Cognitive Function
Continued from page 7


dition and all-cause mortality were assessed, with adjustment for demographics and di-
alysis and cardiovascular (CV) risk factors. Test results were broken down into domain
scores representing memory and executive function.

There were 145 deaths during a median follow-up time of 2.1 years. Each one SD
increase in executive function score was associated with a 35 percent reduction in
mortality—hazard ratio (HR) 0.65. The as-
sociation remained significant after adjust-
ment for demographics and dialysis-related
factors (HR 0.81) but lost significance after
adjustment for CV disease and heart failure.
In time-dependent models, the unadjusted
HR was 0.62, and the association remained
significant after adjustment for demograph-
ic, dialysis, and CV factors (HR 0.79).

On univariate analysis, better memory
scores were associated with lower mortality:
HR 0.82 per one SD. However, this asso-
ciation became nonsignificant after adjust-
ment for demographics.

Many hemodialysis patients have cogni-
tive impairment, which is associated with
increased morbidity. The new study shows
that impaired performance on neurocog-
nitive testing is associated with increased
mortality. The association with memory ap-
ppears to be explained by demographic fac-
tors, whereas the association with executive function may partly reflect the effects of CV
disease. The authors call for new approaches
to improving or stabilizing cognitive impair-
ment in dialysis patients [Drew DA, et al.
Cognitive function and all-cause mortal-
ity in maintenance hemodialysis patients.

BRIEF SUMMARY
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 Overload: Iron absorption from AURYXIA may lead to excessive elevations in iron stores. Increases in serum ferritin and transferrin saturation (TSAT) have been observed in clinical trials. In a 52-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 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 mostly readily ascertained by 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. Among these trials, 557 unique patients were treated with AURYXIA, dosage 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, 62 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 being systematically 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 (19%).

AURYXIA is associated with discolorated feces (dark stools) related to the iron content, but this staining is not clinically relevant and does not affect laboratory tests for occult bleeding, which detect heme rather than non-heme iron in the stool.

Drug Interactions
Doxycycline is an oral drug that has to be taken at least 1 hour before AURYXIA. Oral drugs that can be administered concomitantly with AURYXIA are: (1) aspirin, atorvastatin, calcium carbonate, dipyridamole, digoxin, docusate sodium, eflornithine, fenofibrate, loperamide, metoprolol, pravastatin, propranolol, sitagliptin, and warfarin. There are no empirical data on avoiding drug interactions between AURYXIA and most concomitant oral drugs. For oral medications where a reduction in the bioavailability of that medication would have a clinically significant effect on its safety or efficacy, consider separation of the timing of the administration of the two drugs. The duration of separation depends upon the absorption characteristics of the medication concomitantly administered, such as the time to reach peak systemic levels and whether the drug is an immediate release or an extended release product. Consider monitoring clinical responses or blood levels of concomitant medications that have a narrow therapeutic range.

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.

The effect of AURYXIA on the absorption of vitamins and other nutrients has not been studied in pregnancy. An overdose of iron in pregnant women may carry a risk for spontaneous abortion, gestational diabetes, and fetal malformation.

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

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

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

Geriatric Use: Clinical studies of AURYXIA included 106 subjects aged 65 years and older (33 subjects aged 75 years and older). Overall, the clinical study experience has not identified any obvious differences in responses between the elderly and younger patients in the tolerability or efficacy of AURYXIA.

OVERDOSAGE
No data are available regarding overdose of AURYXIA in patients. In patients with chronic kidney disease on dialysis, the maximum dose studied was 2,520 mg ferrous iron (12 tablets of AURYXIA) per day. Iron absorption from AURYXIA may lead to excessive elevations in iron stores, especially when concomitant IV iron is used. 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.

PATIENT COUNSELING INFORMATION
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.

Adverse Reactions: Advise patients that AURYXIA may cause discolorated (dark) stools, but this staining of the stool is considered normal with oral medications containing iron.

AURYXIA may cause diarrhea, nausea, constipation, and vomiting. Advise patients to report severe or persistent gastrointestinal symptoms to their physician.

Findings

Kidney Donors at Increased Risk of Gestational Hypertension and Pre-eclampsia

Women who become living kidney donors are at increased risk of gestational hyperten-
sion and pre-eclampsia, suggests a study in the New England Journal of Medicine.

The retrospective cohort analysis included 85 women in Ontario who donated a kidney between 1992 and 2010 and sub-
sequently became pregnant. The median age at donation was 29 years; the women had a total of 131 pregnancies after enter-
ing the cohort.

They were matched to 510 healthy nondonors for age, year, urban versus rural residency, income, number of pregnancies, and time to first pregnancy. The control women had a total of 788 pregnancies. The rates of hospital-diagnosed gestational hypertension or pre-eclampsia were com-
pared for donors versus nondonors, along with other maternal and fetal outcomes.

The primary outcome of gestational hy-
pertension or pre-eclampsia was more than twice as frequent among women who do-
nated a kidney: 11 percent versus 5 percent of pregnancies: odds ratio 2.4. The odds ratios for the individual outcomes were 2.5 and 2.4, respectively.

Other maternal and fetal outcomes were similar between groups, including preterm birth and low birth weight. There were no cases of maternal death, stillbirth, or neonatal death among the donors.

Young women who are considering liv-

ing kidney donation commonly ask about the possible effects on future pregnancies. Some studies have reported an increased risk of gestational hypertension and pre-ec-
lampsia after donation, but these findings have been controversial.

The new study finds a significantly in-
creased risk of gestational hypertension or pre-eclampsia in pregnancies occurring in woman after living kidney donation com-
pared with similar healthy nondonors. The authors believe that this information should be included in clinical practice guidelines and shared in the informed con-