



EVIDENCE-BASED

## Comprehensive Guidelines for Management of COVID-19 in **CHILDREN** (below 18 years)

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## Asymptomatic

- Suspected contact [RAT or RTPCR negative or not available]
- Incidentally detected [RAT or RTPCR positive]
- Take 6 min walk test in children above 12 years under supervision of parents/guardian; See **6-minute walk test – at a glance**

### Home isolation (tele consultation SOS)

### Mainstay of Treatment

- Infants and younger children to stay under immediate care of parents/guardians
- No specific medication required for COVID-19 infection
- Continue medications for other conditions, if any
- Promote COVID appropriate behaviour (mask, strict hand hygiene, physical distancing); please see **Children and masks guide**
- Fluids and feeds: ensure oral fluids to maintain hydration and give a nutritious diet
- Advise older children and family to stay connected and engage in positive talks through phone, video-calls, etc.
- Parent/caregivers to contact the doctor in case of deterioration of symptoms

### Investigations

- No investigations are needed

## Mild

- Sore throat or rhinorrhoea
- Cough with no breathing difficulty
- SPO<sub>2</sub> ≥ 94% on room air
- Take 6 min walk test in children above 12 years under supervision of parents/guardian; please see **6-minute walk test – at a glance**
- For other symptoms, see **COVID-19 symptoms – at a glance**

### Home isolation (tele consultation SOS)

### Mainstay of Treatment

- Promote COVID appropriate behaviour (mask, strict hand hygiene, physical distancing); please see **Children and masks guide**
- For fever, give paracetamol 10-15mg/kg/dose; may repeat every 4-6 hours
- For cough: throat soothing agents and warm saline gargles in older children and adolescents
- Fluids and feeds: ensure oral fluids to maintain hydration and give a nutritious diet
- No other COVID-19 specific medication needed
- Antimicrobials are not indicated
- Maintain monitoring chart including counting of respiratory rate 2-3 times a day, look for chest indrawing, bluish discoloration of body, cold extremities, urine output, oxygen saturation, fluid intake, activity level, especially for young children
- Advise older children and family to stay connected and engage in positive talks through phone, video-calls, etc.
- Parent/caregivers to contact the doctor in case of deterioration of symptoms

### Investigations

- No investigations are needed

## Moderate

- In addition to symptoms in mild cases, check for pneumonia which may not be apparent
- Rapid respiration (**age-based**): <2 months RR >60/min; 2-12 months, RR >50/min; 1-5 years, RR >40/min; >5 years, RR >30/min
- SpO<sub>2</sub>: 90-93 % on room air
- For other symptoms, see **COVID-19 symptoms – at a glance**

### Admit in DCHC or COVID-19 Hospital

### Mainstay of Treatment

- Initiate immediate oxygen therapy
- Maintain fluid and electrolyte balance
  - Encourage oral fluids (breast feeds in infants)
  - Initiate intravenous fluid therapy if oral intake is poor
- Corticosteroids are not required in all children with moderate illness; they may be administered in rapidly progressive disease
- Anticoagulants may also be indicated
- **Exercise caution and see use of corticosteroids and anti-coagulants guide**
- For fever (temperature >38°C or 100.4°F): Paracetamol 10-15mg/kg/dose; may repeat every 4-6 hours
- Anti-microbials to be administered if there is evidence/strong suspicion of superadded bacterial infection. See **anti-microbial use guide**
- Supportive care for comorbid conditions, if any

### Activate the Hospital Infection Control Committee

### Investigations

- Baseline lab investigations: CBC, Blood Glucose, urine routine, LFT, KFT, CRP, S. Ferritin, D-Dimer, LDH, CPK.
- Repeat investigations: CRP and D-Dimer 48 to 72 hourly; CBC, KFT, LFT 24 to 48 hourly; IL-6 (subject to availability)
- Investigations may have to be repeated more frequently in ICU settings; serial CXR should be at least 48 hours apart
- HRCT chest to be done ONLY if there is worsening of symptoms, please see **rational use of HRCT imaging guide**

## Severe

- SpO<sub>2</sub> < 90% on room air
- Signs of severe pneumonia, acute respiratory distress syndrome, septic shock, multi-organ dysfunction syndrome, or pneumonia with cyanosis, grunting, severe retraction of chest, lethargy, somnolence, seizure; assess for thrombosis, hemophagocytic lymphohistiocytosis (HLH)
- Please see **COVID-19 symptoms – at a glance**

