

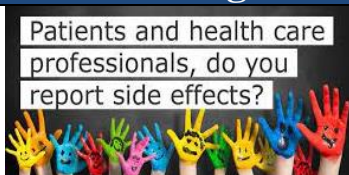


Better Pharmacist Knowledge

Jordan Drug Information and Toxicology Center 2023

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SGLT2 inhibitors in patients with nondiabetic proteinuric chronic kidney disease

In patients with chronic nondiabetic kidney disease with proteinuria (albuminuria ≥ 300 mg/day or proteinuria ≥ 500 mg/day), we recommend treatment with a sodium-glucose co-transporter 2 (SGLT2) inhibitor.

Sodium-glucose co-transporter 2 (SGLT2) inhibitors are recommended in patients with diabetic kidney disease; previously, only one large trial examined their effects in nondiabetic chronic kidney disease. In the EMPA-KIDNEY trial, 6609 patients with estimated glomerular filtration rate (eGFR) 20 to 44 mL/min/1.73 m² (regardless of albuminuria) or 45 to 89 mL/min/1.73 m² (if albumin-to-creatinine ratio was at least 200 mg/g) were randomly assigned to **empagliflozin** 10 mg daily or placebo. At two years, empagliflozin reduced the incidence of end-stage kidney disease, the incidence of a sustained decline in eGFR to <10 mL/min/1.73 m², and the incidence of a sustained decrease in eGFR of 40 percent or more; the risks of all-cause mortality and nonfatal cardiovascular events were similar between groups. The benefit from empagliflozin was larger in patients with albumin-to-creatinine ratio ≥ 300 mg/g and substantially less in patients with lower albumin excretion. **We now recommend SGLT2 inhibitor therapy in patients with nondiabetic chronic kidney disease and albuminuria.** [1]

Persistence of asthma control after stopping omalizumab therapy (November 2022)

Omalizumab, an anti-IgE monoclonal antibody, is an effective add-on therapy for uncontrolled moderate-to-severe asthma but the optimal duration of therapy and the persistence of benefit after discontinuation are unclear. In an analysis of the French national healthcare database that included over 19,000 patients with asthma (over 2000 children) who received omalizumab for a median duration of approximately 4.5 years, rates of asthma hospitalizations were reduced by 75 percent and the need for oral corticosteroids by 30 percent after two years of treatment [1].

Among patients with asthma control during treatment, symptoms remained controlled in a significant percentage one, two, and three years after discontinuation (76, 44, and 33 percent in children and 70, 39, and 24 percent in adults, respectively). These findings **indicate a lasting benefit after discontinuation of omalizumab in patients with controlled asthma and provide a basis for anticipatory guidance for those who discontinue treatment.** [2]

Insulin resistance in severe asthma (November 2022)

Several studies have identified an increased prevalence of asthma and difficult-to-control asthma among obese individuals, although the exact reason for the association is not known. A recent study of patients with severe asthma included extensive metabolic phenotyping as well as long-term follow-up. **Patients with insulin resistance demonstrated more rapid decline in lung function and increased resistance to beta-agonist and oral glucocorticoid therapies compared with patients having normal insulin sensitivity.** Whether targeting insulin resistance can impact these severe asthma features requires further investigation. [3]

Risk of drug overdose in young people prescribed benzodiazepines for sleep disorders (December 2022)

Prescription database studies indicate that benzodiazepines are commonly prescribed for insomnia, despite risks and the availability of safer options. In a recent cohort study in the United States that included over 90,000 children and young adults (age 10 to 29 years) with a sleep disorder who were prescribed a new insomnia medication, benzodiazepines were associated with increased risk of drug overdose in the next six months compared with alternative insomnia medications (**trazodone**, **hydroxyzine**, **zolpidem**, **zaleplon**, **eszopiclone**). Risk was highest among individuals who had also received an opioid prescription in the preceding three months. **We do not prescribe benzodiazepines for insomnia in patients taking opioids or in those with a substance use disorder.** [4]

References:

1. Practice Changing UpToDate; SGLT2 inhibitors in patients with nondiabetic proteinuric chronic kidney disease, accessed online via uptodate, cited on 28 Dec 2022.
2. What's new in allergy and immunology; Persistence of asthma control after stopping omalizumab therapy (November 2022), accessed online via uptodate, cited on 29 Dec 2022.
3. What's new in allergy and immunology; Insulin resistance in severe asthma (November 2022), accessed online via uptodate, cited on 29 Dec 2022.
4. Adverse reactions and warning; risk of drug overdose in young people prescribed benzodiazepines for sleep disorders (December 2022), accessed online via uptodate, cited on 29 Dec 2022.

