Why is it important to treat hyperphosphatemia?

Akebia THERAPEUTICS

Hyperphosphatemia is a common condition in patients with CKD on dialysis[1-3]

43%

43% of in-center dialysis **patients have phosphorus levels above the KDOQI recommended range** (3.5 to 5.5 mg/dL)[1,2,4]

In a 9-month retrospective analysis of 47,742 patients who were new to hemodialysis[5]

- **85% did not maintain** mean serum phosphorus levels within the KDOQI range

  Only 52% received phosphate binders despite inadequate control in the majority of patients

Observational data have shown that **hyperphosphatemia is associated with vascular calcification**[6]

Although some patients may not experience symptoms of hyperphosphatemia, if left untreated it can lead to: **bone and joint pain**, **daily itching**, **nausea**, **vomiting**, **fatigue**, **seizures**, and **kidney stones**[2,3,7-11]

CKD=chronic kidney disease; KDOQI=Kidney Disease Outcomes Quality Initiative.

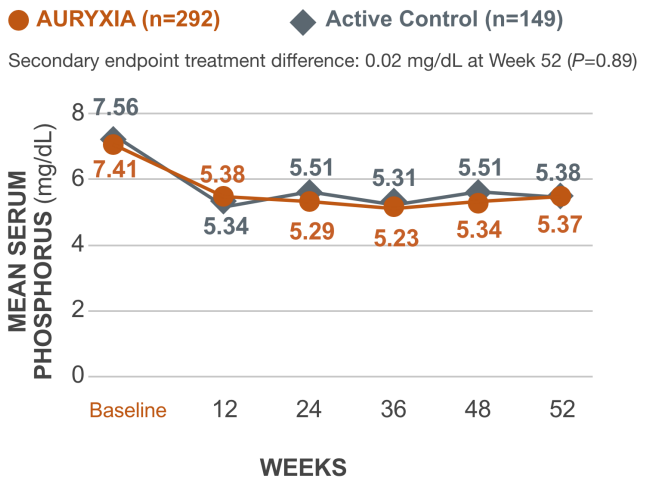
Auryxia® (ferric citrate) tablets

AURYXIA was effective in getting patients to goal when used as a monotherapy[12,13]

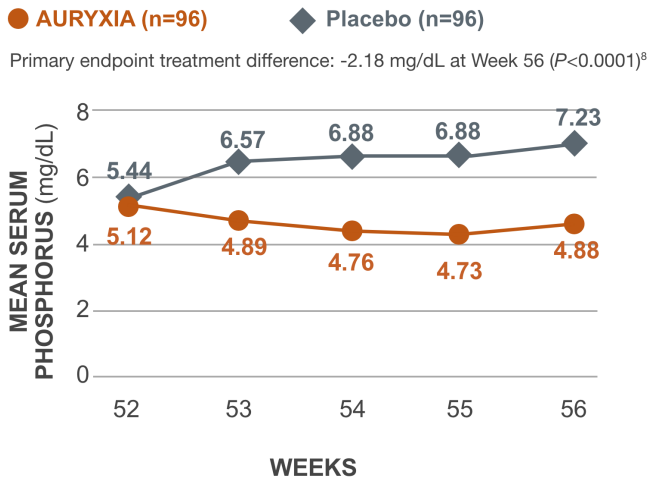
In a 56-week trial, AURYXIA delivered strong efficacy in an iron-based, non-calcium tablet[12,13]

STRONG AND SUSTAINED PHOSPHORUS REDUCTIONS FOR MORE THAN A YEAR OF TREATMENT[12,13]

AURYXIA had similar reductions in serum phosphorus compared to Active Control[12,13]



AURYXIA maintained significant reductions compared to placebo[12,13]



AURYXIA Arm Re-randomization

Patients on AURYXIA:

- Maintained mean serum phosphorus levels between 3.5 and 5.5 mg/dL after a year of treatment (up to Week 56)[12,13]
- Had a mean serum phosphorus level of 7.41 mg/dL at baseline and 4.88 mg/dL at Week 56[13]

CKD=chronic kidney disease; Active Control=sevelamer carbonate and/or calcium acetate.

