PRESCRIBING INFORMATION
Sinora 0.08 mg/ml and 0.16 mg/ml solution for infusion

Presentation: Sinora 0.08 mg/ml; 1ml contains 0.08 mg of noradrenaline. Each 50ml vial contains 4mg of noradrenaline. Sinora 0.16 mg/ml; 1ml contains 0.16mg noradrenaline. Each 50ml vial contains 8mg of noradrenaline.

Indication: On-going treatment of hypotensive emergencies in adult patients weighing >50kg with escalating noradrenaline requirements.

Dosage and Administration: For intravenous infusion into a central vein via cannula. Should be used with a suitable syringe driver pump capable of accurately and consistently delivering the minimum specified volume at a strictly controlled rate of infusion. Should only be administered by those familiar with its use. Should not to be used for initiating vasopressor treatment; consider for use in patients already established on noradrenaline therapy whose dose requirements are clinically confirmed to be escalating. Sinora 0.08 mg/ml solution for infusion may be commended at a flow rate of 1.5ml/h and Sinora 0.16 mg/ml solution for infusion may be commenced at a flow rate of 0.75ml/h. Blood pressure control should be monitored carefully for the duration of therapy, and preferably controlled by arterial blood pressure monitoring. Initiation should be performed using a less concentrated noradrenaline solution to enable more accurate titration, by 0.05 and 0.1 mcg/kg/min steps. The initial dose is usually between 0.05 and 0.15 mcg/kg/min. The recommended maintenance dose is between 0.05 to 1 mcg/kg/min and should be titrated in steps of 0.05 to 0.1 mcg/kg/min as necessary with the aim to establish low normal systolic pressure (100 to 120 mmHg) or adequate mean arterial pressure (>65 mmHg – depending on the patient's condition). Infusion rates and relative adjustments must be determined according to the required posology. Manual bolus for priming when initiating an infusion is not recommended. Caution is required during syringe relay to avoid haemodynamic instability. Continuous noradrenaline infusion through a double pump system and an extension set reducing dead-space volume should be encouraged. Administration should continue until high-dose vasoactive support is no longer needed. Abrupt withdrawal can result in acute hypotension, therefore the infusion should be gradually reduced and switched to a lower concentration infusion. The solution for infusion should not be diluted before use. It should not be mixed with other medicines. Where it is necessary to administer noradrenaline at the same time as total blood or plasma, the latter must be administered in a separate drip. There is no experience in treating patients with renal or hepatic impairment. Elderly patients may be more sensitive to the effects of noradrenaline. Efficacy and safety in children and adolescents have not been established.

Contraindications: Hypersensitivity to noradrenaline or to any of the excipients, hypotension due to hypovolaemia, use with caution in patients receiving cyclopropane or halothane anaesthesia, or any other cardiac sensitising agent or who exhibit profound hypoxia or hypercarbia.

Precautions and Warnings: Noradrenaline should be used in conjunction with appropriate blood volume replacement. During infusion, blood pressure and rate of flow should be monitored frequently to avoid hypertension. Prolonged administration may result in plasma volume depletion which should be continuously corrected by fluid and electrolyte replacement therapy. Failure to do so may result in hypotension when noradrenaline is discontinued or maintenance of blood pressure with the risk of severe peripheral and visceral vasoconstriction with reduced blood flow and tissue perfusion with subsequent tissue hypoxia, lactic acidosis and possible ischaemic injury. Care should be taken to avoid extravasation and injection site should be changed in the event of injection site blanching. In the event of extravasation, the injection site should be irrigated using a fine needle with 10 to 15ml of physiological salt solution containing 5 to 10mg phentolamine mesilate. Caution is recommended in patients with hyperthyroidism or diabetes mellitus, major left ventricular dysfunction associated with acute hypotension, patients with coronary, mesenteric or peripheral vascular thrombosis, patients with hypotension following myocardial infarction and patients with Prinzmetal´s variant angina. Dosage must be reduced if arrythmia occurs during treatment. The product contains 165.3 mg sodium per 50 ml vial, equivalent to 8.3% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Interactions: Concomitant use with volatile halogen anaesthetics should be avoided due to the risk of severe ventricular arrhythmia. Concomitant use with imipramine or serotoninergic-adrenergic antidepressants should be avoided due to the risk of paroxysmal hypertension and possibility of arrythmia. Use with caution with MAO-inhibitors and linezolid due to the potential increase in pressor action. Use with alpha-blockers may reduce the vasopressor effect of noradrenaline. Use with beta-blockers may reduce the stimulating effect of noradrenaline on the heart and increase the risk of severe hypertension. Use with caution with thyroid hormones, cardiac glycosides and antiarrhythmic agents due to the risk of increased cardiac effects by these drugs. Ergot alkaloids or oxytocin may enhance the vasopressor and vasoconstrictive effects of noradrenaline.

Pregnancy and Lactation: Use in pregnancy may impair placental perfusion and induce foetal bradycardia, with the potential to exert a contractile effect on the uterus leading to foetal asphyxiation in late pregnancy. The risk to the foetus should be weighed against the benefit to the mother. No information is available on use in lactation.

Undesirable effects: Anxiety, insomnia, confusion, weakness, psychotic state, headache, tremor, acute glaucoma (very frequent in those predisposed), tachycardia, bradycardia, arrythmias, palpitations, increase in cardiac muscle contractility, acute cardiac insufficiency, stress cardiomyopathy, arterial hypertension, tissue hypoxia, ischaemic injury (including gangrene of the extremities) resulting in coldness and paleness of the members and the face, respiratory insufficiency or difficulty, dyspnoea, nausea, vomiting, urine retention, injection site irritation and injection site necrosis. The frequency of these adverse reactions cannot be estimated from available data. Continuous administration in the absence of blood volume replacement may cause severe peripheral and vascular vasoconstriction, reduced renal blood flow and urine production, hypoxia and increased serum lactate levels.

Overdose: Overdosage may result in severe hypertension, reflex bradycardia, marked increase in peripheral resistance and decreased cardiac output. These may be accompanied by violent headache, photophobia, retrosternal pain, pallor, intense sweating and vomiting. In the event of overdosage, treatment should be withdrawn, and appropriate corrective treatment initiated.

Please refer to full SmPC for Sinora before prescribing.

Legal Category: POM

Basic NHS Cost: 0.08 mg/ml; 1 x 50ml vial £9.97. 0.16 mg/ml; 1 x 50ml vial £14.22

Marketing Authorisation Numbers: Sinora 0.08 mg/ml solution for infusion - PL 46926/0003. Sinora 0.16 mg/ml solution for infusion - PL 46926/0004.

Marketing Authorisation Holder: Sintetica Limited, 30th Floor, 40 Bank Street, Canary Wharf, London, E14 5NR, United Kingdom

Date of Review: March 2020

Adverse events should be reported to the local regulatory authority. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Sintetica Limited Medical Information on 01748 827269 or via e-mail to SinteticaGB@EU.ProPharmaGroup.com