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Severe complications of button battery ingestion in children (October 2022)

Button battery (BB) ingestion with esophageal impaction in children is a true emergency that can cause life-threatening complications. In a systematic review of 361 pediatric cases of BB ingestion resulting in severe complications (95 percent with esophageal impaction), death occurred in 19 percent of patients. Hemorrhage from vascular injuries, primarily aortoesophageal fistulae, was the most common cause of death. Among patients with vascular injuries, those who died had a longer duration of impaction than those who survived (median 144 versus 11 hours, respectively). **These findings highlight the importance of timely recognition of BB ingestion with esophageal impaction and emergency BB removal.** [5]

Trial of discontinuing ACE inhibitors and ARBs in advanced CKD (December 2022)

In patients with chronic kidney disease (CKD) who take angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) chronically, the question of whether to discontinue these agents when patients progress to advanced CKD is debated. Theoretically, the acute decline in glomerular filtration rate (GFR) occurring after initiation of therapy could be regained when these drugs are stopped, thereby delaying the onset of end-stage kidney disease (ESKD). In a large trial in which over 400 patients with advanced CKD (median estimated GFR 18 mL/min/1.73 m²) on chronic therapy with an ACE inhibitor or ARB were randomly assigned to continue or discontinue therapy with these drugs, patients who discontinued therapy were more likely to develop ESKD at three years, although this was not statistically significant; rates of death and cardiovascular events were similar between the groups. **These data support continuing these agents in patients with advanced CKD.** [6]

Oral antihyperglycemic agents and prevention of COPD exacerbations (November 2022)

Glucagon-like peptide 1 (GLP-1) receptor agonists and sodium-glucose co-transporter 2 (SGLT-2) inhibitors are antihyperglycemics increasingly used for the treatment of type 2 diabetes not controlled by metformin. In a recent study of patients with chronic obstructive pulmonary disease (COPD) and new initiation of an antihyperglycemic agent, patients who began

GLP-1 receptor agonists or SGLT-2 inhibitors were less likely to be hospitalized for COPD exacerbations than similar patients receiving sulfonylureas, through as yet undefined mechanisms. Future trials are needed to determine whether use of **GLP-1 receptor agonists or SGLT-2 inhibitors are preferable to other antihyperglycemic agents in patients with diabetes mellitus and risk for COPD exacerbations.** [7]

تعميم من مؤسسة الغذاء والدواء الصادر في 2022/12/14 إشارة الى معلومات الأمانة الدوائية المستجدة و الصادرة من قبل السلطة الدوائية الأوروبية (EMA) بتاريخ 2022/9/30 و المتعلق بالأدوية المحتوية على المادة الفعالة (Terlipressin) حيث ورد التالي:

- A higher than previously known risk of **respiratory failure** has been reported when using terlipressin-containing medicines for the treatment of type 1 hepatorenal syndrome (HRS-1). In addition, a **new risk of sepsis** has been identified with the use of terlipressin - containing medicines for HRS-1. Terlipressin -containing medicines should **be avoided** in patients with advanced renal dysfunction (serum creatinine \geq 442 μ mol/l (5.0mg/dl) and in patients with acute -on chronic liver failure grade 3 and/or model for end-stage liver disease (MELD) score \geq 39 MELD score, unless the benefits outweigh the risks.
- Patients with new onset of breathing difficulties or worsening of existing respiratory disease should be stabilized before treatment with terlipressin-containing medicines and should be closely monitored during treatment. **If patients develop respiratory symptoms, dose reduction of human albumin should be considered, if applicable. If symptoms are severe or do not resolve, terlipressin should be discontinued.**
- Patients should be closely monitored for **symptoms of infection.**
- In addition, healthcare professionals can consider giving terlipressin- containing medicines as **continues intravenous infusion** as an alternative to bolus injection, as continues infusion may reduce the risk of severe adverse events compared to bolus injection.[8]

References:

5. What's new in emergency medicine; Severe complications of button battery ingestion in children (October 2022), accessed online via uptodate, cited on 29 Dec 2022.
6. Acute and chronic kidney disease; trial of discontinuing ACE and ARBs in advanced CKD (December 2022), accessed online via uptodate, cited on 2 Jan 2023.
7. Oral antihyperglycemic agents and prevention of COPD exacerbations (November 2022), accessed online via uptodate, cited on 4 Jan 2023.
8. 2022/12/14 في 2022/9/30 و المتعلق بالأدوية المحتوية على المادة الفعالة (Terlipressin) حيث ورد التالي:

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