



**For distributive shock
including vasoplegia**

READY. SET. REACH TARGET MAP. FAST.

GIAPREZA®
(angiotensin II)
injection for intravenous infusion

Rapidly stabilize MAP in a median of 5 minutes.

For septic or other distributive shock, act fast with GIAPREZA®—
the first and only vasopressor designed to regulate RAAS in your patients.¹

MAP=mean arterial pressure; RAAS=renin-angiotensin-aldosterone system.

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.

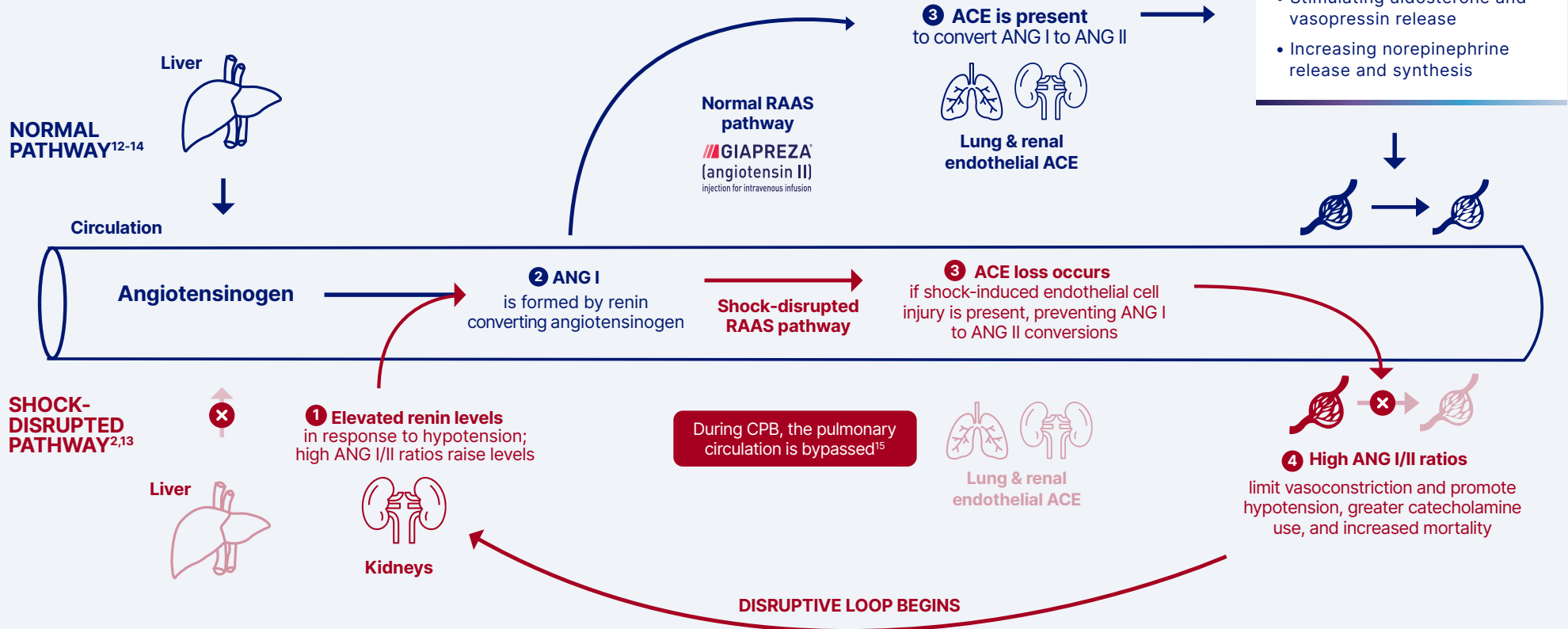
QUICKLY REGULATE RAAS TO IMPROVE PATIENT SURVIVAL

In patients with shock, the RAAS pathway may be disrupted by an ACE deficiency, leading to abnormally high ANG I/II ratios. This disruption can trap patients in a potentially fatal cycle.^{2,3} Vasoplegia is a type of distributive shock that can occur in up to 27% of patients who undergo cardiopulmonary bypass.^{4,5} In groups with predisposing factors, the rate can be as high as 50%.⁵ It is characterized by normal to high cardiac output and low systemic vascular resistance that generally occurs during or within 24 hours of CPB.⁶