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATION

AURYXIA® (ferric citrate) is contraindicated in patients with iron overload syndromes, e.g., hemochromatosis

WARNINGS AND PRECAUTIONS

- **Iron Overload:** Increases in serum ferritin and transferrin saturation (TSAT) were observed in clinical trials with AURYXIA in patients with chronic kidney disease (CKD) on dialysis treated for hyperphosphatemia, which may lead to excessive elevations in iron stores. Assess iron parameters prior to initiating AURYXIA and monitor while on therapy. Patients receiving concomitant intravenous (IV) iron may require a reduction in dose or discontinuation of IV iron therapy

Please see full Important Safety Information and full Prescribing Information, or go to AURYXIAHCP.com

Auryxia® (ferric citrate) tablets

IN A POOLED SAFETY ANALYSIS WHICH INCLUDED A 52-WEEK PIVOTAL STUDY,

the most common adverse reactions reported with AURYXIA were[12]:

Adverse reactions in >5% of patients	AURYXIA N=557
Diarrhea	21%
Discolored feces	19%
Nausea	11%
Constipation	8%
Vomiting	7%
Cough	6%

- In a pooled safety analysis of the pivotal Phase III trial and 3 short-term trials (N=557), the majority of diarrhea cases (56%) resolved within 2 weeks from onset[12,14,15]

WHO MAY BE APPROPRIATE FOR AURYXIA?

Adults with CKD receiving dialysis in need of phosphorus control, who

- are above the target phosphorus range per clinical guidance, ***or***
- may be noncompliant with their current binder, ***or***
- prefer nonchewable tablets, ***or***
- have concerns about calcium-based binders, ***or***
- are on in-center or home dialysis

CKD=chronic kidney disease; HP=hyperphosphatemia; DD=dialysis dependent.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Risk of Overdosage in Children Due to Accidental Ingestion:** Accidental ingestion and resulting overdose of iron-containing products is a leading cause of fatal poisoning in children under 6 years of age. Advise patients of the risks to children and to keep AURYXIA out of the reach of children

Please see full Important Safety Information and full Prescribing Information, or go to AURYXIAHCP.com

Need a different choice for HP in adults with CKD-DD? Reach for AURYXIA.

Auryxia® (ferric citrate) tablets

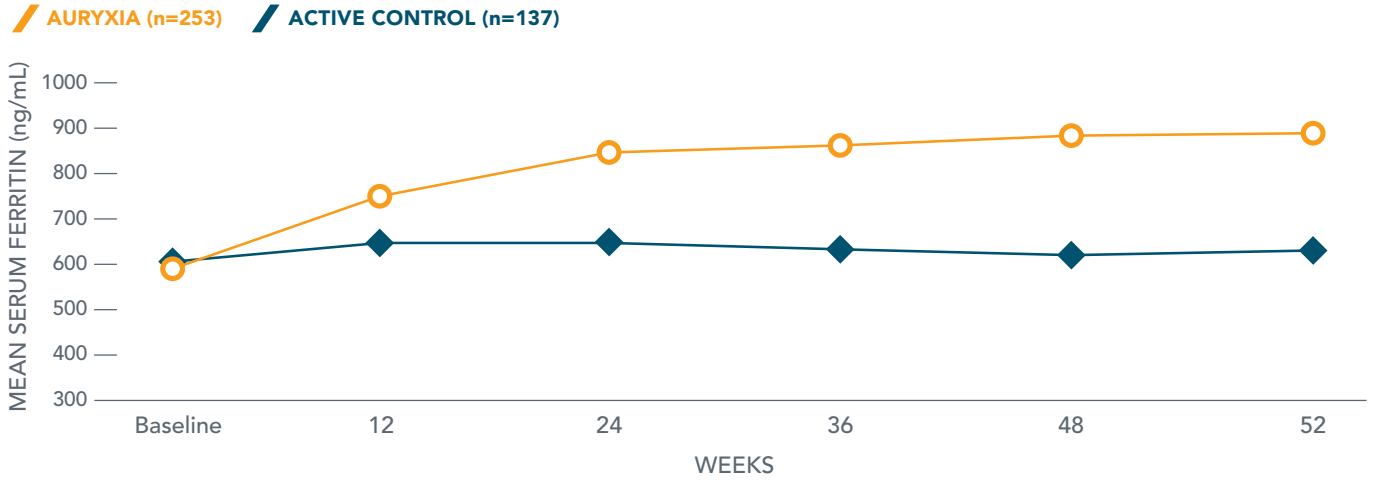
SAFETY
PHARMACODYNAMICS: AURYXIA HAS BEEN SHOWN TO INCREASE IRON PARAMETERS INCLUDING TSAT AND FERRITIN[12]