### Admit in HDU/ICU of COVID-19 Hospital

### Mainstay of Treatment

- Initiate immediate oxygen therapy
- Maintain fluid and electrolyte balance
- Corticosteroids therapy to be initiated
- Anticoagulants may also be indicated
- **Exercise caution and see use of corticosteroids and anti-coagulants guide**
- In case Acute Respiratory Distress Syndrome (ARDS) develops, necessary management to be initiated; see ARDS and Shock guide
- In case shock develops, necessary management to be initiated; see ARDS and Shock guide
- Anti-microbials to be administered if there is evidence/strong suspicion of superadded bacterial infection. See anti-microbial use guide
- May need organ support in case of organ dysfunction, e.g. renal replacement therapy



### COVID-19 SYMPTOMS in children – at a glance

Symptoms*	Asymptomatic	Mild	Moderate	Severe
Fever	×	+	++	+++
Cough	×	+	+	++
Rhinorrhoea	×	+	+/-	+/-
Sore throat/throat irritation	×	+	+/-	+/-
Body ache/headache	×	+	+	++
Malaise/weakness	×	+	+	++
Diarrhoea/gastro-intestinal upset	×	+/-	+/-	+/-
Anorexia/nausea/vomiting	×	+/-	+/-	+/-
Loss of sense of smell and/or taste	×	+/-	+/-	+/-
Shortness of breath/breathlessness	×	×	++	+++
Respiratory rate/min	normal with age dependent variation	age dependent variation	rapid respiration (age based) <2 months >60/min; 2-12 months >50/min; 1-5 years >40/min; >5 years >30/min	rapid respiration (age based) <2 months >60/min; 2-12 months >50/min; 1-5 years >40/min; >5 years >30/min
Cyanosis	×	×	×	+/-
SpO <sub>2</sub> on room air	≥94%	≥ 94%	90% – 93%	< 90%
Grunting, severe retraction of chest, ,	×	×	×	+/-
lethargy, somnolescence	×	×	×	+/-
Seizure	×	×	×	+/-

\* Possible symptoms, signs and findings have been listed; patients in each category may have one or many of these

### 6-MINUTE WALK TEST – at a glance

- **To be used in children above 12 years under supervision of parents/guardian**
- It is a simple clinical test to assess cardio-pulmonary exercise tolerance, and is used to unmask hypoxia
- Attach pulse oximeter to his/her finger and ask the child to walk in the confines of their room for 6 minutes continuously
- Positive test: any drop in saturation < 94%, or absolute drop of more than 3–5% or feeling unwell (lightheaded, short of breath) while performing the test or at end of 6 minutes
- Children with positive 6-minute walk test may progress to become hypoxic and early admission to hospital is recommended (for observation and oxygen supplementation)
- The test can be repeated every 6 to 8 hours of monitoring in home setting; avoid the test in patients with uncontrolled asthma



## Acute Respiratory Distress Syndrome (ARDS) and Shock management guide

### Management/treatment of ARDS

ARDS may be classified based on Pediatric Acute Lung Injury Consensus Conference (PALICC) definition into mild, moderate and severe

- **Mild ARDS:** high flow nasal oxygen, non-invasive ventilation may be given
- **Moderate to severe ARDS:** lung protective mechanical ventilation may be initiated
  - Low tidal volume (4-8 ml/kg); peak pressure <28-30 cmH<sub>2</sub>O; MAP <18-20 cmH<sub>2</sub>O; driving pressure <15 cmH<sub>2</sub>O; PEEP 6-10 cmH<sub>2</sub>O (or higher if severe ARDS); FiO<sub>2</sub> <60%; sedoanalgesia ± neuromuscular blockers; cuffed ETT, inline suction, heat and moisture exchange filters (HMEF), avoid frequent disconnection, nebulization/metered dose inhaler
  - Restricted fluids, calculate fluid overload percentage (FO%) and keep it <10%
  - Awake prone position may be considered in older hypoxemic children if they are able to tolerate it
  - Daily assessment for weaning and early extubation; enteral nutrition within 24 hours, achieve full feeds by 48 hours
  - Transfusion trigger Hb <7g/dL if stable oxygenation and haemodynamics and <10 g/dL if refractory hypoxemia or unstable shock
- If the child does not improve, may consider high frequency oscillatory ventilation (HFOV), extracorporeal membrane oxygenation (ECMO) if available

