose: 300 mg daily.

Weight kg	Daily isoniazid (INH) 100 mg tablet
>2–3.4 kg	¼ tablet
>3.5–6.9 kg	½ tablet
>7–9.9 kg	1 tablet
>10–14.9 kg	1½ tablets
>15–19.9 kg	2 tablets
>20–24.9 kg	2½ tablets
>25 kg	3 tablets

**Note:** For adults and adolescents initiating a DTG-containing ART regimen, isoniazid daily for 12 months is the preferred regimen. For patients who are already virally suppressed on a DTG-based regimen, a weekly combination of isoniazid (900mg if weight >30 kg) plus rifapentine (900mg if weight >30 kg) for three months may be preferred. Do not use rifapentine-containing TPT in patients on protease inhibitor-based ART, or in women on hormonal contraceptives. [See the therapeutic interchange database for details regarding the rifapentine-containing TPT regimen].

LoE:IIb<sup>38</sup>

### Preventive therapy in case of drug-resistant TB contact:

Isoniazid mono-resistant contact:

- Rifampicin, oral, 15 mg/kg daily for 4 months.

Rifampicin mono-resistant contact:

LoE:IVb<sup>39</sup>

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

LoE:IVb<sup>40</sup>

Children living with HIV or malnutrition or existing neuropathy taking isoniazid:

**ADD**

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

LoE:IVb<sup>41</sup>

**REFERRAL**

Children with drug resistant TB contacts for expert advice.

### **17.4.2.2 TB CONTROL PROGRAMME: MEDICINE REGIMENS IN CHILDREN**

A15.0-3/A15.7-8/A16.0-2/ A16.4/A16.7-8 + (B20.0)

The employment of directly observed therapy (DOT) with short-course, fixed medicine combinations are recommended. Treatment should be given daily in both the intensive (initial) and continuation phases.

Recommended dose ranges		
	Daily (mg/kg)	Maximum daily dose
H	10–15	300 mg
R	10–20	600 mg
Z/ PZA	30–40	2 g
E/EMB	15–25	1 200 mg

### **UNCOMPLICATED PULMONARY TB**

Includes smear negative pulmonary TB with no more than mild to moderate lymph node enlargement and/or lung field opacification, or simple pleural effusion on chest x-ray.

Children ≤ 8 years of age or <25 kg):

Weight (kg)	2 months intensive phase given daily			4 months continuation phase given daily
	RH	PZA		RH
	60/60 mg	150 mg* OR 150 mg/3 mL	500 mg	60/60 mg
2–2.9 kg	½ tablet	1.5 mL	expert advice on dose	½ tablet
3–3.9 kg	¾ tablet	2.5 mL	¼ tablet	¾ tablet
4–5.9 kg	1 tablet	3 mL	¼ tablet	1 tablet
6–7.9 kg	1½ tablets		½ tablet	1½ tablets
8–11.9 kg	2 tablets		½ tablet	2 tablets
12–14.9 kg	3 tablets		1 tablet	3 tablets
15–19.9 kg	3½ tablets		1 tablet	3½ tablets
20–24.9 kg	4½ tablets		1½ tablet	4½ tablets
25–29.9 kg	5 tablets		2 tablets	5 tablets

\* For each dose, dissolve 150 mg dispersible (1 tablet) in 3 mL of water to prepare a concentration of 50 mg/mL (150 mg/3 mL).

Note: Give PZA 150 mg or 500 mg, and not both.

LoE:IVb<sup>42</sup>

**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	

**ADD**

- Pyridoxine, oral, daily for 6 months if living with HIV, malnourished, or has existing neuropathy:
  - Child <5 years old: 12.5 mg.
  - Child ≥5 years old: 25 mg.

LoE:IVb<sup>43</sup>Children ≥ 8 years and adolescents (and ≥25 kg)

Pre-treatment body weight kg	2 months intensive phase given daily	4 months continuation phase given daily	
	RHZE (150/75/400/275)	RH (150/75)	RH (300/150)
25–37.9 kg	2 tablets	2 tablets	
38–54.9 kg	3 tablets	3 tablets	
55–70 kg	4 tablets		2 tablets
>71 kg	5 tablets		2 tablets

**AND**If living with HIV, malnourished or has existing neuropathy:

- Pyridoxine, oral, daily for 6 months.
  - Child ≥ 5 years old: 25 mg.
- » Adjust treatment dosages to current body weight.
- » If calculating dosages, rather give ½ tablet more than ½ tablet less.

LoE:IVb<sup>44</sup>**COMPLICATED PULMONARY TB**

- » Includes all other forms of pulmonary TB, such as smear positive TB, cavitating pulmonary TB, bronchopneumonic TB, large lesion pulmonary TB, and tuberculous empyema.
- » Refer all cases of miliary TB for exclusion of TB meningitis.