During the 52-week Active Control Period in the Phase III trial in which concomitant use of IV iron was permitted[12]:

- Because iron absorption from AURYXIA may lead to excessive elevations in iron stores, ferritin and TSAT should be monitored while on AURYXIA[12]
- Examination of serum iron parameters showed that there is a systemic absorption of iron from AURYXIA[12]
- Gradual increases in iron parameters occurred over the first 3-6 months and then plateaued[16]

Assess iron parameters prior to initiating AURYXIA as a phosphate binder and monitor while on therapy[12] AND **In patients receiving IV iron, a reduction in dose or discontinuation of IV iron therapy may be required[12]**

Mean serum ferritin levels for AURYXIA vs Active Control[17]



- Mean serum ferritin increased from 593 ng/mL at baseline to 895 ng/mL at Week 52 (302 ng/mL)[17]
- Mean TSAT increased from 31.3% at baseline to 39.2% at Week 52 (~8%)[17]

TRIAL DESIGN[12,18]

A multicenter, randomized, open-label trial evaluated the ability of AURYXIA to lower serum phosphorus in patients with CKD on dialysis over 56 weeks. Eligible patients had serum ferritin <1000 ng/mL, serum TSAT <50%, and serum phosphorus ≥2.5 and ≤8.0 mg/dL at the screening visit. Phosphate binders other than the study drugs were not permitted during the study.

The safety and efficacy of AURYXIA were studied in the 52-week active-controlled period (AURYXIA n=292, Active Control n=149), then patients were re-randomized to either continue AURYXIA treatment or receive a placebo during the placebo-controlled period, weeks 52-56 (AURYXIA n=96, Placebo n=96).

The primary endpoint was the change in serum phosphorus from baseline (Week 52) to Week 56 between AURYXIA and placebo. The key secondary endpoint was the change in serum phosphorus from baseline (Week 0) to Week 52 between AURYXIA and sevelamer carbonate and/or calcium acetate.

CKD=chronic kidney disease; IV=intravenous; TSAT=transferrin saturation; Active Control=sevelamer carbonate and/or calcium acetate.

SELECT IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

The most common adverse reactions reported with AURYXIA in clinical trials were:

- Diarrhea (21%), discolored feces (19%), nausea (11%), constipation (8%), vomiting (7%) and cough (6%)

Please see full Important Safety Information and full Prescribing Information, or go to AURYXIAHCP.com

Akebia cares®

BROAD INSURANCE COVERAGE FOR PATIENTS WITH HYPERPHOSPHATEMIA

AURYXIA is covered through the majority of commercial health plans and widely available through Medicare Part D plans[19,20]*

- A coverage determination may be required

The majority of eligible patients with commercial insurance **pay as little as $0** for AURYXIA†

All Medicare full Low-Income Subsidy (LIS)/dual-eligible patients **pay no more than $10.00 per fill** of AURYXIA

