AURYXIA™ (ferric citrate) tablets contain 210 mg of ferric iron equivalent to 1 g ferric citrate for oral use.

**INDICATIONS AND USAGE**
AURYXIA is a phosphate binder indicated for the control of serum phosphorus levels in patients with chronic kidney disease on dialysis.

**CONTRAINDICATIONS**
AURYXIA is contraindicated in patients with iron overload syndromes (eg, hemochromatosis).

**WARNINGS AND PRECAUTIONS**
Iron supplements containing iron (eg, AURYXIA) may lead to excessive elevations in iron stores, increases in serum ferritin and transferrin saturation (TSAT) levels were observed in clinical trials. In a 56-week safety and efficacy trial in which concomitant use of AURYXIA and IV iron was permitted, 55 (19%) patients treated with AURYXIA had a ferritin level >1500 ng/mL as compared with 13 (9%) patients treated with active control. Assess iron parameters (eg, serum ferritin and TSAT) prior to initiating AURYXIA and monitor iron parameters while on therapy. Patients receiving IV iron may require a reduction in dose or discontinuation of IV iron therapy.

**Accidental Overdose of Iron**: Accidental overdose of iron-containing products is a leading cause of fatal poisoning in children under 6 years of age. Keep this product out of the reach of children. In case of accidental overdose, call a doctor or poison control center immediately.

**Patients with Gastrointestinal Bleeding or Inflammation**: Patients with inflammatory bowel disease or active, symptomatic gastrointestinal bleeding were excluded from clinical trials. Safety has not been established in these populations.

**ADVERSE REACTIONS**
Adverse reactions to a drug are most readily ascertained by comparison with placebo, but there is little placebo-controlled experience with AURYXIA, so this section describes adverse events with AURYXIA, some of which may be disease-related, rather than treatment-related. A total of 289 patients were treated with AURYXIA and 149 patients were treated with active control (sevelamer carbonate and/or calcium acetate) during the 52-week, randomized, open-label, active control phase of a trial in patients on dialysis. A total of 322 patients were treated with AURYXIA for up to 28 days in three short-term trials. Across these trials, 557 unique patients were treated with AURYXIA, dosages regimens in these trials ranged from 210 mg to 2,520 mg of ferric iron per day, equivalent to 1 to 12 tablets of AURYXIA. In these trials, adverse events reported for AURYXIA were similar to those reported for the active control group. Adverse events reported in more than 5% of patients treated with AURYXIA in these trials included diarrhea (21%), nausea (11%), constipation (8%), vomiting (7%), and cough (4%).

During the 52-week active control period, 60 patients (21%) on AURYXIA discontinued study drug because of an adverse event, as compared to 21 patients (14%) in the active control arm. Patients who were previously intolerant to any of the active control treatments (calcium acetate and sevelamer carbonate) were not eligible to enroll in the study. Gastrointestinal adverse events were the most common reason for discontinuing AURYXIA (14%). AURYXIA is associated with discoloration of the teeth, which can only be corrected by a dental professional. Adverse reactions to drugs include: nausea, vomiting, diarrhea, constipation, abdominal pain, dyspepsia, bloating, flatulence, metallic taste, constipation, diarrhea, increased frequency of stools, rectal bleeding, and pain in the rectum.

**USE IN SPECIFIC POPULATIONS**
**Pregnancy**: Pregnancy Category B. There are no adequate and well-controlled studies in pregnant women. It is not known whether AURYXIA can cause fetal harm when administered to a pregnant woman. Animal reproduction studies have not been conducted.

**Lactation**: It is unknown whether AURYXIA is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when AURYXIA is administered to a nursing woman.

**Nursing Mothers**: Data from rat studies have shown the transfer of iron into milk by divalent metal transporter-1 (DMT-1) and ferroporin-1 (FPN-1). Hence, there is a possibility of infant exposure when AURYXIA is administered to a nursing woman.

**Labor and Delivery**: The effects of AURYXIA on labor and delivery are unknown.

**Pediatric Use**: The safety and efficacy of AURYXIA have not been established in pediatric patients.

**Drug Interactions**
Iron absorption from AURYXIA may lead to excessive elevations in iron stores, especially when concomitant use of IV iron and AURYXIA is employed. In clinical trials, one case of elevated iron in the liver as confirmed by biopsy was reported in a patient administered IV iron and AURYXIA.