Children ≤8 years of age (or <25 kg):

- » Intensive phase: Standard dose 4-drug therapy daily (RHZE) for 2 months.

**THEN**

- » Continuation phase: Standard dose 2-drug therapy daily for 4 to 7 months.

Weight kg	Intensive phase: 2 months			Continuation phase: 4–7 months***	
	RH	PZA	EMB	RH	
	60/60	150 mg* <b>OR</b> 150 mg/3 mL	500 mg	400 mg tablet <b>OR</b> 400 mg/8 mL** solution	60/60

2–2.9 kg	$\frac{1}{2}$ tablet	1.5 mL	Expert advice on dose	1 mL	$\frac{1}{2}$ tablet
3–3.9 kg	$\frac{3}{4}$ tablet	2.5 mL	$\frac{1}{4}$ tablet	1.5 mL	$\frac{3}{4}$ tablet
4–5.9 kg	1 tablet	3 mL	$\frac{1}{4}$ tablet	2 mL	1 tablet
6–7.9 kg	$1\frac{1}{2}$ tablet		$\frac{1}{2}$ tablet	3 mL	$1\frac{1}{2}$ tablets
8–11.9 kg	2 tablets		$\frac{1}{2}$ tablet	$\frac{1}{2}$ tablet	2 tablets
12–14.9 kg	3 tablets		1 tablet	$\frac{3}{4}$ tablet	3 tablets
15–19.9 kg	3 $\frac{1}{2}$ tablets		1 tablet	1 tablet	3 $\frac{1}{2}$ tablets
20–24.9 kg	4 $\frac{1}{2}$ tablets		$1\frac{1}{2}$ tablet	1 tablet	4 $\frac{1}{2}$ tablets
25–29.9 kg	5 tablets		2 tablets	$1\frac{1}{2}$ tablets	5 tablets

\* PZA: For each dose, dissolve 150 mg dispersible (1 tablet) in 3 mL of water to prepare a concentration of 50 mg/mL (150 mg/3mL).  
\*\* EMB: For each dose, crush 400 mg (1 tablet) to a fine powder and dissolve in 8 mL of water to prepare a concentration of 400mg/8mL. Discard unused solution.  
**Note:** Give PZA 150 mg or 500 mg, and not both.  
\*\*\* Continuation phase may be prolonged to 7 months in slow responders and children with HIV.

**AND**

If living with HIV, malnourished or has existing neuropathy:

- Pyridoxine, oral, daily for 6–9 months.
  - Child <5 years old: 12.5 mg.
  - Child ≥5 years old: 25 mg.

LoE:IVb<sup>45</sup>

#### Children ≥ 8 years and adolescents (and >25 kg)

Weight kg	2 months intensive phase given daily	4 months continuation phase given daily	
	RHZE (150/75/400/275) mg	RH (150/75) mg	RH (300/150) mg
25–37.9 kg	2 tablets	2 tablets	
38–54.9 kg	3 tablets	3 tablets	
55–70 kg	4 tablets		2 tablets
>71 kg	5 tablets		2 tablets

**AND**

If living with HIV, malnourished, or has existing neuropathy:

- Pyridoxine, oral, daily for 6 to 9 months.
  - Child ≥5 years old: 25 mg.
- » Weigh at each visit and adjust treatment dosages to body weight. If calculating dosages, rather give  $\frac{1}{2}$  tablet more than  $\frac{1}{2}$  tablet less.
- » Ensure that the correct dose and duration of treatment are adhered to.

LoE:IVb<sup>46</sup>**REFERRAL**

Disseminated forms of TB.

All patients who cannot be managed on an ambulatory basis.

Children <12 years of age for a chest X-ray for diagnostic purposes.

Children with previously treated TB requiring re-treatment.

Children who are contacts of patients with drug resistant TB.

### 17.4.3 TB, HIV AND AIDS

B20.0

People living with HIV (PLHIV) with suspected TB should have one negative sputum TB-NAAT test or two negative sputum smears, before sputum is sent for culture.

Advise PLHIV to present to a clinic if they develop common TB symptoms:

- » active cough (any duration)
- » night sweats
- » fever
- » loss of weight

PLHIV with concomitant TB should be treated according to the standard TB treatment protocol.

Medicine interactions may occur with ART. (See Sections 11.1: Antiretroviral therapy, adults and adolescents; 11.8: Opportunistic infections, treatment in children.)

### 17.4.4 DRUG-RESISTANT TUBERCULOSIS (MDR TB)

Drug-resistant TB (DR-TB) guidelines are updated regularly.  
Consult the most recent National DR-TB Programme Guidelines.