Free AURYXIA may be available for patients who are uninsured, patients who have Medicare Part D insurance but cannot afford their copays, and patients whose insurance does not cover AURYXIA‡

COVERAGE SOLUTIONS MADE *SIMPLE*

REIMBURSEMENT HELP
One-on-one support for assistance with insurance questions and challenges

COPAY CARD
Financial assistance for patients with commercial insurance†

- Visit AkebiaCaresHCP.com for copay enrollment

*Depending on the Medicare Part D insurance plan, a medical exception or prior authorization form may be required.

†Restrictions may apply. Copay assistance is not valid for prescriptions reimbursed under Medicare, Medicaid, or similar federal or state programs.

‡Medicare Part D patients with an annual income of ≤150% of the Federal Poverty Level may be eligible for LIS assistance (also called "Extra Help").

CHOOSE AURYXIA—give your patients the confidence of **sustained phosphorus control**[12,13]

AURYXIA helped patients reach and stay in the KDOQI range during a 56-week trial.[2,12,13]

KDOQI=Kidney Disease Outcomes Quality Initiative.

SELECT IMPORTANT SAFETY INFORMATION

SPECIFIC POPULATIONS

- **Pregnancy and Lactation:** There are no available data on AURYXIA use in pregnant women to inform a drug-associated risk of major birth defects and miscarriage. However, an overdose of iron in pregnant women may carry a risk for spontaneous abortion, gestational diabetes and fetal malformation. Data from rat studies have shown the transfer of iron into milk, hence, there is a possibility of infant exposure when AURYXIA is administered to a nursing woman

Please see full Important Safety Information and full Prescribing Information, or go to AURYXIAHCP.com

Auryxia® (ferric citrate) tablets

INDICATION

AURYXIA® (ferric citrate) is indicated for the control of serum phosphorus levels in adult patients with chronic kidney disease on dialysis

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION

AURYXIA® (ferric citrate) is contraindicated in patients with iron overload syndromes, e.g., hemochromatosis

WARNINGS AND PRECAUTIONS

- **Iron Overload:** Increases in serum ferritin and transferrin saturation (TSAT) were observed in clinical trials with AURYXIA in patients with chronic kidney disease (CKD) on dialysis treated for hyperphosphatemia, which may lead to excessive elevations in iron stores. Assess iron parameters prior to initiating AURYXIA and monitor while on therapy. Patients receiving concomitant intravenous (IV) iron may require a reduction in dose or discontinuation of IV iron therapy
- **Risk of Overdosage in Children Due to Accidental Ingestion:** Accidental ingestion and resulting overdose of iron-containing products is a leading cause of fatal poisoning in children under 6 years of age. Advise patients of the risks to children and to keep AURYXIA out of the reach of children

ADVERSE REACTIONS

The most common adverse reactions reported with AURYXIA in clinical trials were:

- Diarrhea (21%), discolored feces (19%), nausea (11%), constipation (8%), vomiting (7%) and cough (6%)

SPECIFIC POPULATIONS

- **Pregnancy and Lactation:** There are no available data on AURYXIA use in pregnant women to inform a drug-associated risk of major birth defects and miscarriage. However, an overdose of iron in pregnant women may carry a risk for spontaneous abortion, gestational diabetes and fetal malformation. Data from rat studies have shown the transfer of iron into milk, hence, there is a possibility of infant exposure when AURYXIA is administered to a nursing woman

DRUG INTERACTIONS

When clinically significant drug interactions are expected, e.g., Ciprofloxacin or Doxycycline, separate timing of administration.

