sulfaDiazine
Newborn use only

2022

Alert	Increased risk of haemolysis in G6PD deficiency. Discontinue use at first sign of rash (including Stevens-Johnson syndrome, toxic epidermal necrolysis) Discontinue use immediately if blood disorders develop (including leucopenia, thrombocytopenia, megaloblastic anaemia, eosinophilia).
Indication	Congenital toxoplasmosis
Action	Inhibits bacterial folic acid synthesis through competitive antagonism of p-aminobenzoic acid (PABA).[1]
Drug type	Antibiotic
Trade name	Tablets: Multiple brands available through Special Access Scheme
Presentation	500 mg tablets 100 mg/mL oral suspension prepared by pharmacy[11]
Dose	Anti-toxoplasma therapy is for **12 months** and as follows: [2,3] **Pyrimethamine** First 2 days: 1 mg/kg/dose every 12 hours followed by From Day 3 to 6 months: 1 mg/kg/dose once daily followed by 7th month to 12 months: 1 mg/kg/dose three-times a week. **Sulfadiazine** 50 mg/kg every 12 hours from day 1 of treatment to 12 months and **Calcium folinate (folinic acid)** 10 mg three times a week for 12 months until 1 week following cessation of pyrimethamine treatment.
Dose adjustment	Therapeutic hypothermia – Not applicable. ECMO – Not applicable. Renal impairment – Limited data. Caution may be required. [1] Avoid in severe renal impairment due to risk of crystalluria. Hepatic impairment - Caution is required.[1]
Maximum dose	
Total cumulative dose	-
Route	Oral
Preparation	100 mg/mL oral suspension (prepared by pharmacy)[11]
Administration	Administer on an empty stomach. Sulfadiazine should be given concurrently with pyrimethamine.[4]
Monitoring	Full blood count twice a week
Contraindications	History of hypersensitivity to sulfadiazine or any of the components of the preparation.
Precautions	Hepatic impairment: Liver is the main route of metabolism. Caution is required. Risk of kernicterus. Renal impairment: Dosage modification may be required. G6PD deficiency: Use with caution in patients with possible G6PD deficiency.
Drug interactions	
Adverse reactions	Haematologic: Eosinophilia, hypoprothrombinaemia, agranulocytosis, aplastic anaemia, haemolytic anaemia, neutropenia, leucopenia, thrombocytopenia, pancytopenia.[5,6] Central nervous system & neurological: Irritability, nerve disorders, vertigo, aseptic meningitis, kernicterus (in neonates), headache, idiopathic intracranial hypertension, dizziness, tinnitus, drowsiness, seizures.[7] Gastrointestinal: Anorexia, diarrhoea, glossitis (atrophic), vomiting, pancreatitis, pseudomembranous enterocolitis. Dermatologic: Severe cutaneous adverse reactions (SCARs), skin reactions, systemic lupus erythematosus (SLE), photosensitivity reaction, erythema nodosum, rash.[4] Renal: Haematuria, renal impairment, crystalluria, renal tubular necrosis, tubulointerstitial nephritis, nephrotoxicity. Systemic: Serum sickness-like reaction, vasculitis. Cardiovascular: Myocarditis. Endocrine & metabolic: Hypothyroidism, hypoglycaemia. Respiratory, hepatic & other: Cough, dyspnoea, hepatitis, jaundice, fever, cyanosis.
Compatibility	Not applicable
Incompatibility	Not applicable

