

amLODIPine
Newborn use only

2022

Alert	Amlodipine should NOT be used for hypertensive emergencies.
Indication	Hypertension.
Action	Calcium channel blocker.(1) Inhibits the influx of calcium ions into cardiac and vascular smooth muscle. Mainly acts on arteriolar smooth muscle to reduce peripheral vascular resistance and blood pressure.
Drug type	Calcium channel blocker.
Trade name	Norvasc, multiple other brands
Presentation	Tablets: 5 mg and 10 mg Oral suspension prepared by pharmacy: 1 mg/mL
Dose	0.05 - 0.3 mg/kg/ dose DAILY.*(2-5) *Up to 0.6 mg/kg/ day - can be used in 2 divided doses if required (5)
Dose adjustment	Therapeutic hypothermia – No information. ECMO – No information. Renal impairment – No dosage adjustment is required.(6) Hepatic impairment - Caution in patients with liver failure, may require dose reduction.
Maximum dose	0.6 mg/kg/ day (2,5)
Total cumulative dose	N/A
Route	Oral
Preparation	Oral suspension: 1 mg/mL preparation compounded by pharmacy. 5 mg tablet: Disperse ONE tablet in 10 mL of water for injection to make 0.5 mg/mL. The tablet will disperse within 4 minutes. Mix well to obtain an even dispersion. Measure the desired dose and administer immediately. Prepare a fresh solution for each dose. 10 mg tablet: Disperse ONE tablet in 20 mL of water for injection to make 0.5 mg/mL. The tablet will disperse within 4 minutes. Mix well to obtain an even dispersion. Measure the desired dose and administer immediately. Prepare a fresh solution for each dose.
Administration	Oral
Monitoring	Blood pressure monitoring is recommended. Liver function tests.
Contraindications	Not to be used in hypotensive or septic neonates. Hypersensitivity to amlodipine or components of the formulation.
Precautions	Congestive heart failure Hepatic impairment Severe aortic stenosis
Drug interactions	May increase the serum concentration of CYP3A4 substrates such as Nifedipine – blood pressure monitoring is warranted. Blood pressure lowering agents may enhance the hypotensive effect of amlodipine. Use with caution with CYP3A4 inhibitors (e.g. erythromycin, azole antifungals) as they may increase plasma concentration of amlodipine and increase risk of adverse effects.
Adverse reactions	Reflex tachycardia(5) Peripheral oedema, hypotension, flushing, hypersensitivity reactions (Steven Johnson syndrome, dermatitis, angioedema) Cholestatic jaundice, hepatitis, toxic epidermal necrolysis, acute interstitial nephritis.
Compatibility	Not applicable.
Incompatibility	Not applicable.
Stability	Oral suspension of 1 mg/mL: 60 day expiry (15) Tablet dispersed in water: Prepare a fresh solution for each dose. Discard unused portion.
Storage	Tablets: Store below 25°C Compounded oral suspension: 2-8°C
Excipients	Norvasc brand: Microcrystalline cellulose, calcium hydrogen phosphate, sodium starch glycolate, magnesium stearate.
Special comments	It may take up to 5-7 days (half-life 35-50 hours) to see the full antihypertensive effect of amlodipine and an interval of 5-7 days may be required prior to any dose adjustment.

