Acetazolamide (AZA)

Dosage:

- epilepsy: 8–30 mg/kg/d (as stated in the Summary of Product Characteristics, SPC)
- type 2 episodic ataxia: 5–10 mg/kg/d (off-label)
- idiopathic intracranial hypertension/pseudotumor cerebri (off-label)
  - infants: initial dose 8 mg/kg/d as 3 separate doses, increase if required to a maximum of 100 mg/kg/d
  - children: start with 25 mg/kg/d, increase by 25 mg/kg/d if required (max. 100 mg/kg/d or 2 g/d)
  - adolescents: start with 25 mg/kg/d, increase by 25 mg/kg/d if required (max. 100 mg/kg/d or 2 g/d)
- central respiratory disorder with accompanying hypoxemia: 7.5–10.0 mg/kg/d (caution: metabolic decompensation)

Neuropaediatric indications:

- reduction of cerebrospinal fluid (CSF) production with increase of intracranial pressure (ICP) (including posthemorrhagic ventricular dilatation and idiopathic intracranial hypertension)
- alternative therapy for partial, generalized or absence epilepsy (short-term)
- type 2 episodic ataxia
- central respiratory disorder with accompanying hypoxemia

Mechanism of action:

- carbonic anhydrase inhibitor

Relevant contraindications:

- hypokalemia, hyponatremia

Relevant side effects and interactions:

- metabolic acidosis
- frequent urination
- skin rash
- paresthesia
- hypercalciuria/nephrolithiasis
- nephrotoxic in combination with NSAIDs
- increase of Carbamazepine level
- (rarely) Stevens-Johnson syndrome

Approval status: –

Sources:

- **Germany – SPC:** –
- **USA – T:**
  - **epilepsy**
    - oral
    - 4–16 mg/kg/d as 1–4 separate doses, not to exceed 30 mg/kg/d or 1 g/d; extended release capsule is not recommended for treatment of epilepsy
  - **oedema**
    - oral or IV
    - 5 mg/kg/d as a SD or 150 mg/m²/d as a SD
- **United Kingdom – BNFC:**
  - **epilepsy**
    - oral or by slow intravenous injection
      - **neonate:** initial dose 2.5 mg/kg 2–3 times daily; maintenance dose 5–7 mg/kg 2–3 times daily
      - **children 1 month–12 years:** initial dose 2.5 mg/kg 2–3 times daily, followed by 5–7 mg/kg 2–3 times daily, max. 750 mg/d (maintenance dose)
      - **children 12–18 years:** 250 mg 2–4 times daily
  - **raised intracranial pressure**
    - oral or by slow intravenous injection
      - **children 1 month–12 years:** initial dose 8 mg/kg 3 times daily, increasing as necessary to max. 100 mg/kg/d

Comment:

- careful use of long term administration
- frequent control of acid-base homeostasis as well as electrolytes

Acetylsalicylic acid (ASA)

Dosage:

- stroke prophylaxis: 1–3 mg/kg/d
  - initial dose for acute stroke treatment or in case of temporary symptoms: 3–5 mg/kg/d (information only for adults available, not for children)
  - after 3–6 months of LMWH therapy following the clinically acute phase, in a stable situation: 3–5 mg/kg/d (no information on dosage and tolerability of ASA available for newborns)
- acute tension-type headache treatment: 10–15 mg/kg p.o./IV
- acute migraine treatment: 10–15 mg/kg p.o./IV
- migraine prophylaxis: 2–3 mg/kg/d p.o.
- Kawasaki disease with fever: 50 mg/kg/d or 80–100 mg/kg/d as 4 separate doses over 48–72 h, followed by 3–5 mg/kg/d; discontinue treatment after 6–8 weeks

Neuropaediatric indications:

- primary and secondary stroke prevention/prophylaxis
- tension-type headache
- acute migraine treatment
- migraine prophylaxis
- Kawasaki disease

Mechanism of action:

- inhibition of platelet aggregation through inhibition of cyclo-oxygenase with consecutive reduction of thromboxane A2 and prostacyclin synthesis

Relevant contraindications:

- severe liver or renal failure
- children and adolescents with feverish illness

Relevant side effects and interactions:

- very rare at low dose
- nausea, heartburn, vomiting
- bronchoconstriction
- mucosal irritation, gastrointestinal bleeding and peptic ulcer
- relapse of (chronic) inflammatory bowel diseases
- Reye syndrome in children (and adolescents) with feverish illness (historical)

Approval status:

- varies depending on product (see SPC)

Sources:

- **Germany – SPC:**

Age:	**Single dose (SD):**
7–9 years	1 tablet, i.e. 250 mg
9–12 years	1–1½ tablet, i.e. 250–375 mg
> 12 years	2–3 tablets, i.e. 500–750 mg

  - The SD can be given every 4–8 h, if necessary.
- **USA – T:**
  - **Kawasaki disease**
    - oral
      - 80–100 mg/kg/d divided into 4 doses, i.e. 20–25 mg/kg, administered every 6 h for up to 14 d (until fever resolves for at least 48 h); then decrease the dose to 3–5 mg/kg/d once daily. In patients without coronary artery abnormalities, continue with the low dose for 6–8 weeks. In patients with coronary artery abnormalities, maintain the low-dose treatment indefinitely (in addition to therapy with Warfarin).
  - **analgesic**
    - oral, rectal, IV
      - 10–15 mg/kg every 4–6 h, max. dose: 4 g/d
  - **anti-inflammatory**
    - oral
      - initially: 60–90 mg/kg/d divided into several doses
      - usual maintenance dose: 80–100 mg/kg/d given in appropriate doses every 6–8 h
      - monitor ASA serum concentration
  - **antiplatelet effects**
    - adequate paediatric studies have not been performed; paediatric dosage is derived from adult studies and clinical experience and is not well established
    - Suggested doses have ranged from 1–5 mg/kg/d to 5–10 mg/kg/d as a SD. Doses are typically rounded to a convenient amount.
  - **arterial ischemic stroke, recurrent:** 1–5 mg/kg/d as a SD after anticoagulation therapy has been discontinued.
- **United Kingdom – BNFC:**
  - **Kawasaki disease**
    - oral
      - **neonates:** initially 32 mg/kg/d as 4 separate doses for 2 weeks or until afebrile, followed by 5 mg/kg/d as a SD for 6–8 weeks; if no evidence of coronary lesions after 8 weeks, discontinue treatment or seek expert advice
      - **children 1 month–12 years:** initally 30–50 mg/kg/d as 4 separate daily doses for 2 weeks or until afebrile, then 2–5 mg/kg/d as a SD for 6–8 weeks; if no evidence of coronary lesions after 8 weeks, discontinue treatment or seek expert advice
  - **inhibition of platelet aggregation, prevention of thrombus formation after cardiac surgery**
    - oral
      - **neonates:** 1–5 mg/kg/d as a SD
      - **children 1 month–12 years:** 1–5 mg/kg/d (usual max. 75 mg) as a SD
      - **children 12–18 years:** 75 mg/d as a SD

IV comment:

- increased (potentially/historical) risk of developing Reye syndrome (< 12 years)
- should not be administered during acute febrile disease (especially varicella disease and influenza)
- optional monitoring of anticoagulation: platelet function testing

Aciclovir

Dosage:

- suspected HSV-1 or -2 encephalitis: 45 mg/kg/d as 3 separate doses (with neonatal infection: 60 mg/kg as 3 separate doses) over 21 d
- up to age 12 as IV therapy
- with confirmed HSV encephalitis or with immunosuppression, doses should be doubled and treatment continued for 14 d (newborns 21 d)

Neuropaediatric indications:

- confirmed or suspected herpes simplex or varicella zoster encephalitis
- varicella zoster virus with facial nerve paralysis

Mechanism of action:

- antimetabolite, inhibition of viral DNA polymerase
- phosphorylated by viral thymidine kinase and further phosphorylated to acyclo-GTP by cellular kinase
- by incorporating and using acyclo-GTP instead of GTP for DNA replication via DNA polymerase, no more deoxyribonucleotides (dNTP) can be attached as acyclo-GTP has no 3'-OH group and termination of DNA synthesis occurs

Relevant contraindications:

- none

Relevant side effects and interactions:

- reduced dose in renal disease to lower the risk of toxic encephalopathy

Approval status:

- varies depending on product (see SPC)

Sources:

- **Germany – SPC:**
  - **Herpes simplex infection**
    - **children > 2 years:** see dose recommendation for adults
    - **children < 2 years:** half dose of adults' dose
    - **adults:** 800 mg/d as 4 separate doses (alternatively as 2 separate doses). This is the recommended dose for prophylaxis in immunocompromised patients.
    - **note:** For severely immunocompromised patients (e.g. after organ transplantation) a dose of 1,600 mg/d as 4 separate doses may be indicated.
- **USA – T:**
  - **Herpes zoster in immunocompetent host**
    - oral
      - **children ≥ 12 years:** initiate treatment within 48 hours of rash onset using 4000 mg/d as 5 separate doses for 5–7 d
    - IV
      - **infants 1 month–< 1 year:** 30 mg/kg/d as 3 separate doses for 7–10 d
      - **children ≥ 1 year:** 30 mg/kg/d as 3 separate doses or 1500 mg/m²/d as 3 separate doses for 7–10 d
  - **Herpes zoster in immunocompromised host**
    - IV
      - 30 mg/kg/d as 3 separate doses for 7–10 d; note: the AIDS info guidelines recommended duration of therapy is 10–14 d
  - **HSV encephalitis**
    - IV
      - **infants 1–3 months:** 60 mg/kg/d as 3 separate doses for 14–21 d
      - **children 3 months–12 years:** 60 mg/kg/d as 3 separate doses for 14–21 d; some clinicians recommend 45 mg/kg/d or 1500 mg/m²/d as 3 separate doses for 14–21 d
      - **children ≥ 12 years:** 30 mg/kg/d as 3 separate doses for 14–21 d
  - **Varicella-zoster in immunocompromised host**
    - IV
      - **infants < 1 year:** 30 mg/kg/d as 3 separate doses for 7–10 d
      - **children 1–12 years:** 1500 mg/m²/d or 30 mg/kg/d as 3 separate doses for 7–10 d
      - **children ≥ 12 years:** 30–45 mg/kg/d as 3 separate doses for 7–10 d
  - **Varicella-zoster-virus in immunocompetent host** (initiate treatment within the first 24 h of rash onset)
    - oral
      - **children ≥ 2 years and ≤ 40 kg:** 80 mg/kg/d as 4 separate doses for 5 d, max. 3200 mg/d
      - **children > 40 kg:** 3200 mg/d as 4 separate doses for 5 d
- **United Kingdom – BNFC:**
  - **Herpes simplex treatment**
    - oral
      - **children 1 month–2 years:** 500 mg/d as 5 separate doses usually for 5 d (longer if new lesions appear during treatment or if healing incomplete); double the dose for immunocompromised patients or if absorption is impaired
      - **children 2–18 years:** 1000 mg/d as 5 separate doses usually for 5 d (longer if new lesions appear during treatment or incomplete healing); double the dose for immunocompromised patients or if absorption is impaired
    - by intravenous infusion
      - **neonate:** 60 mg/kg/d as 3 separate doses for 14 d (21 d if CNS involvement)
      - **children 1–3 months:** 60 mg/kg/d as 3 separate doses for 14 d (21 d if CNS involvement)
      - **children 3 months–12 years:** 750 mg/m²/d as 3 separate doses usually for 5 d; double the dose to 500 mg/m² given every 8 h if CNS involvement (given for up to 21 d) or if immunocompromised
      - **children 12–18 years:** 15 mg/kg/d as 3 separate doses usually for 5 d; double the dose to 30 mg/kg/d as 3 separate doses if CNS involvement (given for up to 21 d) or if immunocompromised

