

Patient Counseling for Finerenone

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ABSTRACT

Finerenone is a nonsteroidal mineralocorticoid receptor antagonist, which is used to retard the progression of chronic kidney disease in persons with type 2 diabetes. This communication describes the various aspects of patient counseling needed to ensure safe and effective usage of the molecule. It utilizes the 5C checklist: Confirmation of clinical indication; Caveats and contraindications; Concerns and checkpoints; Caution and use with concomitant medication; and Constraints and cost, to create a simple, yet comprehensive tool for clinical use.

Keywords: Aldosterone antagonist, chronic kidney disease, diabetic kidney disease, mineralocorticoid receptor antagonist, patient-centered care, person-centered care, type 2 diabetes

Finerenone is a novel nonsteroidal mineralocorticoid receptor antagonist, which has been approved for use in persons with chronic kidney disease (CKD) and type 2 diabetes (diabetic kidney disease or DKD), to retard the progression of DKD.¹

Finerenone offers an alternative pathway to treat CKD associated with type 2 diabetes by blocking mineralocorticoid receptor overactivation, which contributes to CKD progression and cardiovascular damage. The development of finerenone represents a major breakthrough in the prevention and management of DKD, as it has proven cardiovascular and renal benefits in two long-term renal and cardiovascular outcome trials (CVOTs). Two large CVOTs, FIDELIO and FIGARO, along with their pre-specified analysis, FIDELITY, have demonstrated a statistically significant improvement in various cardiocentric and renocentric composite outcomes.²⁻⁴

SHARING INFORMATION AND DECISION-MAKING

Shared and informed decision-making is ingrained in modern medical practice, and persons living with diabetes should be active partners in their management.⁵ Therapeutic patient education, per se, has been shown to improve long-term results in persons with diabetes.⁶

It would be good clinical sense, therefore, to discuss the education counseling, and support that is required while prescribing finerenone to a person living with diabetes.

THE 5C CHECKLIST

We have used the 5C rubric (Box 1) to list the Clinical indications; Caveats and contraindications; Concerns and check points; Cautionary advice, including usage with concomitant medication; and Constraints and cost-associated with finerenone usage.

This simple framework assists health care professionals in discussing and explaining finerenone usage in persons with DKD. The format also works as a useful checklist, not only for finerenone, but for all other interventions in medical practice.

THE WAY FORWARD

Finerenone usage is endorsed by the American Diabetes Association (ADA) and American Association of Clinical Endocrinology (AACE) clinical practice guidelines, which suggest its use in patients with CKD who are at increased risk for cardiovascular events or CKD progression or in those who do not tolerate sodium-

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glucose co-transporter-2 (SGLT2) inhibitors. The ADA recommends targeting a $\geq 30\%$ reduction in urinary albumin-creatinine ratio (UACR), though it does not specify a time frame for this.^{7,8}

As finerenone usage increases, the need for patient counseling will increase. We hope that the 5C counseling checklist will assist physicians in offering the best possible care to all persons living with diabetes and DKD.

Box 1. Counseling for Finerenone

Confirmation of Clinical Indications

- Statistically significant improvement in cardiovascular and renal outcomes, in persons with type 2 diabetes and DKD, as reported by the FIDELIO, FIGARO and FIDELITY results.
- Finerenone is indicated to reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end-stage kidney disease, cardiovascular death, nonfatal myocardial infarction and hospitalization for heart failure in adult patients with CKD associated with type 2 diabetes.
- Initiation of finerenone treatment is recommended in CKD and type 2 diabetes persons with an eGFR >25 mL/min/1.73 m², or with UACR >30 mg/g, and with normokalemia.

Caveats and Contraindications

Caveats

- No approved so far on persons with type 1 diabetes.
- No approved so far on persons with non-DKD.
- Not indicated for use in heart failure or refractory hypertension.

Contraindications

- End-stage renal disease.
- Initiation is not recommended if serum potassium >5.0 mmol/L (5 mEq/L).
- Severe hepatic impairment (Child-Pugh C).
- Addison's disease.
- Preconception, pregnancy and lactation.

Concerns and Checkpoints

Concerns

- The risk of side effects is less with finerenone than with earlier mineralocorticoid receptor antagonists such as spironolactone and eplerenone.
- Hyperkalemia leading to permanent discontinuation may occur in $\approx 2\%$ of patients and the risk of sexual and other side effects is minimal.

Checkpoints

- Serum potassium must be monitored 1 month after onset of therapy, at regular (≈ 4 monthly) intervals thereafter, and whenever a change in electrolyte levels is anticipated or suspected, e.g., vomiting, diarrhea, addition of diuretics, renotoxic drugs, other concomitant medication, which may interfere with finerenone metabolism.
- While there is no specific recommendation for the frequency and regularity of monitoring UACR, it would be prudent to assess this 4 months after onset of therapy. More frequent assessment may be justified if it can help allay patient anxiety and/or inform changes in choice and/or dosage of finerenone/concomitant therapy.

Caution and Concomitant usage

Caution during use

- Finerenone is a once-daily oral tablet that can be taken at any time of the day.
- Begin with 10 mg/day finerenone in persons with eGFR <60 mL/min/1.73 m², and 20 mg/day in those with eGFR >60 mL/min/1.73 m².
- If potassium levels are normal (<4.8 mEq/L) after 1 month, up-titrate to 20 mg/day.
- If potassium levels are >5.5 mEq/L, withhold finerenone; check potassium after a few days (as it has a short half-life), and restart 10 mg/day if serum potassium ≤ 5.0 mEq/L.
- If potassium levels are between 4.8 and 5.0 mEq/L, maintain the dose and take an individualized, case-based decision, keeping in mind the risk benefit ratio of continuing finerenone and assessing the ability to screen for hyperkalemia, and manage it if needed.

