# **Newborn use only**

Alert	Avoid in preterm neonates until term corrected age for the treatment of hypertension due to concern
	of impaired kidney development, hyperkalemia and acute kidney injury.(1).
	May cause rapid drop in BP.(1-3)
Indication	Congestive heart failure
	Treatment of hypertension: Calcium channel blockers (e.g. Amlodipine) or peripheral vasodilators
	(hydralazine) are better alternatives.
	Congenital nephrotic syndrome – To reduce proteinuria.(4-6)
Action	Angiotensin-converting enzyme inhibitor (ACEI).
7.00.011	Heart failure: Peripheral vasodilator - Reduces afterload (blood pressure (BP) and systemic vascular
	resistance) and preload (right atrial pressure and left ventricular filling pressure) and increases cardiac
	output.
	Hypertension: Several mechanisms of action: (1) inhibits formation of angiotensin II, (2) decreases
	bradykinin degradation and, (3) inhibits norepinephrine release from sympathetic nerve endings. All
	these effects produce significant vascular relaxation, reduction of after-load and improvement in
	cardiac output.
	<b>Proteinuria:</b> The mechanism of the anti-proteinuric effect is not clearly understood. Reduction of
	systemic and intraglomerular pressures and improved size selectivity of glomerular basement
	membrane have been proposed.(7) Proteinuria reduction may also occur by a dose dependent
	hemodynamic effect on the efferent arteriole which can result additionally in reduction of glomerular
	filtration rate (GFR). (8)
Drug type	Angiotensin-converting enzyme inhibitor (ACEI).
Trade name	Capoten
Presentation	5mg/mL oral solution.
Dose	Hypertension  Starting does 0.01.0.1 mg/kg/does. Sinct does may save varied due n in DD (1)
	Starting dose: 0.01-0.1 mg/kg/dose. First dose may cause rapid drop in BP.(1)
	Maintenance dose: 0.01–0.5 mg/kg/dose 8 hourly.(1)
	Congestive heart failure
	Starting dose: 0.05-0.1 mg/kg (lower range if combined with diuretics or other vasoactive agents)
	Maintenance dose: 0.1 mg/kg/dose 8 hourly and titrate to 0.3 mg/kg/dose 8 hourly*#
	*Doses up to 2 mg/kg/dose 8 hourly are used in children (9).  #6-hourly frequency (but with same daily dose) may occasionally be used at the discretion of
	cardiology.
	Congenital nephrotic syndrome Starting dose: 0.1
Daga adimeters and	Starting dose: 0.1 – 0.3 mg/kg/dose 8 hourly. Gradually increase to 1-2 mg/kg/dose 8 hourly (4)  Therapeutic hypothermia – No information.
Dose adjustment	ECMO – No information.
	Renal impairment - If GFR >50 ml/min/1.73m <sup>2</sup> – no dose adjustment is needed.
	If GFR 10-50 ml/min/1.73m <sup>2</sup> – 50% of recommended dose.
	If GFR <10 ml/min/1.73m² – Avoid it (ANMF consensus)
	Hepatic impairment – No studies to recommend dose adjustment but hepatic failure is known in adults.
Maximum dose	
iviaximum dose	Hypertension: 2 mg/kg/day (1)
Total aumanilatina	Nephrotic syndrome: 6 mg/kg/day (4)
Total cumulative dose	Not applicable
	Oral
Route	Oral
Preparation	Dilute 1 mL (= 5mg) of captopril 5 mg/mL oral solution with 4 mL of water for injection to make 1
	mg/mL solution
Administration	ORAL before feeds
Monitoring	Close monitoring of blood pressure –
	BP is measured at 10 minute intervals for 30-40 minutes following the first dose and 15 and 30
	minutes following the first dose of any increase in dosage.
	BP is monitored twice daily once a maintenance dose is achieved.
	Regular monitoring of serum potassium and creatinine (1)
	White cell count (neutropenia)

