Clinical Guideline for Acute Encephalitis Syndrome (AES)

(Version 1)(4-8-2023)

Major criteria: Fever with reduced conscious level/ altered mental status >24 hours plus
One of the following ***minor criteria:***
- Seizures/abnormal movement/behavioural problems/change in sleep pattern

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Assess ABC, active seizures, raised ICP → Annex A & B

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Blood: FBC, CRP, Blood C&S, U&E, RBS, *Ca & *Mg, Dengue/ JE serology, MP
Nasopharyngeal swab for influenza/Covid -19 viruses, ***rectal swab*** for enteroviruses
CSF (if patient's condition is favourable): RE, Gram & ZN stain, viral PCR (if available), (Store 2-3 ml of extra CSF in sterile container for further antibodies testing at 2-8˚C)
Neuroimaging: CT/MR brain (if available)

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Infectious etiology:
- **HSV**: IV aciclovir 20 mg/kg 8 H x 21 days
- **Influenza**: consider Oseltamivir (preferably within 48 hr after onset of symptoms) for 5-7 days. Refer Annex C for dosage.
- **Bacteria**: IV ceftriaxone 80-100 mg/kg 1 or 2 divided doses x 7-14 days
- **Scrub typhus** if cutaneous eschar positive (Annex D): oral or IV azithromycin 10mg/kg/day x 5 days

Para-infectious etiology:
ADEM or ANEC or AHLE
- Multifocal, bilateral, asymmetric white matter demyelination pattern in neuroimaging (+)
- Viral serology or PCR may or may not be (+)
- CSF pleocytosis may be (+) in RE
- Anti-MOG, Anti-AQP4 antibodies may be (+)
- Give IV methylprednisolone 20-30 mg/kg x 5 days or IVIG 2G/kg in 2-5 days (if refractory or contraindicated to methylpred.)

Suspect Autoimmune encephalitis:
- Refractory seizure
- Abnormal movement
- Change in personality or behaviour
- Change in sleep pattern
- Speech reduction

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Consult with Paed. Neurology team

*__Investigation__: consider only when there is refractory seizure control despite adequate doses of anti-seizure medications

Abbreviations: *ADEM* – acute disseminated encephalomyelitis; *ANEC* – acute necrotizing encephalitis of childhood; *AHLE* – acute hemorrhagic leukoencephalitis; *Anti-MOG* – anti myelin oligodendrocyte glycoprotein; *anti-AQP4* – anti aquaporin 4

Annex A

Algorithm for treatment of active seizures

***Benzodiazepines**
PR Diazepam – 0.5 mg/kg #
IM Midazolam – 0.2 mg/kg #
Nasal Midazolam – 0.3 mg/kg #
Buccal Midazolam – 0.3 mg/kg #
IV Diazepam – 0.3 mg/kg
IV Lorazepam – 0.1 mg/kg
preferable if available

Maximum doses for Benzodiazepine

Midazolam
Child 1 mth-1 year – 2.5 mg
Child 1-5 years – 5 mg
Child 5-10 years – 7.5 mg
above 10 years – 10 mg

Diazepam
Child 1 mth-2 year – 5 mg
Child 2-5 years – 7.5 mg
Child 5-12 years – 10 mg

Lorazepam
Child 1 mth-12 years – 4 mg

Seizures

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- Lateral Position
- O_2
- Suction if required
- Obtain IV access (as early as possible)
- Blood Glucose Level

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Unwitnessed onset/ >5 min duration

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*Benzodiazepines (**First line**)

↓ Wait for 5min

↓ If ongoing seizure

**2nd dose of Benzodiazepines

**Parenteral route is preferable

↓ Wait for 5min

***Use pheno if already on oral phenytoin and vice versa (if possible)

***Second line** (go to third line if not available)
IV/IO Phenobarbitone 20 mg/kg over 20 min (OR)
IV/IO Phenytoin 20 mg/kg over 20 min (OR)
IV Levetiracetam 40-50 mg over 5-20 min (dilute with 50-100 ml 0.9% N/S or 5% dextrose, max. 9 mcg/kg/min)

↓ 20 min after giving drug

Third line (preferable should be in ICU)
- IV diazepam infusion 100 mcg/kg/hr increasing to a maximum of 400 mcg/kg/hr (OR)
- IV Midazolam 0.2 mg/kg bolus (at 2 mg/min; max 10 mg), followed by IV infusion of 1 mcg/kg/minute (increased by 1 mcg/kg/minute every 15 minutes) until seizures controlled; max 9 mcg/kg/minute

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Rapid sequence induction of anaesthesia (RSI)
- IV Atropine 0.02 mg/kg/dose (maximum 1 mg)
- IV Suxamethonium 1-2 mg/kg/dose
- IV Thiopentone 4 mg/kg/dose then 2-8 mg/kg/hour by continuous intravenous infusion