#### DESCRIPTION

Isoniazid monoresistant TB is TB disease caused by *M. tuberculosis* that is resistant to isoniazid, but susceptible to rifampicin.

Rifampicin resistant tuberculosis (RR-TB) is TB disease caused by *M. tuberculosis* that is resistant to rifampicin, with or without resistance to other anti-TB drugs.

Pre-XDR TB is TB disease caused by a strain of *M. tuberculosis* that is resistant to rifampicin and at least one fluoroquinolone (either levofloxacin or moxifloxacin).

Extensively drug-resistant TB (XDR-TB) is TB disease caused by a strain of *M. tuberculosis* that is resistant to rifampicin AND at least one fluoroquinolone (levofloxacin or moxifloxacin) AND either bedaquiline or linezolid. LoE:IVb<sup>47</sup>

#### 17.4.4.1 ISONIAZID MONO-RESISTANT TUBERCULOSIS IN ADULTS

A15.0-3/A15.7-8/A16.0-2/A16.4/A16.7-9 + (U50.00-01+U50.10-11) + (B20.0)

#### MEDICINE TREATMENT

Confirmed isoniazid mono-resistant TB:

- RHZE at standard doses. (See Section 17.4.1: Pulmonary Tuberculosis (TB) in adults.)

#### AND

- Levofloxacin, oral, daily
  - 30–45 kg: 750 mg.
  - ≥46 kg: 1 000 mg.

Confirmed isoniazid monoresistant TB AND contraindication to isoniazid:

- 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 to 45 kg: 750 mg
- >46 kg: 1 000 mg

LoE:IIb<sup>48</sup>

Treatment should be given for at least 6 months.

## REFERRAL

All drug resistant TB patients to medical officer at primary care level for initiation of therapy.

### 17.4.4.2 RIFAMPICIN-RESISTANT TUBERCULOSIS (RR TB), IN ADULTS

A15.0-3/A15.7-8/A16.0-2/A16.7-8 + (U50.00-01+U50.20-21) + (B20.0)

**Never treat for drug resistant TB without laboratory confirmation, either by molecular or phenotypic (culture and sensitivity) results.**

## GENERAL MEASURES

Counsel and educate patients about the disease and its treatment, including treatment duration.

Screen all close contacts for signs and symptoms of drug-resistant TB and by sputum sampling to detect early disease.

Infection control and cough etiquette is important to limit spread.

## MEDICINE TREATMENT

### Drug resistant TB prophylaxis

The effectiveness of preventive therapy in adults exposed to drug resistant TB bacteria is not currently known. Consult a specialist for management.

### RR-TB and Pre-XDR TB treatment

Consult the most recent national drug resistant TB programme guidelines.  
Treatment for 6–18 months is required.

Management of drug resistant TB should be conducted in dedicated drug resistant TB clinics and hospitals with appropriate infection control measures.

### XDR-TB treatment

Patients with XDR-TB should be discussed with the National Clinical Advisory Committee (NCAC - [NCAC@witshealth.co.za](mailto:NCAC@witshealth.co.za)) and referred to a TB hospital for an individualised regimen of at least 4 effective medicines, based on susceptibility tests

and treatment history. Infection control to prevent airborne transmission is essential to prevent nosocomial transmission.

## REFERRAL

All drug resistant TB patients to medical officer at primary care level for initiation of therapy.

### 17.4.4.3 RIFAMPICIN-RESISTANT (RR), PRE-XDR AND XDR TUBERCULOSIS, IN CHILDREN

A15.0-3/A15.7-8/A16.0-2/A16.7-8 + (U50.00-01+U50.20-21) + (B20.0)

**Never treat for drug resistant TB without laboratory confirmation, either by molecular or phenotypic (culture and sensitivity) results.**

**All cases should be discussed with a designated specialist drug resistant TB centre.**

## GENERAL MEASURES

Suspect drug-resistant TB when any of the features listed below is present:

- » A known source case (or contact) with drug resistant TB or high-risk source case, e.g. on TB therapy who was recently released from prison.
- » A patient with confirmed treatment adherence that remains smear positive after 2 months of 1<sup>st</sup> line TB treatment.
- » Any severely ill child with TB who failed to improve, or got worse on TB treatment.
- » Patients who defaulted TB treatment (>2 months).
- » History of treatment interruption (<1 month) or relapse at some point during their TB therapy.
- » With recurrent TB disease after completion of TB treatment (re-treatment case).

Management of drug resistant TB should be conducted in dedicated drug resistant TB clinics and hospitals with appropriate infection control measures. Initiate treatment in consultation with a designated expert. An uninterrupted medicine supply, direct supervision with proper education and counselling is necessary.

## REFERRAL

All children with suspected drug resistant TB to a medical officer at primary care level for initiation of therapy.