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PHARMACOLOGICAL PROFILE OF EMPAGLIFLOZIN: MECHANISM OF ACTION AND THERAPEUTIC APPLICATIONS

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ABSTRACT

The prevalence of diabetes mellitus rose in 2014, partly due to the release of new treatments. Empagliflozin, a very successful therapy for type 2 diabetes mellitus, was granted FDA clearance in 2014. The objective of this study is to assess the suitable commencement, contraindications, and adverse effects of empagliflozin. Empagliflozin can be provided either as a monotherapy or in conjunction with metformin and other drugs, such as linagliptin. Although the price is expensive, these combinations are recommended to decrease mortality and control blood glucose levels when lifestyle changes and metformin alone are not enough. In 2016, the FDA granted approval for the use of empagliflozin in lowering the risk of cardiovascular death among individuals diagnosed with type 2 diabetes. This study will examine the indications, administration, side effects, and monitoring necessary for empagliflozin medication, highlighting the need of interprofessional teamwork in maximising patient outcomes.

INTRODUCTION

EMPAGLIFLOZIN

A rise in diabetes mellitus patients was seen in 2014 due to the large number of new medications identified during the pharmaceutical development phase. Among the most effective antidiabetic medications used to treat type 2 diabetes mellitus, empagliflozin was

officially authorized by the FDA in 2014, and many other treatments are now in the trial phase. There are antidiabetic medications that are used either alone or in conjunction with other agents. It is also possible to provide empagliflozin alone or in combination with metformin and another medication, such as linagliptin or empagliflozin alone.

While these combinations can be costly and put a strain on patients' finances, they are prescribed to patients to help reduce mortality as an additional treatment option or as a second line of defense following metformin. When exercise and dietary changes alone aren't enough to control a patient's blood sugar levels, the next step in diabetes treatment is lifestyle modification. However, when a patient's A1c level is more than 9%, doctors will prescribe a combination therapy that includes metformin. In 2016, A new usage for empagliflozin has been authorized by the US Food and Drug Administration (FDA). Cardiovascular complications, including heart failure, are less likely and hospitalization is less frequent in those with type 2 diabetes. As a result, it is the medicine of choice for managing this condition. When administered in this context, empagliflozin is most effective:

The goals of this study are as follows:

- Determine when empagliflozin treatment should begin.
- Describe the situations in which empagliflozin treatment is not appropriate.
- List both the usual and unusual side effects of using empagliflozin. When prescribing or ordering empagliflozin medication, it is important to review interprofessional techniques that will improve results.[1]

Indications

Adults diagnosed with type 2 diabetes mellitus use the antidiabetic medicine empagliflozin. Its 2014 FDA approval sealed the deal. You can use empagliflozin on its own or combine it with other antidiabetic medications. Empagliflozin and linagliptin are combo products, as is empagliflozin with metformin. Due to patient financial concerns, clinicians may be hesitant to prescribe these newer medications because of their potential higher cost. On the other hand, after metformin, the American Diabetes Association (ADA) is requesting medications that have reduced death rates in a clinical trial. Among these agents are liraglutide and empagliflozin. Managing one's lifestyle and exercising regularly are the mainstays of diabetic therapy, with metformin following closely behind. If the A1c is more than 9%, The Standards of Medical Care for Diabetes recommend using metformin in conjunction with other diabetes

treatments. In 2016, researchers approved empagliflozin for a new use: lowering the risk of cardiovascular mortality in persons with type 2 diabetes and cardiovascular disease. Hospitalizations and fatalities caused by cardiovascular disease are reduced when empagliflozin is used. Prescribers should be knowledgeable of the advantages of empagliflozin due to the elevated risk of cardiovascular death in individuals with type 2 diabetes.

To summarise, the following situations may warrant the use of empagliflozin.

- When those with heart failure and obvious atherosclerotic cardiovascular disease are unable to attain optimal glycemic control with metformin and lifestyle modifications. You can use this medication as a second-line treatment for inadequate glycemic control when insulin is not an option for metformin users and complications such as weight gain and hypoglycemia persist. It is also a last resort when two oral medications or insulin plus metformin fail to achieve adequate glycemic control in cases of nephropathy(urine albumin-to-creatinine>300mg/g).[2-4]

Mechanism Of Action

To exert its therapeutic effect, empagliflozin binds to and blocks the proximal tubule-resident sodium-glucose co-transporter-2 (SGLT-2). Because it inhibits SGLT2, empagliflozin causes the kidneys to reabsorb less glucose and excrete more glucose in the urine. The drug's ability to reduce glucose levels does not rely on insulin. Patients with type 2 diabetes saw an approximately 64 g/d increase in urine glucose excretion with a dosage of 10 mg empagliflozin and a 78 g/d rise with a 25 mg dose. The diuretic and natriuretic effects of empagliflozin lead to intravascular constriction by lowering salt and volume loads. In addition to lowering blood pressure without elevating heart rate, empagliflozin is linked to decreased body fat.[5]

Administration

Empagliflozin is an oral drug, hence the recommended daily dosage is 10 or 25 mg administered orally. Take 10 mg first thing in the morning daily, with or without meals. The suggested dosage is 25 mg, with the right volume depletion before delivery as needed, assuming it is well-tolerated.[6]

Patient with renal impairment

Dosage adjustments are not necessary until your glomerular filtration rate (GFR) falls below 45 mL/min/1.75 m^2.

Adverse Effects

Low blood pressure, ketoacidosis, renal damage, vaginal mycotic infections, aberrant lipid profiles, pyelonephritis, and Fournier gangrene are some of the notable adverse effects of empagliflozin when used with insulin.