### Management of shock

- Consider crystalloid fluid bolus 10-20 ml/kg over 30-60 minutes (fast in presence of hypotension) with early vasoactive support (epinephrine)
- Consider inotropes (milrinone or dobutamine) if poor perfusion and myocardial dysfunction persists despite fluid boluses and vasoactive drugs and achievement of target mean arterial pressure (MAP)
- Once stabilized proceed for restricted fluids and early de-resuscitation
- Hydrocortisone may be added if there is fluid refractory catecholamine resistant shock (avoid if already on dexamethasone or methylprednisolone)
- Initiate enteral nutrition; sooner the better
- Transfusion trigger Hb <7g/dL if stable oxygenation and haemodynamics, and <10 g/dL if refractory hypoxemia or unstable shock



## Multisystem Inflammatory Syndrome (MIS-C) management guide

**Multi System Inflammatory Syndrome in Children (MIS-C)** is a new syndrome in children characterized by unremitting fever  $>38^{\circ}\text{C}$  and epidemiological linkage with SARS-CoV-2. It usually occurs after 2–4 weeks of recovery from acute COVID-19

### Diagnostic criteria (WHO)

- Children and adolescents 0–18 years of age with fever  $\geq 3$  days
- **And any two** of the following:
  - Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet)
  - Hypotension or shock
  - Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP)
  - Evidence of coagulopathy (PT, PTT, elevated D-Dimer)
  - Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain)
- **And** elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin
- **And** no other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes
- **And** evidence of recent COVID-19 infection (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19

**Treatment**– The child needs appropriate supportive care preferably in ICU for treatment of cardiac dysfunction, shock, coronary involvement, multi-organ dysfunction. Drugs to be used are:

- Intravenous immunoglobulin (IVIG): 2g/kg over 12 to 24 hours
- Steroids: methylprednisolone 1-2mg/kg/day
- Empirical broad spectrum antimicrobials

If the child does not improve with the above treatment or deteriorates, options include:

- Repeat IVIG
- High dose corticosteroid (methylprednisolone 10-30 mg/kg/day for 3-5 days); have to be tapered over 2 to 3 weeks while monitoring inflammatory markers
- Aspirin: 3mg/kg/day to 5 mg/kg/day, max 81mg/day (if thrombosis or coronary aneurysm score is  $>2.5$ )
- Low molecular weight heparin (Enoxaparin): 1mg/kg twice daily subcutaneously (if patient has thrombosis or giant aneurysm with absolute coronary diameter  $\geq 8$  mm or  $\geq 10$  Z score (coronary aneurysm score  $\geq 10$ ) or LVEF  $< 30\%$  or D-Dimer  $\geq 5$  ULN); clotting factor Xa should be between 0.5 to 1 IU/ml

- Use of biologicals only after expert consultation and should be used at tertiary care only

For children with cardiac involvement, repeat ECG 48 hourly & repeat ECHO at 7–14days and between 4 to 6 weeks (and after 1 year if initial ECHO was abnormal)



### Suggested proforma for monitoring in children

Name: ..... Age: ..... Sex: ..... Date: .....

#	Co-morbid conditions (if any)	Controlled (Y/N)	Drugs being taken
1			
2			
3			

#### Record of symptoms

Time	Lethargy/malaise*	SoB**	Temperature	BP#	Respiratory rate##	Bluish nails or lips	Chest indrawing	SpO <sub>2</sub> *** & pulse rate	Physical activity (normal or lower)
08:00 am									
12:00 noon									
04:00 pm									
08:00 pm									

\*Malaise: feeling of unwellness; \*\*SoB: shortness of breath/breathing difficulty/ breathlessness; record as Yes/No

\*\*\*SpO<sub>2</sub>: oxygen levels to be measured by pulse oximeter; # measure BP if age appropriate BP cuffs are available; ## record respiratory rate in a clam or sleeping child

**Take the 6-minute walk test** (as detailed in the 6-minute walk test – at a glance)



**INFECTION PREVENTION AND CONTROL (IPC) and WHAT-TO-DO – at a glance**

IPC interventions and what-to-do	Asymptomatic	Mild	Moderate	Severe
Standard precautions	✓	✓	✓	✓
Droplet precautions	✓	✓	✓	✓
Airborne precautions	✓	✓	✓	✓
Contact precautions and hand hygiene	✓	✓	✓	✓
Wear triple layer mask (for patient)^	✓	✓	✓	✓
N95 mask for care givers (home/hospital)	✓	✓	✓	✓
Physical distancing	✓	✓	✓	✓
Cough etiquette/respiratory hygiene	✓	✓	✓	✓
Well ventilated rooms	✓	✓	✓	✓
Cleaning/disinfection – frequently touched surfaces	✓	✓	✓	✓
Safe disposal of BMW	✓	✓	✓	✓
Activation of hospital infection control committee	✗	✗	✓	✓
Monitor healthcare associated infections	✗	✗	✓	✓
Anti-pyretic (paracetamol)	✗	✓	✓	✓
Anti-tussive (SOS)	✗	✓	✓	✓
Oxygen support	✗	✓	✓	✓
Monitoring (CXR/HRCT/Lab tests) *#	✗	✗	✓	✓
Anticoagulation #	✗	✗	✓	✓
Anti-inflammatory therapy #	✗	✗	✓	✓

