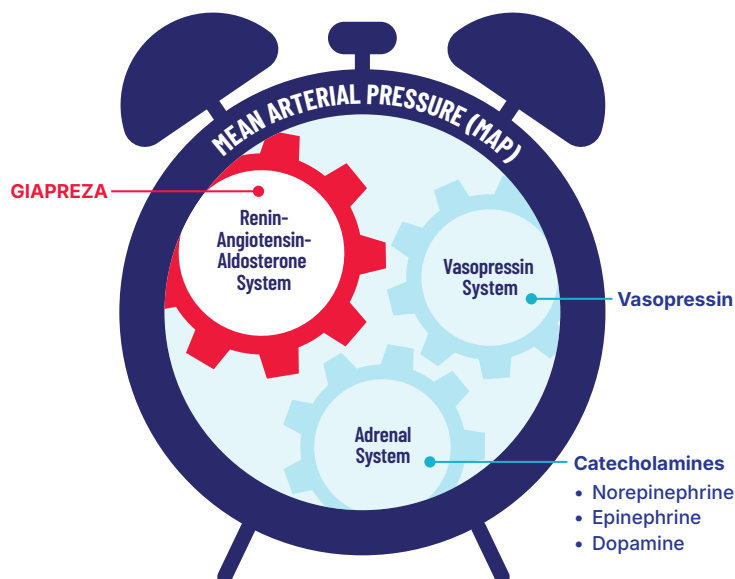


COULD NEGLECTING RAAS *COMPROMISE PATIENT OUTCOMES* IN DISTRIBUTIVE SHOCK?



> RAAS is the essential third mechanism for optimal MAP control¹⁻³

The renin-angiotensin-aldosterone system (RAAS) produces **angiotensin II (ANG II)**, a **naturally occurring peptide hormone** that triggers vasoconstriction and increases blood pressure.^{4,5}



Traditional SOC vasopressors only address the adrenergic and vasopressin systems that regulate blood pressure, and therefore may be insufficient for some patients.^{2,3,6,7}

RAAS complements the adrenergic and vasopressin systems as a key regulator of MAP.⁸

Increased exposure to high-dose catecholamines and vasopressin is associated with adverse physiologic and clinical effects, including⁸⁻¹¹

- Tachyphylaxis and reduced vascular responsiveness
- Cardiovascular and ischemic adverse effects
- Worsening organ dysfunction
- Increase in mortality risk—potentially by up to 80%

With the risk of worsening organ dysfunction, why wait to engage the RAAS pathway and rapidly restore MAP?

MAP=mean arterial pressure; SOC=standard of care.

SELECTED IMPORTANT SAFETY INFORMATION

Indication

GIAPREZA® (angiotensin II) increases blood pressure in adults with septic or other distributive shock.

Contraindications

None.

Warnings and Precautions

The safety of GIAPREZA was evaluated in 321 adults with septic or other distributive shock in a randomized, double-blind, placebo-controlled study, ATHOS-3. There was a higher incidence of arterial and venous thrombotic and thromboembolic events in patients who received GIAPREZA compared to placebo-treated patients in the ATHOS-3 study (13% vs. 5%). The major imbalance was in deep venous thromboses. Use concurrent venous thromboembolism (VTE) prophylaxis.

Please see additional Important Safety Information throughout.

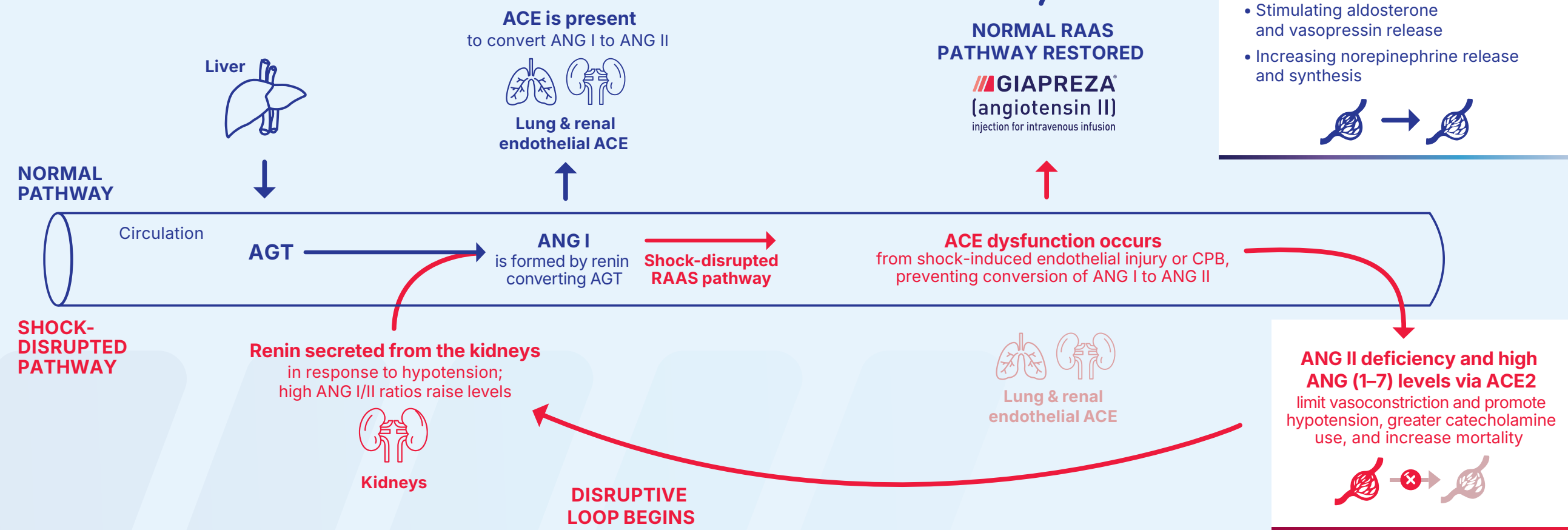
Before administering, please see the [Full Prescribing Information](#) for GIAPREZA.