- **Herpes simplex prophylaxis in immunocompromised patients**
  - oral
    - **children 1 month–2 years:** 400–800 mg/d as 4 separate doses
    - **children 2–18 years:** 800–1600 mg/d as 4 separate doses
- **Herpes simplex suppression**
  - oral
    - **children 12–18 years:** 800 mg/d as 2 or 4 separate doses; increase to 1,200 mg/d as 3 separate doses if symptoms recur on standard suppressive therapy or for suppression of genital herpes during late pregnancy (from 36 weeks gestation); stop therapy every 6–12 months to reassess recurrence frequency – consider restarting after two or more recurrences
- **prophylaxis of chickenpox after delivery**
  - by intravenous infusion
    - **neonates:** 30 mg/kg/d as 3 separate doses; continued until serological tests confirm absence of virus
- **chickenpox and herpes zoster infection**
  - oral
    - **children 1 month–2 years:** 800 mg/d as 4 separate doses for 5 d
    - **children 2–6 years:** 1600 mg/d as 4 separate doses for 5 d
    - **children 6–12 years:** 3200 mg/d as 4 separate doses for 5 d
    - **children 12–18 years:** 4000 mg/d as 5 separate doses for 7d
  - by intravenous infusion
    - **neonates:** 30–60 mg/kg/d as 3 separate doses for at least 7 d
    - **children 1–3 months:** 30–60 mg/kg/d as 3 separate doses for at least 7 d
    - **children 3 months–12 years:** 750 mg/m²/d as 3 separate doses usually for 5 d, double the dose for immunocompromised patients
    - **children 12–18 years:** 15 mg/kg/d as 3 separate doses for 5 d, double the dose for immunocompromised patients
    - **note:** to avoid excessive dose in obese patients, parenteral dose should be calculated on the basis of ideal weight for the patient's height
- **attenuation of chickenpox if administration of anti-varicella-zoster immunoglobulin preparation contraindicated**
  - oral
    - **children 1 month–18 years:** 40 mg/kg/d as 4 separate doses for 7 d starting 1 week after exposure

IV comment:

- IV therapy over 60 min, as fast infusion/injection increases risk of kidney damage; ensure adequate hydration

ACTH

(Tetracosactide)

Dosage:

- 15–30 U/m² IM as a SD (maximum 60 U/d)
- duration of therapy has not yet been systematically examined in studies.
- ACTH is usually intramuscularly administered each day over a period of 2–3 weeks, after that the dosage is reduced and/or the administration interval increased over a period of 1–15 weeks to gradually discontinue the medication

Neuropaediatric indications:

- West syndrome, epileptic encephalopathy

Mechanism of action:

- as a glandotropic hormone, the drug controls synthesis and release of corticosteroids

Relevant contraindications:

- acute systemic infection
- do not use in newborns (depot preparation contains benzyl alcohol)

Relevant side effects and interactions:

- hypertonia, cardiomyopathy, nephrocalcinosis, hypokalemia
- anaphylaxis
- frequent hyperglycemia
- irritability
- increased appetite and weight gain
- increased risk of infection due to immunosuppression
- gastrointestinal bleeding
- osteoporosis
- iatrogenic Cushing's syndrome
- enhanced efficacy of cardiac glycosides
- increased potassium excretion due to diuretics
- decreased efficacy of anti-diabetic medications and coumarins
- decreased efficacy in patients on comedication with Rifampicin, barbiturates, Phenytoin
- increased risk of gastrointestinal bleeding in patients on comedication with salicylates
- increase of stereoidal efficacy by Theophylline and Propranolol
- attenuation of cortisol release by Omeprazole and Dexamethasone
- liver damage possible in patients on comedication with anticonvulsants