^ for children >12 years and for those between 6-11 years if masks can be tolerated and safely used by them; \* please see detailed guidelines for HRCT

# to be done in hospital settings/as per the guidance of treating physician



## ANTIMICROBIAL USE guide

COVID-19 is a viral infection, and antimicrobials have no role in prevention or treatment of uncomplicated COVID-19 infection

**Asymptomatic and mild cases:** antimicrobials are not recommended for therapy or prophylaxis

**Moderate and severe cases:** antimicrobials should not be prescribed unless there is clinical suspicion of a superadded infection; hospital admission increases risk of healthcare-associated infections with multidrug-resistant organisms

**Septic shock:** empirical antimicrobials (according to body weight) are frequently added to cover all likely pathogens based on clinical judgement, patient host factors and local epidemiology and antimicrobial policy of the hospital, and are usually needed when there is leucocytosis with neutrophilia, very high inflammatory markers, or raised procalcitonin (which may also be raised in severe trauma, burns, multiorgan failure, major surgery or chronic kidney disease)

**Antimicrobial stewardship** is a coordinated program that promotes the appropriate use of antimicrobials (including antibiotics), improves patient outcomes, reduces drug resistance, and decreases the spread of infections caused by multidrug-resistant organisms; it should be integrated into the pandemic response across the broader health system through the following:

1. **Reduce/eliminate unnecessary antimicrobial use**– through careful selection of antimicrobials as per national/hospital treatment guidelines for their empiric use in children
2. **AWaRe (Access, Watch and Reserve)** classification in the Essential List of Medicines is a tool for antibiotic stewardship – antimicrobials are divided into 3 categories based on their indication for common infections, their spectrum of activity and their potential for increasing antimicrobial resistance; use access group AMs for community acquired infections
3. **Strengthen microbiology laboratories to reduce turnaround time** of COVID-19 testing and other infections by improving test methods and expanding testing facilities
4. **Diagnostic stewardship** – collect blood cultures and other appropriate samples for culture before starting antimicrobials, which should preferably be administered within 1 hour of clinical assessment, with daily assessment for de-escalation and substituting IV route to oral once patient is stabilized
5. **Infection prevention and control**– implement/strictly enforce standard/transmission-based precautions, surveillance of HAI and other IPC measures
6. **Monitor trends of antimicrobial resistance and antibiotic consumption/use**, including Remdesivir, through audits/review and share/feedback of results and impact of interventions
7. **Education and training** to improve clinical competence among health workers treating COVID-19 patients – key competencies include ability to identify signs and symptoms of severe COVID-19 and those of a superimposed bacterial or fungal disease, and evaluating the need for medical devices that increase risk of healthcare associated infections (HAI)
8. **Ensure continuity of essential health services** and regular supply of quality assured and affordable antimicrobials, including antiretroviral/tuberculosis drugs and vaccines
9. **Use biocides** cautiously for environmental and personal disinfection – prioritize biocidal agents without, or with a low, selection pressure for antimicrobial resistance
10. **Address gaps in research** to ensure that antimicrobial stewardship activities become an integral part of the pandemic response and beyond; research agenda includes rapid and affordable diagnostic tests that differentiate between bacterial and viral respiratory tract infections; short- and long-term impact of wide use of biocides for environmental and personal disinfection including cross resistance to antimicrobials; and R&D for newer drugs, vaccines (COVID-19 and others) and potential alternatives to antimicrobials

These measures would reduce the emergence of untreatable multi-drug resistant infections and diseases that could potentially lead to another public health emergency





### Guide for use of Remdesivir

#### **Remdesivir (an emergency use authorization drug) is NOT recommended in children**

There is lack of sufficient safety and efficacy data with respect to Remdesivir in children below 18 years of age

