

Norepinephrine

Norepinephrine Bitartrate - Potent Alpha-1 & Beta-1 Inotrope / Vasopressor

Vasopressors & Inotropes / Vasopressors

Evidence status: current

ICU High-Yield Summary

Norepinephrine is the recommended first-line vasopressor for septic shock and is widely used for other vasodilatory shock states. In cardiogenic shock, vasopressor/inotrope selection depends on blood pressure, cardiac output and shock phenotype rather than a universal first-line rule.

Mechanism of Action

Alpha-1 Vascular Smooth Muscle & Beta-1 Cardiomyocyte Agonism

1. Binds vascular alpha-1 adrenergic receptors, inducing intense arterial and venous vasoconstriction. 2. Increases Systemic Vascular Resistance (SVR) and Mean Arterial Pressure (MAP). 3. Stimulates cardiac beta-1 adrenergic receptors, increasing myocardial contractility and stroke volume. 4. Minimal beta-2 receptor activation, preventing unwanted peripheral vasodilation.

ICU Clinical Reasoning

Why I Choose It

First-line recommended vasopressor in Surviving Sepsis Campaign guidelines for Septic Shock. | Increases MAP primarily via SVR elevation while preserving or increasing cardiac output. | Lower arrhythmia risk compared to Dopamine.

Why I Avoid / Key Limitations

Extravasation causes severe local tissue ischemic necrosis. | Excessive vasoconstriction in hypovolemia causes visceral and digital ischemia. | Increases myocardial oxygen demand.

Bedside Pearl

Norepinephrine is the first-line vasopressor for septic shock. When the norepinephrine requirement is escalating, SSC 2026 suggests adding vasopressin rather than relying on a universal numeric trigger; follow the local fixed-dose vasopressin protocol and reassess shock phenotype.

Dosing & Administration

Routine ICU Dosing

Septic shock: titrate norepinephrine promptly to the perfusion/MAP target (SSC uses an initial MAP target around 65 mmHg for most adults), using the institution's standardized concentration and weight-based or non-weight-based protocol. Do not equate 0.02-0.05 mcg/kg/min with a fixed 2-5 mcg/min across body weights. Current U.S. norepinephrine labeling for acute hypotension starts 8-12 mcg/min and lists a typical maintenance dose of 2-4 mcg/min; ICU sepsis protocols commonly use different weight-based starting schemes. There is no universal evidence-based maximum in refractory shock.

Hemodialysis

No dialysis-specific dose is established in the U.S. label; titrate continuously to hemodynamic effect rather than applying a renal replacement dose table.

CRRT

No CRRT-specific dose is established; titrate continuously to hemodynamic effect.

Renal Dose Table

Any CrCl: No renal adjustment required; titrate to target MAP.

Organ Failure Considerations

Renal Failure & AKI

Use to restore an appropriate perfusion pressure; do not claim a predictable increase in GFR. Renal response depends on baseline perfusion, congestion, autoregulation and overall shock resuscitation.

Hepatic Impairment

Titrate to hemodynamic effect; no universal hepatic dose adjustment is used in shock, but critical illness can alter response.

Toxicity & Safety

Major Warnings

Peripheral extravasation causes severe ischemic tissue necrosis. | Severe organ hypoperfusion if given without adequate volume resuscitation in hypovolemia. | Arrhythmias and myocardial ischemia.

Organ Toxicities

Vascular & Tissue: Ischemic necrosis upon extravasation, digital gangrene in refractory shock. | Cardiovascular: Tachycardia, atrial/ventricular arrhythmias, myocardial ischemia.

Drug Interactions

Bedside Interactions

MAO Inhibitors / Tricyclic Antidepressants: Inhibition of catecholamine breakdown; consequence: Severe hypertensive crisis; ICU action: Titrate norepinephrine extremely cautiously at low initial doses.

Monitoring & TDM

Monitoring

Continuous arterial blood pressure (arterial line preferred) | Heart rate and ECG rhythm | Perfusion markers (lactate, urine output, ScvO₂) | IV site for extravasation

Evidence & Source Traceability

Claim-Level Citations

Surviving Sepsis Campaign 2026 recommends norepinephrine as the first-line vasopressor for adults with septic shock. - Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2026.

(<https://sccm.org/clinical-resources/guidelines/guidelines/surviving-sepsis-campaign-international-guidelines-for-management-of-sepsis-and-septic-shock-2026>)

Guideline IDs

shock-guideline-esicm-2025