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Page 1 of 4

# **Newborn use only**

	Watch for angioedema
Contraindications	Severe renal impairment
	Hypersensitivity to captopril or components of the formulation.
	Angioedema.
	Preterm neonates until term corrected age age, because of impaired nephrogenesis risk (1) (ANMF
	consensus)
Precautions	Neutropenia
	Renal impairment
Drug interactions	ACE-inhibitors will increase the effect of diuretics.
	Combination of ACE inhibitor, diuretic and NSAID may precipitate acute renal failure.
	Potassium supplements or drugs which increase potassium level (eg spironolactone) – risk of
	hyperkalaemia
	Antihypertensive medications in combination with captopril will increase risk of hypotension.
Adverse	Hypotension
reactions	Neutropenia, agranulocytosis
	Hyperkalemia, raised serum creatinine and renal failure(2, 3)
	Angioedema and anaphylaxis
	Hepatic impairment
	Isolated dry cough in infants and children(10)
Compatibility	Not applicable
Incompatibility	Not applicable
Stability	28 days after opening.
Storage	Store in refrigerator at 2-8°C.
Excipients	Citric acid, sodium citrate dihydrate, disodium edetate, sodium benzoate and water (pH adjusted with
	sodium hydroxide and hydrochloric acid)
Special	
comments	
Evidence	Efficacy
	Hypertension (Control of the Control
	O'dea et al, in a small retrospective study of neonates found an initial dose of 0.01 mg/kg was
	effective.(2) Tack et al, in their retrospective study of sick premature infants with chronic lung disease
	who received captopril (0.3 mg/kg) for systemic hypertension noted significant fall in BP after the initial
	dose necessitating halving the dose subsequently. Some of the infants developed oliguria and neurologic signs (seizures, lethargy, apneas) with fall in BP.(3)
	Gantenbein et al investigated side effects of captopril in 43 newborn and young infants with congenital
	heart disease after cardiac surgery treated with captopril for heart failure.(11) Initial median dose of
	captopril was 0.17 mg/kg/day (range 0.05-0.55 mg/kg/day), slowly increased over 3-33 days to a
	maximal median dose of 1.86 mg/kg/day (range 0.2-2.3 mg/kg/day). All patients were simultaneously
	treated with diuretics. They reported renal impairment, hypotension and desaturations. These side
	effects were not dose related and all were reversible.
	Heart failure
	ACEIs prevent, attenuate, or possibly reverse the pathophysiological myocardial remodeling. In
	addition, they decrease afterload by antagonizing the rennin-angiotensin-aldosterone system.(9) The
	International Society of Heart and Lung Transplantation on the management of paediatric heart failure
	recommends ACEIs in all patients with heart failure and left ventricular systolic dysfunction. Therapy
	with ACE inhibitors should be started at low doses with a subsequent up-titration to the target dose
	with careful monitoring of blood pressure, renal function, and serum potassium. (9,12)
	Congenital nephrotic syndrome
	ACEI and prostaglandin inhibitors have been shown to reduce proteinuria. The effect of ACEI reaches
	optimal after 4-8 weeks of treatment. A combination of captopril and indomethacin was successfully
	used (4-6). In a case series, Kovacevic et al reported young infants with congenital nephrotic
	syndrome treated with unilateral nephrectomy, captopril and indomethacin. Treatment with
	captopril and indomethacin was commenced at a median age of 2.3 months (range 0.2–5.2 months), and was given prior to unilateral nephrectomy in six children and 2 weeks after unilateral

## **Newborn use only**

	nephrectomy in one child. Captopril was started at a low median dose of 0.3 (range 0.3-0.75) mg/kg
	per day divided in three doses and gradually increased to a maximum median dose of 3.4 (range 1.0–
6.0) mg/kg per day. The initial median dose of indomethacin was 0.8 (range 0.3–1.2) mg/	
	divided in two doses given to a maximum median dose of 2.8 (range 1.2–3.0) mg/kg per day.(4)
	Pharmacokinetics
	Onset of action is within 15 minutes with a maximum effect in 1-2 hours. Most of the drug is eliminated
	through kidneys.(2, 3, 11, 13)
Practice points	Hypertension
Traduce points	Captopril is not recommended as the first line antihypertensive agent for neonatal hypertension
	because of concerns with kidney development and other side effects.(GOR B, LOE IV) (1-3, 11)
	Heart failure
	ACE inhibitors are recommended in all patients with HF and left ventricular systolic dysfunction.
	Therapy with ACE inhibitors should be started at low doses with a subsequent up-titration to the target
	dose with careful monitoring of blood pressure, renal function, and serum potassium.(9,12) ACE
	inhibitors are considered relatively safe for children with heart failure irrespective of etiology of heart
	failure, but renal impairment, hypotension and hyperkalemia are common adverse reaction.(14) This
	treatment is based on the assumption that blocking of the renin-angiotensin-aldosterone system has a
	positive effect on morbidity and mortality, as it does in adults with heart failure. The dose of captopril
	ranged from 0.07-2.5 mg/kg/day with a duration of treatment up to 3 years. (15,16)
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