### Guide for using Masks

- Children aged **5 years and under** should not be required to wear masks
- Children aged **6-11 years** may wear a mask depending on the ability of child to use a mask safely and appropriately under direct supervision of parents/guardians
- Children aged **12 years and over** should wear a mask under the same conditions as adults
- Ensure hands are kept clean with soap and water, or an alcohol based hand rub, while handling masks



## USE of STEROIDS and ANTI-COAGULANTS guide

### Steroids

- **Steroids are not indicated and are harmful in asymptomatic and mild cases of COVID-19**
- Indicated only in hospitalized moderately severe and critically ill COVID-19 cases **under strict supervision**
- Steroids should be used **at the right time, in right dose and for the right duration**
- **Self-medication of steroids must be avoided**
- **Indications and recommended dose:** Corticosteroids may be used in rapidly progressive moderate and severe cases. The recommended dose is as below: .
  - Dexamethasone 0.15 mg/kg per dose (maximum 6 mg) twice a day or equivalent dose of methylprednisolone may be used if dexamethasone is unavailable, for 5–14 days depending on clinical assessment on daily basis
- It must be remembered that steroids prolong viral shedding and hence caution is required in their use.

### Anti-coagulants

#### Recommended dose in severe COVID-19 and MIS-C

- Aspirin: 3 mg/ kg/day to 5 mg/kg/day max 81 mg/ day (if thrombosis or Coronary aneurysm score  $\geq 2.5$ )
- Low molecular weight heparin (Enoxaparin): 1mg/kg twice daily subcutaneously
- Clotting factor Xa should be between 0.5–1 IU/ml (if patient has thrombosis or coronary aneurysm score  $>10$  or LVEF  $<30\%$ )



## **RATIONAL USE of HRCT IMAGING** guide

**High-resolution CT (HRCT)** scan of chest provides better visualization of the extent and nature of lung involvement in patients with COVID-19

However, any additional information gained from HRCT scan of chest often has little impact on treatment decisions, which are based almost entirely on clinical severity and physiological impairment

Therefore, treating physicians should be highly selective in ordering HRCT imaging of chest in COVID-19 patients

### **Routine HRCT imaging of chest in COVID-19 patient is NOT recommended**

- Nearly two-thirds of persons with asymptomatic COVID-19 have abnormalities on HRCT chest imaging which are nonspecific, and most of them do not progress clinically
- HRCT imaging of chest done in first week of illness might often underestimate the extent of lung involvement, giving a false sense of security
- Correlation between extent of lung involvement by HRCT imaging of chest and hypoxia is imperfect; often, young individuals with extensive lung involvement will not develop hypoxia, while elderly individuals with minimal/ less extensive lung involvement are likely to develop hypoxia
- Radiation exposure due to repeated HRCT imaging may be associated with risk of cancer later in life

### **HRCT imaging of chest NOT be done for following situations**

- Not to be done for diagnosing/screening Covid-19 infection (diagnosis of COVID-19 should be done only by using approved laboratory tests as recommended by ICMR)
- Not indicated in asymptomatic and mild cases of COVID-19
- Not needed to initiate treatment in COVID-19 patients with hypoxia and an abnormal chest radiograph
- Not needed to assess response to treatment; more often, the lung lesions show radiological progression despite clinical improvement

### **Indications for HRCT imaging of chest in COVID-19 patients**

- Suspected or confirmed cases of moderate COVID-19 who continue to deteriorate clinically even after initiation of appropriate therapy especially with high risk of invasive fungal infection

**In view of the above, treating pediatricians should exercise caution while advising HRCT imaging of chest**



## MUCORMYCOSIS guide

**Mucormycosis** is a serious fungal disease seen in patients with the underlying/predisposing factors such as immunosuppression, poorly controlled diabetes mellitus (especially diabetic ketoacidosis), misuse/overuse of steroids, cancer, organ/stem cell transplantation, and those under prolonged ICU treatment.

**Mode of infection** is usually through inhalation of fungal spores present in dust/air and it is not contagious; presentation is variable but usually occurs in third week after onset of COVID-19 symptoms

### Signs and symptoms

#### Rhino-cerebral mucormycosis

- Facial pain, pain over sinuses, periorbital swelling
- Conjunctival injection or chemosis, blurring of vision/diplopia
- Paraesthesia/decreased sensation over half of face
- Blackish discolouration of skin over nasolabial groove/alae nasi; nasal crusting and nasal discharge which could be blackish, or blood tinged
- Loosening of teeth, pain in teeth and gums
- Discoloration (pale) of palate/turbinates insensitive to touch, eschar over palate
- Worsening of respiratory symptoms, haemoptysis, and chest pain; headache, alteration of consciousness and seizures etc.