Relative angiotensin II deficiency (as measured by high levels of renin and angiotensin I to II ratios during vasoplegia):

- contributes to a reduction of vascular tone, leading to vasodilation and subsequent organ hypoperfusion⁶⁻⁸
- has been associated with a significantly greater risk of mortality⁹

Risk factors for vasoplegic shock include renal failure, use of ACEi/ARB, duration of bypass, or previous cardiac surgery.^{6,10,11}



This figure is based on post hoc exploratory and animal studies.^{2,16}

ACE=angiotensin-converting enzyme; ACEi=ACE inhibitor; ANG=angiotensin; ARB=angiotensin II receptor blockers; 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.

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REGULATING RAAS CAN **STABILIZE MAP FAST**

GIAPREZA®
(angiotensin II)
injection for intravenous infusion



Not an actual patient.

Sam | 48



Undergoes coronary artery bypass grafting

Medical history: hypertension, obesity, type 2 diabetes mellitus, and hypercholesterolemia

Admitted for: non-ST-segment elevation myocardial infarction

Imaging: indicates triple-vessel disease

0 min
Post-op MAP drops to 56 mmHg

5 min
MAP drops to 54 mmHg

10 min
MAP drops to 53 mmHg

20 min
MAP drops to 52 mmHg

Sam develops vasoplegia coming out of surgery.
Norepinephrine is initiated at **0.05 mcg/kg/min.**

Post-operative cardiac index: 3.3 L/min/m²
Hemoglobin: 8.4 g/dL

Norepinephrine is titrated to **0.10 mcg/kg/min.**
Vasopressin is initiated at **0.04 units/min.**

After cardiopulmonary bypass, for every 10 min of MAP <55 mmHg, mortality risk increases by 30%.¹⁷

A MAP <65 mmHg for >10 min is associated with higher rates of stroke and renal replacement therapy.^{18,19}

START GIAPREZA® EARLY—rapidly stabilize MAP in a median of 5 minutes.²⁰

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.

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

WHEN MAP DROPS, ACT FAST WITH GIAPREZA®

The first and only synthetic human ANG II treatment, designed specifically to regulate RAAS and stabilize MAP fast¹



Regulate RAAS to help increase survival, reduce catecholamine use, and shorten days in the ICU^{2,21}



Rapidly achieve and sustain target MAP in a median of 5 minutes²¹



Initiate GIAPREZA early—survival benefit was greater with lower vasopressor doses^{20,*}

*Exploratory post hoc analysis.²⁰

DON'T WAIT

GIAPREZA is a catecholamine-sparing agent that can rapidly stabilize MAP and may help save lives^{2,22}