To report suspected adverse reactions, contact Akebia Therapeutics, Inc. at 1-844-445-3799

Please see full Important Safety Information and full Prescribing Information, or go to AURYXIAHCP.com

References: 1. US-DOPPS Practice Monitor, May 2021. Serum phosphorus (most recent), categories. Accessed November 29, 2022. http://www.dopps.org/DPM/Files/phosphmgdl_c_overallTAB.htm **2.** National Kidney Foundation. K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. *Am J Kidney Dis.* 2003;42(4 Suppl 3):S1-S201. doi:10.1053/S0272-6386(03)00905-3 **3.** Pai AB. Disorders of calcium and phosphorus binders. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM, eds. *Pharmacotherapy: A Pathophysiologic Approach*, 10e. McGraw-Hill Education; 2017:chap 50. **4.** US-DOPPS Practice Monitor, October 2020. DPM sampling, study design, and calculation methods. Accessed November 29, 2022. https://www.dopps.org/dpm/Data_Sources_Methods.pdf **5.** Farrand KF, Copley JB, Heise J, Fridman M, Keith MS, Poole L. Analysis of serum phosphate control and phosphate binder utilization in incident hemodialysis patients. *Int J Nephrol Renovasc Dis.* 2014;7:261-269. doi:10.2147/IJNRD.S58037 **6.** Palit S, Kendrick J. Vascular calcification in chronic kidney disease: role of disordered mineral metabolism. *Curr Pharm Des.* 2014;20(37):5829-5833. doi:10.2174/1381612820666140212194926 **7.** Combs SA, Teixeira JP, Germain MJ. Pruritus in kidney disease. *Semin Nephrol.* 2015;35(4):383-391. doi:10.1016/j.semnephrol.2015.06.009 **8.** Shirazian S, Aina O, Park Y, et al. Chronic kidney disease-associated pruritus: impact on quality of life and current management challenges. *Int J Nephrol Renovasc Dis.* 2017;10:11-26. doi:10.2147/IJNRD.S108045 **9.** Friedman EA. Consequences and management of hyperphosphatemia in patients with renal insufficiency. *Kidney Int Suppl.* 2005;(95):S1-7. doi:10.1111/j.1523-1755.2005.09500.x **10.** Vervloet MG, van Ballegooijen AJ. Prevention and treatment of hyperphosphatemia in chronic kidney disease. *Kidney Int.* 2018;93(5):1060-1072. doi:10.1111/j.1523-1755.2005.09500.x **11.** Taravati S, Cinar E, Akkoc Y. Hyperphosphatemia in a patient with spinal cord injury who received etidronate for the treatment of heterotopic ossification. *Spinal Cord Ser Cases.* 2017;3:17032. doi:10.1038/scsandc.2017.32 **12.** AURYXIA® [Package Insert]. Cambridge, MA: Akebia Therapeutics, Inc. **13.** Data on File 1, Akebia Therapeutics, Inc. **14.** Data on File 11, Akebia Therapeutics, Inc. **15.** Data on File 4, Akebia Therapeutics, Inc. **16.** Umanath K, Jalal DI, Greco BA, et al; for Collaborative Study Group. Ferric citrate reduces intravenous iron and erythropoiesis-stimulating agent use in ESRD. *J Am Soc Nephrol.* 2015;26(10):2578-2587. doi:10.1681/ASN.2014080842 **17.** Data on File 2, Akebia Therapeutics, Inc. **18.** Umanath K, Sika M, Niecestro R, et al; for Collaborative Study Group. Rationale and study design of a three-period, 58-week trial of ferric citrate as a phosphate binder in patients with ESRD on dialysis. *Hemodial Int.* 2013;17(1):67-74. doi:10.1111/j.1542-4758.2012.00711.x **19.** Data on File 24, Akebia Therapeutics, Inc. **20.** Data on File 29, Akebia Therapeutics, Inc.

Akebia Therapeutics®, Auryxia®, AkebiaCares®, and their associated logos are trademarks of Akebia and/or its affiliates.

©2023 Akebia Therapeutics, Inc. All rights reserved. PP-AUR-US-1298 (v3.0) 01/23

Akebia® THERAPEUTICS