**Counseling Information**
**Do not discontinue AURYXIA without consulting your doctor.**

**Adverse Reactions**: Adverse effects of AURYXIA are infrequent and include: abdominal pain, bloating, flatulence, metallic taste, constipation, diarrhea, increased frequency of stools, rectal bleeding, and pain in the rectum.

**Dosing Recommendations**
Inform patients to take AURYXIA as directed with meals and adhere to their prescribed diets. Instruct patients on concomitant medications that should be dosed apart from AURYXIA.

**Drug Interactions**
For children with steroid-sensitive nephrotic syndrome, extending initial steroid therapy from 3 to 6 months does not affect the subsequent relapse rate, reports a trial in *Kidney International*. The randomized trial included 219 children with a first episode of steroid-sensitive nephrotic syndrome, enrolled at five academic hospitals in India. After 3 months of standard therapy with prednisolone, 181 children were assigned to receive 3 additional months of prednisone or 3 months of placebo therapy. The effects of extended steroid therapy on the risk of future relapse were assessed. The cumulative initial prednisolone dosage was about 3500 mg/m² in the 6-month group versus 2800 mg/m² in the 3-month group. On intention-to-treat analysis, the numbers of steroid-sensitive relapses during the year after randomization were 1.26 and 1.54, respectively. The difference was not significant after adjustment for sex, age, and time to initial remission. The rates of sustained remission, frequent relapses, and adverse steroid effects were similar as well. For children with idiopathic nephrotic syndrome, multiple relapses are associated with a risk of chronic kidney disease and medication-related adverse events. Some reports have suggested that a prolonged course of initial prednisolone therapy can reduce the relapse rate, although these studies have had important limitations. The new trial finds no reduction in relapse rate for children with steroid-sensitive nephrotic syndrome assigned to 3 months versus 6 months of initial prednisolone therapy. Although extended treatment can postpone the occurrence of initial relapse, the 1-year relapse rates are similar between groups. A Japanese trial comparing 2 months versus 6 months of prednisolone, published in the same issue (*Kidney Int* 2015; 87:225–232), reaches a similar conclusion (*Kidney Int* 2015; 87:217–224).

**Surgical Robots Linked to Increased Rates of Partial Nephrectomy**
Hospitals acquiring surgical robots are more likely to perform guideline-recommended partial nephrectomy in patients with renal cancer, reports a study in *Medical Care*. The researchers used payer data from seven states to identify nearly 21,600 nephrectomies performed in 2001, 2005, and 2008. Hospital-level rates of partial nephrectomy were analyzed in relation to the hospitals’ acquisition of a surgical robotic system. The association was adjusted for nephrectomy volume, year of surgery, and other hospital factors. Hospitals performed more partial nephrectomies after acquiring surgical robots. For hospitals acquiring robots between 2001 and 2004, the proportion of...
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Partial nephrectomies increased by about 30 percent in 2005 and 35 percent in 2008. A smaller increase of 15.5 percent was noted for hospitals acquiring a surgical robot between 2005 and 2008.

Is Metformin Safe for Patients with Kidney Disease?

Available data support the "cautious expansion" of metformin use for patients with type 2 diabetes and mild to moderate chronic kidney disease (CKD), according to a systematic review in the Journal of the American Medical Association.

A literature search identified 65 publications providing data on the risk of lactic acidosis in metformin-treated patients with impaired renal function. Since its approval in 1994, metformin has been contraindicated for use in patients with "renal disease or renal dysfunction."

However, the evidence suggested that drug levels generally remained in the therapeutic range for metformin-treated patients with mild to moderate CKD (estimated GFR 30 to 60 mL/min/1.73 m²). Despite renal clearance of metformin, the rates of lactic acidosis were low and in the range of the background rate among all patients with diabetes: about three to ten cases per 100,000 person-years.

There were no randomized trials evaluating the safety of metformin in patients with impaired kidney function. Some reports suggested that the guidelines regarding metformin use in kidney disease are "commonly disregarded," with no increase in adverse events. Observational studies suggested beneficial effects on macrovascular outcomes, even in patients with contraindications to metformin use.

On the basis of these data, the authors suggest a change in prescribing guidelines to permit metformin use in patients with mild to moderate CKD. They emphasize that any such strategy would require appropriate dosage reductions and careful monitoring of kidney function [Inzucchi SE, et al. Metformin in patients with type 2 diabetes and kidney disease: a systematic review. JAMA 2014; 312: 2668–2675].

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