Available in a 0.5 mg/mL vial offering flexibility for patient treatment

References: 1. National Center for Biotechnology Information. PubChem Compound Summary for CID 172198, angiotensin I. <https://pubchem.ncbi.nlm.nih.gov/compound/Angiotensin-II-human>. Accessed March 12, 2024. 2. Bellomo R, Forni LG, Busse LW, et al. Renin and survival in patients given angiotensin II for catecholamine-resistant vasodilatory shock. *Am J Respir Crit Care Med*. 2020;202(9):1253-1261. doi:10.1164/rccm.201911-2172OC 3. Supplementary appendix to: Khanna A, English SW, Wang XS, et al. Angiotensin II for the Treatment of Vasodilatory Shock. *N Engl J Med*. 2017;377(5):419-430. doi: 10.1056/NEJMoa1704154 4. Lambden S, Creagh-Brown BC, Hunt J, Summers C, Forni LG. Definitions and pathophysiology of vasoplegic shock. *Crit Care*. (2018) 22:174 doi: 10.1186/s13054-018-2102-1 5. Weis F, Kilger E, Beiras-Fernandez A, et al. Association between vasopressor dependence and early outcome in patients after cardiac surgery. *Anaesthesia*. 2006 Oct;61(10):938-42. doi: 10.1111/j.1365-2044.2006.04779.x 6. Busse LW, Barker N, Petersen C. Vasoplegic syndrome following cardiothoracic surgery—review of pathophysiology and update of treatment options. *Crit Care*. 2020;24:36. doi:10.1186/s13054-020-2743-8 7. Chow JH, Wittwer ED, Wieruszewski PM, Khanna AK. Evaluating the evidence for angiotensin II for the treatment of vasoplegia in critically ill cardiothoracic surgery patients. *J Thorac Cardiovasc Surg*. 2022;163:1407-14. doi:10.1016/j.jtcvs.2021.02.097 8. Papazisi O, Palmen M, Danser AHJ. The use of angiotensin II for the treatment of post-cardiopulmonary bypass vasoplegia. *Cardiovasc Drugs Ther*. 2022;36:739-748. doi:10.1007/s10557-020-07098-3 9. Bellomo R, Wunderink RG, Szerlik H, et al. Angiotensin I and angiotensin II concentrations and their ratio in catecholamine-resistant vasodilatory shock. *Crit Care*. 2020; 24:43. doi: 10.1186/s13054-020-2733-x 10. Dayan V, Cal R, Giangrossi F. Risk factors for vasoplegia after cardiac surgery: a meta-analysis. *Interact Cardiovasc Thorac Surg*. 2019;28(6):838-844. doi:10.1093/icvts/ivy352 11. Liu H, Yu L, Yang L, Green MS. Vasoplegic syndrome: An update on perioperative considerations. *J Clin Anesth*. 2017;40:63-71. doi:10.1016/j.jclinane.2017.04.017 12. Andrews L, Benken J, Benedetti E, et al. Effects of angiotensin II in the management of perioperative hypotension in kidney transplant recipients. *Clin Transplant*. 2022;36(9):e14754. doi: 10.1111/ctr.14754 13. Fountain JH, Kaur J, Lappin SL. Physiology, Renin Angiotensin System. StatPearls Publishing; 2023. <https://www.ncbi.nlm.nih.gov/books/NBK470410/>. Accessed January 22, 2024. 14. Wang Y, Seto SW, Golledge J. Angiotensin II, sympathetic nerve activity and chronic heart failure. *Heart Fail Rev*. 2014;19(2):187-98. doi: 10.1007/s10741-012-9368-1 15. Machin D, Allsager C. Principles of cardiopulmonary bypass. CEACCP. 2006; 6:5 (176-181). doi:10.1093/bjaceaccp/mk1043 16. Wan L, Langenberg C, Bellomo R, et al. Angiotensin II in experimental hyperdynamic sepsis. *Crit Care*. 2009;13(6):R190. doi: 10.1186/cc8185 17. Ristovic V, de Roock S, Mesana TG, et al. The Impact of Preoperative Risk on the Association between Hypotension and Mortality after Cardiac Surgery: An Observational Study. *J Clin Med*. 2020;9(7):2057. doi: 10.3390/jcm9072057 18. Sun LY, Chung AM, Farkouh ME, et al. Defining an Intraoperative Hypotension Threshold in Association with Stroke in Cardiac Surgery. *Anesthesiology*. 2018;129(3):440-447. doi: 10.1097/ALN.0000000000002298 19. Ngu JMC, Jabagi H, Chung AM, et al. Defining an Intraoperative Hypotension Threshold in Association with De Novo Renal Replacement Therapy after Cardiac Surgery. *Anesthesiology*. 2020;132(6):1447-1457. doi: 10.1097/ALN.0000000000003254 20. Wieruszewski PM, Bellomo R, Busse LW, et al. Initiating angiotensin II at lower vasopressor doses in vasodilatory shock: an exploratory post-hoc analysis at the ATHOS-3 clinical trial. *Crit Care*. 2023;27(1):175. doi: 10.1186/213054-023-04446-1 21. Khanna A, English SW, Wang XS, et al. Angiotensin II for the Treatment of Vasodilatory Shock. *N Engl J Med*. 2017;377(5):419-430. doi: 10.1056/NEJMoa1704154 22. Buckley MS, Barletta JF, Smithburger PL, et al. Catecholamine Vasopressor Support Sparing Strategies in Vasodilatory Shock. *Pharmacotherapy*. 2019;39(3):382-398. doi: 10.1002/phar.2199

IMPORTANT SAFETY INFORMATION

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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

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

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