Concomitant medication

- No extra diuresis occurs with finerenone, and it can be used with thiazide, thiazide-like, and loop diuretics.
- Finerenone is not indicated with other mineralocorticoid receptor antagonists, spironolactone and eplerenone.
- In a patient who has been on spironolactone or eplerenone for an indication such as hypertension or heart failure, and now needs finerenone for management of DKD, an individualized needs and priority assessment should be done.

- Finerenone is not contraindicated in patients taking concomitant medications that are strong CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, ritonavir, nelfinavir, cobicistat, clarithromycin, telithromycin and nefazodone).

- Concomitant intake of strong CYP3A enzyme inducers like rifampicin, carbamazepine, phenytoin, phenobarbital and St John's Wort may lead to decrease in plasma concentration of finerenone and results in reduced therapeutic effect and should be avoided.

- Finerenone can be used with all glucose-lowering drugs, including SGLT2 inhibitors.

Constraints and Cost

- Share details about the cost of therapy with the patient, especially in a pay-from-pocket scenario, and assist in performing an informal cost-benefit analysis.
- Explain that the cost of 10 mg and 20 mg tablets is same, to preclude suboptimal dosing.

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Early Diagnosis of Type 1 Diabetes in Young Children is Important to Preempt DKA-associated Cognitive Decline

Mild cognitive decline may occur expeditiously in children aged 3 to 5 years with type 1 diabetes following an episode of diabetic ketoacidosis (DKA), irrespective of the severity of the event, suggests a multicenter clinical trial published in the journal *Endocrinology, Diabetes & Metabolism*.¹

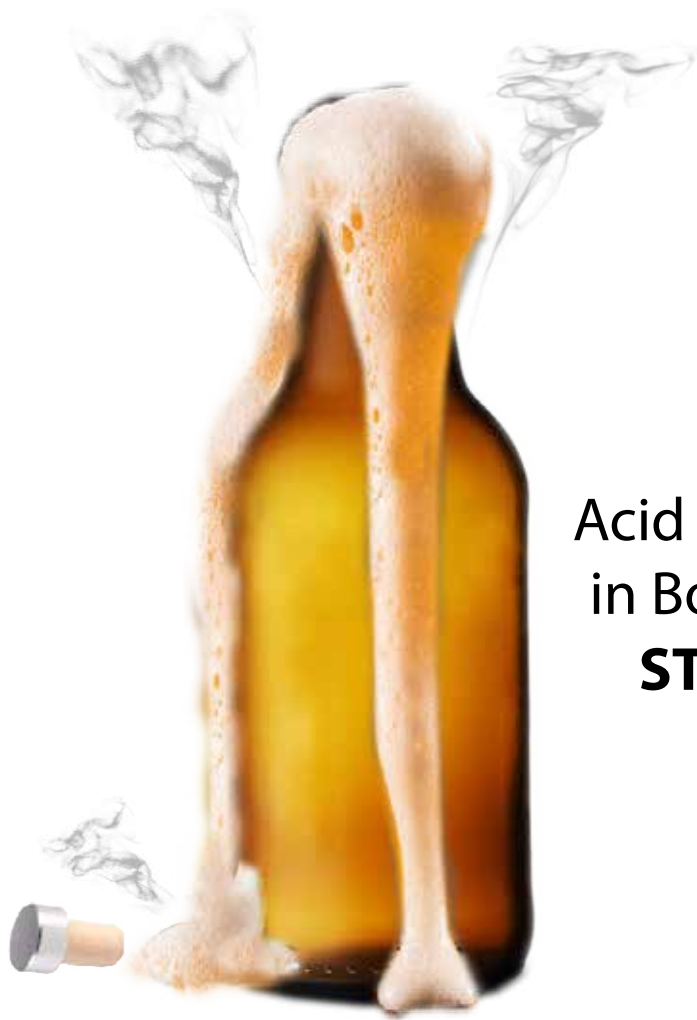
A randomized clinical trial was conducted at 12 hospitals to evaluate the impact of a single episode of DKA on cognitive function in young children. These centers were a part of the Pediatric Emergency Care Applied Research Network (PECARN) Fluid Therapies Under Investigation in DKA (FLUID) trial. For this, researchers selected 22 children with moderate to severe DKA and 24 children with mild DKA with a recent diagnosis of type 1 diabetes, in <2 years of their enrollment. The control group included 27 age- and duration matched children with type 1 diabetes but without DKA. Children with DKA underwent one-time neurocognitive evaluation 2 to 6 months after occurrence of DKA. Children in the control group were evaluated immediately after their enrollment. Children with hypoglycemia (<70 mg/dL) or hyperglycemia (>350 mg/dL) were evaluated at a later date. A pH value from 7.20 to 7.25, or serum bicarbonate between 10 and 15 mmol/L were considered as mild DKA. The features of moderate/severe DKA were pH ≤7.19 or serum bicarbonate ≤9 mmol/L.

Children who developed DKA showed significantly lower IQ scores on the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III) (English version) compared to children who did not have DKA. Severity of the DKA had no impact on this. This effect was seen even after adjusting for ethnicity and socioeconomic status. “Patient demographic variables had no statistical difference as a function of DKA status” observed the authors.

These findings demonstrate the strong association of DKA on cognitive function in young children with type 1 diabetes as those who had had a single episode of DKA were found to exhibit lower IQ scores compared to age-matched patients without DKA just within 6 months of the episode. Hence, “early detection of diabetes and prevention of DKA in young children” assumes great significance.

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