#### Gastro-intestinal mucormycosis

- Symptoms and signs are very non-specific and mimic other gastrointestinal (GI) conditions but have a progressively worsening course
- Unexplained feed intolerance, abdominal distension, GI bleeding in a child with several risk factors (shock, vasopressors, broad-spectrum antibiotics)
- Persistent elevation of serum lactate in the absence of haemodynamic instability, liver dysfunction or other known causes

### Diagnosis

- KOH mount and microscopy, histopathology of debrided tissue – presence of ribbon like aseptate hyphae, 5-15  $\mu$  thick that branch at right angles
- **Positive serologic assays for Galactomannan or (1,3)- $\beta$ -D-glucan** also support the diagnosis of mucormycosis
- Relevant radiological Investigations e.g. contrast enhanced CT of sinuses, CT chest for suspected pulmonary involvement (presence of more than 10 nodules, reverse halo sign, CT bronchus sign, pleural effusion – are highly suggestive of mucormycosis), MRI brain etc. to see the extent of systemic involvement; unstable patients might require repeat CT/MRI scans to assess the progression of disease



## MUCORMYCOSIS guide (continued)

### Management

- Mucormycosis is an aggressive, life-threatening infection that needs a high index of suspicion, prompt diagnosis and early treatment (surgical debridement and antifungal therapy) by a multidisciplinary team to reduce mortality
- Don't wait for culture results to initiate therapy as mucormycosis is an emergency
- Early complete surgical debridement is the cornerstone of treatment, and may be repeated as required
- **Conventional Amphotericin B** (deoxycholate) as a prolonged IV infusion through a central venous catheter or PICC; closely monitor kidney function and electrolytes during treatment
  - Reconstitute in water for injection, and dilute in 5% dextrose (do not use normal saline/Ringer's lactate); start with test dose: 1 mg IV infusion over 20-30 min
  - Loading dose: 0.25–0.5 mg/kg IV infused over 2-6 hours; gradually increase by 0.25 mg-increments/day to reach maintenance dose: 1–1.5 mg/kg/day
- **Liposomal Amphotericin B or Amphotericin lipid complex**, if available; prolonged infusion over 2–3hours through a central venous catheter or PICC and closely monitoring KFT and electrolytes
  - Reconstitute in water for injection, and dilute in 5% dextrose (do not use normal saline/Ringer's lactate); start full dose from first day; **5 mg/kg/day** (10 mg/kg/day in case of CNS involvement)
  - Continue till a favourable response is achieved which may take 3-6 weeks following which step down to oral Posaconazole (delayed release tablets, children  $\geq 3$  years and adolescents  $\leq 17$  years: 5-7 mg/kg/dose twice daily on day 1, followed by 5 to 7 mg/kg/dose daily) or Isavuconazole (not approved below 18 years of age, however if required to be given, the dose for weight  $>30$ kg: 200 mg 1 tablet 3 times daily for 2 days followed by 200 mg daily,  $<30$ kg: half the dose for  $>30$  kg children) may have to be taken for prolonged period as per advice of pediatrician
- **Posaconazole** should be given as salvage therapy in cases who cannot be given Amphotericin B
  - **Injection IV**
    - Children  $\leq 11$  years: loading dose: 7-12 mg/kg/dose IV twice on the first day and maintenance dose: 7-12 mg/kg IV once a day, starting on second day (max: 300 mg/dose)
    - Adolescents: 300 mg IV twice on the first day and maintenance dose 300 mg IV once a day, starting on the second day
  - **Oral delayed release tablets (100 mg) and Oral Suspension (for infants and smaller children)** To be administered with fatty food:
    - Oral delayed release tablets : **Children** 7 to 12 years: initial dose: 200 mg/dose thrice daily; maximum dose: 800 mg/day  
**Adolescents:** 300 mg/dose twice on day 1, followed by 300 mg/dose once daily
    - Oral suspension (for infants and children) as syrup in a strength of 40 mg/ml. The recommended dose for children with body weight  $<34$  kg is 4.5 to 6 mg/kg/dose 4 times daily; maximum dose 800 mg/day. For those children and adolescents with body weights  $>34$  kg the dose is 200 mg/dose 3 times daily (maximum 200 mg 4 times a day)

**Treatment has to be continued until resolution of clinical signs and symptoms as well as radiological signs of active disease; and may have to be given for quite a long period of time**