Alert	Short-acting nifedipine has been abandoned as a treatment for severe hypertension in adults as a result of significant adverse effects.(1) Nifedipine is a poor choice for control of severe hypertension in infants and children because of unpredictable fall in BP after administration. It should only be used in consultation with renal physician, cardiologist or neonatologist. Alternative agents (e.g. IV nicardipine, IV hydralazine or oral captopril) that produce more controlled reductions in blood pressure and that are easier to accurately dose and administer are preferred for short-term control of severe hypertension.(1) Sublingual route is not recommended in neonates.
Indication	Acute severe hypertension – For short term control* *Refer to alert section.
Action	Inhibits 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	Adalat, Adefin, Nifelat (SAS), Ratiopharm (SAS)
Presentation	Tablets: 10 mg and 20 mg (conventional release) Ratiopharm oral solution: 20 mg/mL (SAS product)
Dose	0.05 – 0.25 mg/kg/dose. Can be repeated 6 hourly if required. (1,2,4) *Start with lower end of the dose range to avoid precipitous fall in blood pressure.
Dose adjustment	Therapeutic hypothermia – No information. ECMO – No information. Renal impairment - No dose adjustment is needed (3) Hepatic impairment - May need dose reduction in severe hepatic impairment.
Maximum dose	0.3 mg/kg/dose (higher dosing should be discussed with paediatric nephrologist)
Total cumulative dose	Not applicable
Route	Oral Sublingual route is not recommended in neonates
Preparation	Conventional release 10 mg and 20 mg tablets can be crushed. Modified release tablets can't be crushed.
Administration	Oral
Monitoring	Close monitoring of blood pressure: Continuous monitoring of arterial blood pressure if feasible. Non-invasive BP: Measure every 10 minute for first 30 minutes followed by 30-60 minute intervals for next 4 hours.
Contraindications	Ischaemic conditions or hypovolaemia Hypersensitivity to nifedipine or components of the formulation.
Precautions	Congestive heart failure, aortic stenosis Concomitant use of CYP3A4 inhibitors (e.g. erythromycin, azole antifungals) Hepatic impairment - Mainly protein bound (> 90%) and binding may be significantly reduced in severe hepatic impairment.
Drug interactions	Nifedipine is metabolised by CYP3A4. Inhibitors of CYP3A4 (e.g. erythromycin, fluconazole) may reduce clearance of nifedipine and result in increased plasma concentrations and adverse effects. Concurrent use will require blood pressure monitoring. Inducers of CYP3A4 (e.g. phenytoin) reduces the bioavailability of nifedipine. Clinical response needs to be monitored and dose increase may be necessary. Nifedipine may increase blood pressure lowering effect of other anti-hypertensives including diuretics and may result in reduced digoxin clearance and increased digoxin levels.
Adverse reactions	Hypotension, peripheral oedema, flushing. Reactive tachycardia shortly after use.
Compatibility	Not applicable
Incompatibility	Not applicable
Stability	Ratiopharm: 12 months from the date of opening. Liquid form stability is limited, follow local guidelines. Check with hospital pharmacy for in-house preparation.

Storage	Tablet and oral solution: Store below 25°C. Protect from light.
Excipients	Ratiopharm: Macrogol 200
Special comments	'Sublingual' administration of nifedipine, in reality, does not mean absorption of the drug in the mouth itself; rather, it is likely that all absorption of the drug occurs in the gastrointestinal tract, with 'sublingual' administration leading to more rapid onset of drug effect than administration of an intact capsule.(1)
Evidence	**Efficacy** There are no prospective trials on nifedipine in term and preterm infants with hypertension. There are only retrospective studies reported on the safety and efficacy of nifedipine in paediatric population and most were on the use of sublingual nifedipine.(1) Blaszak et al reported a retrospective review of 117 children (mean age 11.6 ± 5.3 years; range 0.1 – 18.9 years) with severe hypertension. The mean nifedipine dose was 0.23 ± 0.12 mg/kg (range 0.04 – 0.69 mg/kg), and the mean BP reduction within 2 h after the dose was 17% for systolic BP and 23% for diastolic BP. Significantly, BP reductions of > 25% occurred in about a third of children who received > 0.25 mg/kg.(4) Egger et al retrospectively reviewed nifedipine given to 166 hypertensive children (mean age 8.5 years; range 4 months – 18 years).(2) The mean dose was 0.30 mg/kg (range 0.04 – 1.3 mg/kg), and mean BP reduction within 6 h after administration was 17% for systolic BP and 28% for diastolic BP. They also reported that BP response was unpredictable. Adverse events occurred in about 10% of patients, and included neurological events (mostly in patients with acute CNS injury), symptomatic hypotension requiring intervention, and desaturations. Most of the patients who experienced neurological events, and all of the patients with symptomatic hypotension, had experienced BP reductions of > 20%. **Safety** There are several case reports of sudden, profound hypotension in hypertensive children with sublingual nifedipine (8-12). Case reports do not establish causality or give useful information about how frequently such events may occur.(8) The case series published by Blaszak et al suggest that use of short-acting nifedipine appears to be safe but that precipitous BP reductions can occur if doses of > 0.25 mg/kg.(4) Another large series published by Egger et al suggest that short-acting nifedipine is safe in most patients, except perhaps in those with underlying central nervous system injury, but that it should be used with caution. In addition, they reported that, as a result of their experience, they had decreased their starting nifedipine dose to 0.10 mg/kg.(2)
Practice points	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, hypercalcemia, volume overload).(1) Clinical criteria for initiating antihypertensive medications are not well defined in neonates.(1) 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.(5-7)
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