Stability	Oral suspension: 60 days in fridge. [11]
Storage	Tablets: Store below 30°C. Protect from light. Oral suspension: Store 2-8°C. Protect from light.[11]
Excipients	Lactose, maize starch, hydrolysed starch, docusate sodium and magnesium stearate.[1]
Special comments	
Evidence	**Efficacy** Neonates with Congenital toxoplasmosis: Treatment with the following medications is recommended for 12 months: Pyrimethamine: 1 mg/kg every 12 hours for 2 days followed by 1 mg/kg daily for 6 months followed by the same dose, three-times a week to complete 12 months; Sulfadiazine: 50 mg/kg every 12 hours; and Folinic acid: 10 mg three times a week for 12 months. Folinic acid should be administered until 1 week following cessation of pyrimethamine treatment.[2,3] The United States data suggest that risk of recurrent eye disease is around 31% in infants with CT who had received 12 months of postnatal treatment during their first year of life. [8] The French cohort study showed the risk of recurrence of eye disease and within 12 years after the diagnosis of the first eye lesion was around 34%. The French cohort had mothers who were treated during pregnancy and the infants were also postnatally treated.[9] Older children (diagnosed beyond neonatal age) with active disease (Chorioretinitis):[2] Anti-toxoplasma treatment is given for at least 1–2 weeks after resolution of all signs and symptoms of acute chorioretinitis (with sharpening of the lesion borders and/or scarring of the lesion) and for ~4–6 weeks total. Acute eye disease often resolves within 10 to 14 days after initiation of treatment, but there are cases that take a longer time to resolve. Pyrimethamine First 2 days: 1 mg/kg/dose orally twice a day (maximum 50 mg/day) Then: 1 mg/kg/dose orally once daily (maximum 25 mg/day) Sulfadiazine 75 mg/kg/dose orally × 1, followed by 50 mg/kg/dose orally twice a day Folinic acid 10–20 mg orally three times a week Prednisone (severe chorioretinitis) 0.5 mg/kg/dose twice a day (maximum 40 mg/day; rapid taper) **Pharmacokinetics (in adults):** It is 38-48% protein bound. Extensively metabolised in the liver. Plasma half-life is approximately 7-16.8 hours. It is eliminated 30% to 44% unchanged in the urine, while 15% to 40% is eliminated in the acetylated form; both dependent on urine pH.[1] **Safety** Treatment of infants with pyrimethamine/sulfadiazine was associated with adverse events, ranging from 14% to 50% of cases. [5,6] The main adverse effect was neutropenia, reported to occur more often with higher doses and especially when folinic acid was not administered. Seizures have been reported with cases of pyrimethamine overdose resulting from prescription dosing errors.[7]
Practice points	
References	1. Micromedex. Sulfadiazine. Accessed on 31st January 2022. 2. Maldonado YA, Read JS, Committee On Infectious D. Diagnosis, Treatment, and Prevention of Congenital Toxoplasmosis in the United States. Pediatrics. 2017;139. 3. Management of Perinatal Infections. Australasian Society for Infectious Diseases (ASID). 2014. 4. Daraprim. Product information. Accessed on 23 November 2021. 5. Daveluy A, FH, Bricout H, et al; European Toxoprevention Study Group (EUROTOXO). Review of data related to side effects of drugs used in congenital toxoplasmosis. Panel 2: Treatment Issues. August 24, 2005. 6. Schmidt DR, Hogh B, Andersen O, Hansen SH, Dalhoff K, Petersen E. Treatment of infants with congenital toxoplasmosis: tolerability and plasma concentrations of sulfadiazine and pyrimethamine. Eur J Pediatr 2006;165(1):19–25.

	7. Genuini M, Freihuber C, Girard I, de Montgolfi er I, Kieffer F, Mitanchez D. Neonatal intoxication with pyrimethamine: risk due to the absence of pediatric formulation? [in French]. Arch Pediatr 2011;18(10):1084–1086. 8. Phan L, Kasza K, Jalbrzikowski J, Noble AG, Latkany P, Kuo A, Mieler W, Meyers S, Rabiah P, Boyer K, Swisher C. Longitudinal study of new eye lesions in treated congenital toxoplasmosis. Ophthalmology. 2008 Mar 1;115(3):553-9. 9. Wallon M, Garweg JG, Abrahamowicz M, Cornu C, Vinault S, Quantin C, Bonithon-Kopp C, Picot S, Peyron F, Binquet C. Ophthalmic outcomes of congenital toxoplasmosis followed until adolescence. Pediatrics. 2014 Mar 1;133(3):e601-8. 10. Pathmanathan U et al. Stablity of sulfadiaizine oral liquids prepared from tablets and powder. J Pharm Pharm Sci 2004; 7(1): 84-7. 11. Sulfadiazine 100mg/mL Oral Suspension. IJPC. 2011; 15 (5): 426.

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