

**amLODIPine**  
**Newborn use only**

**2022**

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| <b>Alert</b>                 | Amlodipine should <b>NOT</b> be used for hypertensive emergencies.   |
| <b>Indication</b>            | Hypertension.  |
| <b>Action</b>                | Calcium channel blocker.(1)<br>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.   |
| <b>Drug type</b>             | Calcium channel blocker.   |
| <b>Trade name</b>            | Norvasc, multiple other brands   |
| <b>Presentation</b>          | Tablets: 5 mg and 10 mg<br>Oral suspension prepared by pharmacy: 1 mg/mL   |
| <b>Dose</b>                  | 0.05 - 0.3 mg/kg/ <b>dose</b> DAILY.*(2-5)<br>*Up to 0.6 mg/kg/ <b>day</b> - can be used in <b>2 divided doses</b> if required (5)   |
| <b>Dose adjustment</b>       | Therapeutic hypothermia – No information.<br>ECMO – No information.<br>Renal impairment – No dosage adjustment is required.(6)<br>Hepatic impairment - Caution in patients with liver failure, may require dose reduction.   |
| <b>Maximum dose</b>          | 0.6 mg/kg/ <b>day</b> (2,5)  |
| <b>Total cumulative dose</b> | N/A  |
| <b>Route</b>                 | Oral   |
| <b>Preparation</b>           | <b>Oral suspension:</b> 1 mg/mL preparation compounded by pharmacy.<br><b>5 mg tablet:</b> 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.<br><b>10 mg tablet:</b> 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. |
| <b>Administration</b>        | Oral   |
| <b>Monitoring</b>            | Blood pressure monitoring is recommended.<br>Liver function tests.   |
| <b>Contraindications</b>     | Not to be used in hypotensive or septic neonates.<br>Hypersensitivity to amlodipine or components of the formulation.  |
| <b>Precautions</b>           | Congestive heart failure<br>Hepatic impairment<br>Severe aortic stenosis   |
| <b>Drug interactions</b>     | 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.<br>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.  |
| <b>Adverse reactions</b>     | Reflex tachycardia(5)<br>Peripheral oedema, hypotension, flushing, hypersensitivity reactions (Steven Johnson syndrome, dermatitis, angioedema)<br>Cholestatic jaundice, hepatitis, toxic epidermal necrolysis, acute interstitial nephritis.  |
| <b>Compatibility</b>         | Not applicable.  |
| <b>Incompatibility</b>       | Not applicable.  |
| <b>Stability</b>             | Oral suspension of 1 mg/mL: 60 day expiry (15)<br>Tablet dispersed in water: Prepare a fresh solution for each dose. Discard unused portion.   |
| <b>Storage</b>               | Tablets: Store below 25°C<br>Compounded oral suspension: 2-8°C   |
| <b>Excipients</b>            | Norvasc brand: Microcrystalline cellulose, calcium hydrogen phosphate, sodium starch glycolate, magnesium stearate.  |
| <b>Special comments</b>      | 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.   |

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| <b>Evidence</b>        | <p><b>Background</b><br/>Incidence of hypertension in neonates ranges from 0.2 to 3%.<sup>(2)</sup> 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.<sup>(7, 8)</sup> 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.<sup>(8)</sup></p> <p><b>Dose</b><br/>Flynn et al suggest that, as in adults, amlodipine may provide adequate blood pressure control in children when dosed once daily.<sup>(3)</sup> 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.<sup>(4)</sup> 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.<sup>(9)</sup> 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.<sup>(10)</sup></p> <p><b>Pharmacokinetics</b><br/>Amlodipine has slow onset of action (approximately 6 hours) which may be problematic in the acute setting and a prolonged duration of effect.<sup>(2,3,11)</sup> It is well absorbed with peak blood levels between 6-12 hours post dose.<sup>(1)</sup></p>  |
| <b>Practice points</b> | <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).<sup>(5)</sup> Clinical criteria for initiating antihypertensive medications are not well defined however in general sustained BP &gt;99<sup>th</sup> centile is an indication to consider treatment. <sup>(5)</sup> 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.<sup>(12-14)</sup> Amlodipine should not be used for hypertensive emergencies because it has slow onset of action and prolonged duration of effect.<sup>(GOR C; LOE III-3) (3).</sup></p>  |
| <b>References</b>      | <ol style="list-style-type: none"> <li>1. MIMS Online. Amlodipine. Accessed on 14 October 2021.</li> <li>2. Dionne JM, Abitbol CL, Flynn JT. Hypertension in infancy: diagnosis, management and outcome. <i>Pediatric nephrology</i>. 2012; 27(1):17-32.</li> <li>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.</li> <li>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.</li> <li>5. Flynn JT. The hypertensive neonate. <i>Seminars in Fetal and Neonatal Medicine</i>; 2020: Elsevier. <a href="https://doi.org/10.1016/j.siny.2020.101138">https://doi.org/10.1016/j.siny.2020.101138</a>.</li> <li>6. Paediatric Renal Dosing. Dosing guidance for pediatric renal patients. US Kidney disease website. Accessed on 14 October 2021.</li> <li>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.</li> <li>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.</li> <li>9. Flynn JT. Efficacy and safety of prolonged amlodipine treatment in hypertensive children. <i>Pediatric Nephrology</i>. 2005; 20(5):631-5.</li> <li>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.</li> <li>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.</li> <li>12. Flynn JT. Neonatal hypertension: diagnosis and management. <i>Pediatric nephrology</i>. 2000;14(4):332</li> </ol> |

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|  | <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 &amp; 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> |
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