Evidence	<p>Background Incidence of hypertension in neonates ranges from 0.2 to 3%.⁽²⁾ Systolic and diastolic BP values on day 1 of life correlate with gestational age and birth weight, and there is a progressive increase in BP with postnatal age in days.^(7, 8) Zubrows charts for the neonates are used in many nurseries. These charts contain systolic and diastolic BP for gestational age, post-conceptual age and birth weight.⁽⁸⁾</p> <p>Dose Flynn et al suggest that, as in adults, amlodipine may provide adequate blood pressure control in children when dosed once daily.⁽³⁾ Tallian et al performed a study with a starting dose of 0.07±0.04 mg/kg/day. The total daily dose of amlodipine was increased 25%–50% every 5–7 days. They also chose a once daily regimen.⁽⁴⁾ Analysis of Flynn and colleagues revealed that blood pressure reduction was sustained throughout the period of amlodipine treatment, while amlodipine dose remained stable (mean effective daily dose 0.17±0.12 mg/kg.⁽⁹⁾ Andersen and colleagues reported starting doses of amlodipine with a mean of 0.13+/-0.09 mg/kg/day in ages from 4 to 26 years. The dose was increased in two thirds of their study population to 0.23+/-0.13 mg/kg/day with limited side effects. Both once daily and twice daily regimens were effective.⁽¹⁰⁾</p> <p>Pharmacokinetics Amlodipine has slow onset of action (approximately 6 hours) which may be problematic in the acute setting and a prolonged duration of effect.^(2,3,11) It is well absorbed with peak blood levels between 6-12 hours post dose.⁽¹⁾</p>
Practice points	<p>Data on the treatment of hypertension in neonates is limited. The first step in treating neonatal hypertension should be to determine a correctable cause of hypertension (e.g. inotropes, dexamethasone or other corticosteroids, hypercalcemia, volume overload).⁽⁵⁾ Clinical criteria for initiating antihypertensive medications are not well defined however in general sustained BP >99th centile is an indication to consider treatment. ⁽⁵⁾ No data exist on the adverse effects of chronic hypertension in infancy. Treatment options should be tailored to the severity and underlying cause of hypertension, including intravenous and/or oral therapy.⁽¹²⁻¹⁴⁾ Amlodipine should not be used for hypertensive emergencies because it has slow onset of action and prolonged duration of effect.^{(GOR C; LOE III-3) (3).}</p>
References	<ol style="list-style-type: none"> 1. MIMS Online. Amlodipine. Accessed on 14 October 2021. 2. Dionne JM, Abitbol CL, Flynn JT. Hypertension in infancy: diagnosis, management and outcome. <i>Pediatric nephrology</i>. 2012; 27(1):17-32. 3. Flynn JT, Nahata MC, Mahan Jr JD, Portman RJ, Investigators P. Population pharmacokinetics of amlodipine in hypertensive children and adolescents. <i>The Journal of Clinical Pharmacology</i>. 2006; 46(8):905-16. 4. Tallian K, Nahata M, Turman M, Mahan J, Hayes J, Mentser M. Efficacy of amlodipine in pediatric patients with hypertension. <i>Pediatric Nephrology</i>. 1999; 13(4):304-10. 5. Flynn JT. The hypertensive neonate. <i>Seminars in Fetal and Neonatal Medicine</i>; 2020: Elsevier. https://doi.org/10.1016/j.siny.2020.101138. 6. Paediatric Renal Dosing. Dosing guidance for pediatric renal patients. US Kidney disease website. Accessed on 14 October 2021. 7. Pejovic B, Peco-Antic A, Marinkovic-Eric J. Blood pressure in non-critically ill preterm and full-term neonates. <i>Pediatric Nephrology</i>. 2007; 22(2):249-57. 8. Zubrow AB, Hulman S, Kushner H, Falkner B. Determinants of blood pressure in infants admitted to neonatal intensive care units: a prospective multicenter study. Philadelphia Neonatal Blood Pressure Study Group. <i>Journal of Perinatology</i>. 1995; 15(6):470-9. 9. Flynn JT. Efficacy and safety of prolonged amlodipine treatment in hypertensive children. <i>Pediatric Nephrology</i>. 2005; 20(5):631-5. 10. Andersen J, Groshong T, Tobias JD. Preliminary experience with amlodipine in the pediatric population. <i>American journal of therapeutics</i>. 2006; 13(3):198-204. 11. Flynn JT, Pasko DA. Calcium channel blockers: pharmacology and place in therapy of pediatric hypertension. <i>Pediatric Nephrology</i>. 2000; 15(3):302-16. 12. Flynn JT. Neonatal hypertension: diagnosis and management. <i>Pediatric nephrology</i>. 2000;14(4):332

	<p>13. Nickavar A, Assadi F. Managing hypertension in the newborn infants. International journal of preventive medicine. 2014; 5(Suppl 1):S39.</p> <p>14. Sharma D, Farahbakhsh N, Shastri S, Sharma P. Neonatal hypertension. The Journal of Maternal-Fetal & Neonatal Medicine. 2017; 30(5):540-50.</p> <p>15. Nahata MC, Morosco RS, Hipple TF. Stability of amlodipine besylate in two liquid dosage forms. J Am Pharm Assoc (Wash). 1999 May-Jun; 39(3):375-7.</p>
--	---

VERSION/NUMBER	DATE
Original 1.0	11/11/2021
Revised 2.0	25/11/2021
Revised 3.0	2/06/2022
REVIEW	2/06/2027

Authors Contribution

Original author/s	Anke Raaijmakers, Srinivas Bolisetty
Evidence Review	Srinivas Bolisetty
Expert review	Fiona Mackie, Karel Allegaert
Nursing Review	Kirsty Minter, Eszter Jozsa, Priya Govindaswamy
Pharmacy Review	Mohammad Irfan Azeem, Helen Huynh
ANMF Group contributors	Bhavesh Mehta, Nilkant Phad, John Sinn, Cindy Chen, Michelle Jenkins, Joanne Malloy, Simarjit Kaur, Hannah Bell
Final editing	Thao Tran
Electronic version	Cindy Chen, Ian Callander
Facilitator	Srinivas Bolisetty