 **GIAPREZA®**
(angiotensin II)
injection for intravenous infusion

RAAS IS A **CRITICAL PATHWAY** FOR ADDRESSING SEPTIC SHOCK AND VASOPLEGIA¹⁻³

RAAS dysfunction can elevate renin and ANG I and II ratios, contributing to refractory hypotension and increased vasopressor dependence⁵

RAAS PATHWAY^{1,5,12-15,*}



In distributive shock, the following factors can contribute to RAAS dysfunction:

- Organ dysfunction⁵
- Exposure to RAAS-inhibiting medications¹⁶
- CPB¹

*This figure is based on post hoc exploratory analyses and animal studies.
ACE=angiotensin-converting enzyme; AGT=angiotensinogen; CPB=cardiopulmonary bypass.

SELECTED IMPORTANT SAFETY INFORMATION Adverse Reactions

The most common adverse reactions reported in greater than 10% of GIAPREZA-treated patients were thromboembolic events. Adverse reactions occurring in $\geq 4\%$ of patients treated with GIAPREZA and $\geq 1.5\%$ more often than placebo-treated patients in the ATHOS-3 study were thromboembolic events (including deep vein thrombosis), thrombocytopenia, tachycardia, fungal infection, delirium, acidosis, hyperglycemia, and peripheral ischemia.

Please see additional Important Safety Information throughout.
Before administering, please see the [Full Prescribing Information](#) for GIAPREZA.

GIAPREZA is the only vasopressor that directly addresses RAAS dysfunction—restoring a vital, yet often overlooked, pathway to rapidly raise MAP in distributive shock.^{3,4}

GIAPREZA[®] (angiotensin II): **UNIQUELY ENGAGES THE RAAS PATHWAY, CRITICAL FOR MAP CONTROL^{3,4}**

Recognizing and addressing RAAS dysfunction plays a key role in restoring hemodynamic stability^{1-3,7}



Consider patients with distributive shock in whom RAAS dysfunction may be present

- AKI¹⁷
- CKD¹⁸
- ACE inhibitor/ARB exposure⁵
- ARDS¹⁹
- Decompensated liver disease²⁰
- Cardiac surgery where CPB was required¹

Initiating GIAPREZA gives you a multimodal strategy for restoring target MAP and reducing catecholamine burden^{4,6,*}

*GIAPREZA was studied in ATHOS-3, an international, randomized, double-blind, placebo-controlled trial of 321 patients with distributive shock who remained hypotensive despite fluid and vasopressor therapy. Patients received either GIAPREZA (n=163) plus SOC vasopressors or placebo (n=158) plus SOC vasopressors (which included norepinephrine, epinephrine, dopamine, phenylephrine, and vasopressin). The primary endpoint was MAP response defined as an increase in MAP at hour 3 of ≥ 10 mmHg, or a MAP response of ≥ 75 mmHg, without an increase in baseline vasopressor dosing. Doses of GIAPREZA or placebo were titrated to a target MAP of ≥ 75 mmHg during the first 3 hours of treatment while doses of other vasopressors were maintained. From hour 3 to hour 48, GIAPREZA or placebo was titrated to maintain a MAP between 65 and 70 mmHg while reducing doses of other vasopressors. Seventy percent of patients (n=114/163) achieved MAP response with GIAPREZA plus SOC vs 23% of patients (n=37/158) with placebo plus SOC ($P < 0.0001$). Median time to reach target MAP was 5 minutes.^{4,6}

AKI=acute kidney injury; ARB=angiotensin II receptor blocker; ARDS=acute respiratory distress syndrome; CKD=chronic kidney disease.

SELECTED IMPORTANT SAFETY INFORMATION

Drug Interactions

Angiotensin converting enzyme (ACE) inhibitors may increase response to GIAPREZA. Angiotensin II receptor blockers (ARBs) may reduce response to GIAPREZA.

You are encouraged to report negative side effects of prescription drugs to the FDA.

To report SUSPECTED ADVERSE REACTIONS, please contact:

La Jolla Pharmaceutical Company

1-800-651-3861 | medicalinformation@ljpc.com

U.S. Food and Drug Administration

1-800-FDA-1088 | www.fda.gov/medwatch

Please see additional Important Safety Information throughout.

Before administering, please see the Full Prescribing Information for GIAPREZA.

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