Patients with weak renal function, low systolic blood pressure, advanced age, and diuretic use are more likely to experience symptomatic hypotension when taking empagliflozin., ACE inhibitors, or ARBs because of their effects on osmotic diuresis and intravascular volume contraction. With empagliflozin, eGFR decreases, and serum creatinine increases. Hence, it is crucial to promptly evaluate renal function and then keep tabs on it regularly. Using empagliflozin is not recommended. It is not advised to use medication for cases where the glomerular filtration rate (GFR) falls below 45 mL/min or 30 mL/min/1.73 m^2.

Empagliflozin puts people at risk of ketoacidosis, thus they should not take it if they have type 1 diabetes. Ketoacidosis can happen to anybody who has a history of pancreatitis, has had pancreatic surgery, drinks excessively, or has pancreatic sickness.

Your risk of hypoglycemia increases when you use empagliflozin in conjunction with insulin or sulfonylureas. It is recommended to lower the dosage of sulfonylurea and use caution when giving them together.[7]

After using empagliflozin, you're more likely to get genital mycotic infections or urinary tract infections. Upon becoming aware of any symptoms, take the appropriate safety measures. Mycotic disorders can impact males in several ways, including the penile region, the scrotal area, the scrotal cavity, and balanitis. Candida infections affecting the vagina are known as vulvitis and vulvovaginal candidiasis. In terms of genital mycotic infections and UTIs, females outnumbered males.

Fournier gangrene, a kind of necrotizing fasciitis of the perineum, is an extremely uncommon bacterial illness that can be deadly in rare cases. Symptoms can begin anywhere from one week into therapy to two years after the medication is started. It is important to advise

patients on SGLT2 inhibitors of the possibility of perineal necrotizing fasciitis. Notify the FDA if a doctor has diagnosed an infection.

Contraindications

Patients with a glomerular filtration rate (GFR) less than 30 mL/min/1.73m^2 indicate substantial renal impairment and should not be given empagliflozin. If your GFR is 45 mL/min or below, or if you are pregnant during the second or third trimesters, do not use empagliflozin. Not suggested for those with severe empagliflozin hypersensitivity such as those undergoing dialysis or with end-stage renal disease. When the liver is not working properly, empagliflozin may be given. Avoid using empagliflozin if you have type 1 diabetes or diabetic ketoacidosis.[8]

Monitoring

As part of the empagliflozin monitoring program, a hemoglobin A1c (HbA1c) measurement is collected every three to six months. Initial testing should focus on confirming pregnancy as well as assessing lipid profiles, renal function, and blood pressure. When a pregnant woman uses empagliflozin in the second or third trimester, it might harm the developing baby. Due to the effects on intravascular contraction, it is essential to monitor renal function and blood pressure frequently throughout therapy. To make sure that patients don't have mycotic infections or urinary tract infections, doctors should ask whether their patients have any issues with their urine. Deterioration of renal function and fluid loss in the elderly is associated with an elevated risk of adverse consequences. Individuals using insulin, sulfonylureas, or diuretics should have their blood pressure and glucose levels checked regularly for symptoms of hypoglycemia or hypotension.[9]

Toxicity

Dyslipidemia, UTIs, and vaginal mycotic infections were the most often reported adverse effects. It has been noted to induce syncope, hypovolemia, dehydration, and hypotension as a result of its diuretic effects associated with volume depletion. A kind of perineal necrotizing fasciitis known as Fournier gangrene has been warned about by the FDA. Hospitalization and surgical debridement were required in twelve instances in all. Take the patient to the nearest emergency room for a surgical examination if you think it's necessary to cease the medication.[10,11]

Enhancing Healthcare Team Outcomes

The breakthrough study for empagliflozin tested 720 people with type 2 diabetes mellitus, known as the EMPAGLIFE trial. There was a substantial decrease in cardiovascular mortality, heart failure hospitalizations, and deaths due to any co-transporter in the empagliflozin group.[12] Patients at risk for cardiovascular complications due to type 2 diabetes were the first to benefit from this trial's findings, which showed a decrease in cardiovascular mortality. Depending on patient characteristics, EMPAREG and LEADER trial findings show that insulin is losing ground to SGLT2 inhibitors and GLP-1 agonists as the preferred second-line treatment. The EDICT trial found that compared to patients who sequentially took their medications, those who received triple dose combination therapy of metformin, SGLT 2 inhibitor, and pioglitazone for newly diagnosed type 2 diabetes reduced their HbA1c levels more significantly.[13]

The full interdisciplinary healthcare team should carry out Empagliflozin treatment. The primary decision-maker for medication prescriptions will be the endocrinologist or family physician. The nursing staff should be familiar with the medication's adverse event profile and be able to help with monitoring at subsequent appointments, both for therapeutic efficacy and side effects. To avoid prescription interactions, the chemist should verify dosages, offer advice on titration, and reconcile medications. If more glucose control is required, the chemist should recommend other agents. Therapy with empagliflozin will be optimized while risks are minimized by these diverse disciplines working together as a cohesive interprofessional unit.

CONCLUSION

Empagliflozin is a notable breakthrough in the management of type 2 diabetes mellitus, providing advantages beyond regulating blood sugar levels, such as safeguarding cardiovascular health. However, the use of this involves meticulous evaluation of patient-specific variables, possible negative consequences, and cost ramifications. Consistent monitoring and communication among professionals are crucial for maximising treatment results and reducing hazards. Further investigation is required to examine the enduring impacts of empagliflozin and its synergistic effects with other antidiabetic medications in order to enhance treatment procedures.

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