Annex B

Summary of measures to reduce intracranial pressure

- Assessment and management of ABC's
  - Ensure oxygenation- Normoxia (PaO2>60 mmHg, SpO2>92%)
  - Ensure adequate circulating volume- Normovolaemia
  - Maintain normal BP
- Identify the signs of impending brain herniation and treat immediately
- Early intubation if; GCS <8, Evidence of herniation, Apnoea, inability to maintain airway
- Short term hyperventilation using bag ventilation: Target PaCO2: 30–35 mm Hg (suitable for acute, sharp increases in ICP or signs of impending herniation)
- ***If present***, inform ICU team and transfer as soon as possible
- Treatment of underlying cause including surgery
- Head in neutral position with mild head elevation of 15–30° (Ensure that the child is euvolemic)
- Mannitol: 0.5-1.5g/kg (2.5-7.5 mL/kg of 20% solution) every 4-6 hour as per requirement, up to 72 h
- Hypertonic 3% Saline infusion:
  - Preferable in presence of Hypotension, Hypovolemia, Renal failure
  - Dose: 10ml/kg bolus followed by 0.1–1 ml/kg/hr infusion, Target Na+—145–155 mEq/L
- Steroids
  - Especially intracranial SOL with perilesional oedema
  - Dexamethasone IV - 1-1.5 mg/kg/day 4 divided doses; Max- 16 mg/day
- Acetazolamide: Hydrocephalous, benign intracranial hypertension
- Adequate sedation and analgesia
- Prevention and treatment of seizures
- Avoid noxious stimuli
- Control fever: antipyretics, cooling measures
- Maintenance IV Fluids: Only isotonic or hypertonic fluids (Ringer lactate, 0.9% Saline, 5% D in 0.9% NS), No Hypotonic fluids
- Maintain blood sugar: 80–120 mg/dL
- Maintain Hb concentration around 10 g/dl, to help cerebral oxygen delivery
- Refractory raised ICP:
  - Heavy sedation and paralysis
  - Barbiturate coma
  - Hypothermia
  - Decompressive craniectomy

Monitoring

- Monitor continuously for all vital parameters (temperature, HR, RR, BP, MABP, CFT), and level of consciousness, neurological status, herniation signs, oxygenation (SpO2) and PaCO2, hourly.
- Assess adequacy of sedation and analgesia, input and output and bowel sounds.
- After a dose of mannitol, monitor the urine output hourly.
- Random blood sugar should be monitored at least every 6 h. If hypoglycaemia/ hyperglycaemia, monitor blood sugar every 1–2 h.
- Serum sodium should be monitored every 6-8 h, if 3% saline is used.
- EEG (if facility and specialist is available) should be monitored to look for non-convulsive seizure if child is comatose.

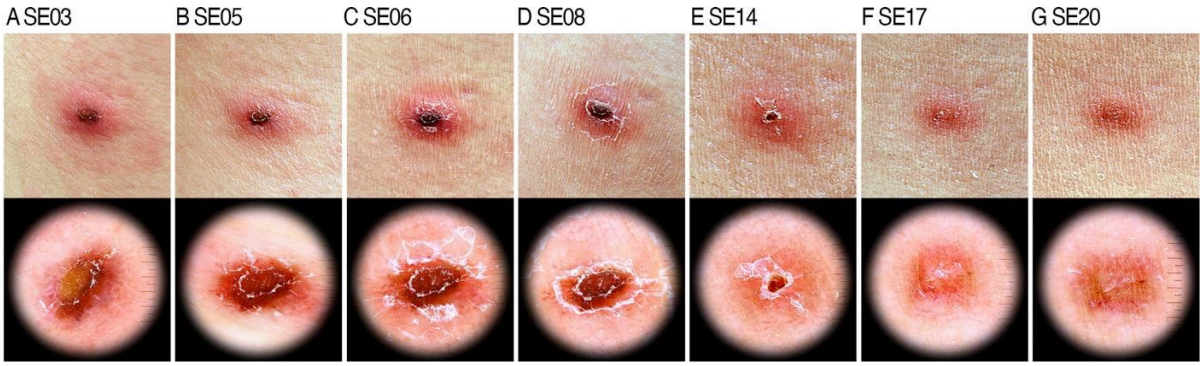
Annex C

Dosage of Oseltamivir

Antiviral Agent	Use	Children	Adults
Oral Oseltamivir	Treatment (5 days)	**If younger than 1 yr old**[1]: 3 mg/kg/dose twice daily[2,3] **If 1 yr or older, dose varies by child's weight:** 15 kg or less, the dose is 30 mg **twice** a day >15 to 23 kg, the dose is 45 mg **twice** a day >23 to 40 kg, the dose is 60 mg **twice** a day >40 kg, the dose is 75 mg **twice** a day	75 mg **twice** daily
	Chemo-prophylaxis (7 days)	If child is younger than 3 months old, use of oseltamivir for chemoprophylaxis is not recommended unless situation is judged critical due to limited data in this age group. **If child is 3 months or older and younger than 1 yr old**[1] 3 mg/kg/dose once daily[2] **If 1 yr or older, dose varies by child's weight:** 15 kg or less, the dose is 30 mg **once** a day >15 to 23 kg, the dose is 45 mg **once** a day >23 to 40 kg, the dose is 60 mg **once** a day >40 kg, the dose is 75 mg **once** a day	75 mg **once** daily

Ref: https://www.cdc.gov/flu/pdf/professionals/antivirals/antiviral-dosage-duration.pdf

Cutaneous eschar in scrub typhus (Annex D)



Ref: Am. J. Trop. Med. Hyg., 95(6), 2016, pp. 1223–1224 doi:10.4269/ajtmh.16-0583

This guideline was developed by *Clinical Management Committee on Vaccine Preventable Diseases, Ministry of Health, Myanmar.*

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