FRONT

3029240

DIAZAC

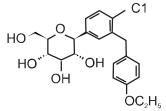
Dapagliflozin Tablets

COMPOSITION
DIAZAC 5 (Dapagliflozin Tablets 5 mg)
Each film coated tablet contains:
Dapagliflozin 5 mg
Excipients q.s.

DIAZAC 10 (Dapagliflozin Tablets 10 mg)
Each film coated tablet contains:
Dapagliflozin 10 mg
Excipients q.s.

DOSAGE FORM
Film coated tablet

DESCRIPTION
Dapagliflozin is described chemically as (1S)-1,5-Anhydro-1-C-[4-chloro-3-[(4 ethoxyphenyl)methyl]phenyl]-D-glucitol (2S,3R,4R,5S,6R)-2-(3-(4-ethoxybenzyl)-4-chlorophenyl)-6-hydroxymethyltetrahydro-2H-pyran-3,4,5-triol and the molecular weight is 408.87. The structural formula is:



EXCIPIENT LIST
Microcrystalline Cellulose, Anhydrous Lactose, Polyoxyl 40 Hydrogenated Castor Oil, Isopropyl Alcohol, Colloidal Silicon Dioxide, Crospovidone, Magnesium Stearate, Methylene Chloride, Opadry Yellow 03B22227.

CLINICAL PARTICULARS
Therapeutic Indications
Dapagliflozin is indicated:
- As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- To reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors.
- To reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure (NYHA class II-IV) with reduced ejection fraction.
- To reduce the risk of sustained eGFR decline, end-stage kidney disease, cardiovascular death, and hospitalization for heart failure in adults with chronic kidney disease at risk of progression.

Limitations of Use
- Dapagliflozin is not recommended for patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.
- Dapagliflozin is not recommended for use to improve glycemic control in adults with type 2 diabetes mellitus with an eGFR less than 45 mL/min/1.73 m^2. Dapagliflozin is likely to be ineffective in this setting based upon its mechanism of action.

Dapagliflozin is not recommended for the treatment of chronic kidney disease in patients with polycystic kidney disease or patients requiring or with a recent history of immunosuppressive therapy for kidney disease. Dapagliflozin is not expected to be effective in these populations.

Posology and Method of Administration
Prior to Initiation of Dapagliflozin
Assess renal function prior to initiation of Dapagliflozin therapy and then as clinically indicated.
Assess volume status and, if necessary, correct volume depletion prior to initiation of Dapagliflozin

Recommended Dosage
See Table 1 for dosage recommendations based on estimated glomerular filtration rate (eGFR).

eGFR (mL/min/1.73 m^2)	Recommended Dose
eGFR 45 or greater	To improve glycemic control, the recommended starting dose is 5 mg orally once daily. Dose can be increased to 10 mg orally once daily for additional glycemic control*. For all other indications, the recommended starting dose is 10 mg orally once daily.
eGFR 25 to less than 45	10 mg orally once daily*.
eGFR less than 25	Initiation is not recommended, however patients may continue 10 mg orally once daily to reduce the risk of eGFR decline, ESKD, CV death and hHF.
On dialysis	Contraindicated.

* Dapagliflozin is not recommended for use to improve glycemic control in adults with type 2 diabetes mellitus with an eGFR less than 45 mL/min/1.73 m^2. Dapagliflozin is likely to be ineffective in this setting based upon its mechanism of action.
hHF: hospitalization for heart failure, CV: Cardiovascular, ESKD: End Stage Kidney Disease.

Pediatric Use
Safety and effectiveness of Dapagliflozin in pediatric patients under 18 years of age have not been established.

Geriatric Use
No Dapagliflozin dosage change is recommended based on age.

Method of Administration
Oral

Contraindications
- History of a serious hypersensitivity reaction to dapagliflozin, such as anaphylactic reactions or angioedema.

Patients on dialysis

Interaction with Other Medicinal Products and Other Forms of Interaction
Positive Urine Glucose Test
Monitoring glycemic control with urine glucose tests is not recommended in patients taking SGLT2 inhibitors as SGLT2 inhibitors increase urinary glucose excretion and will lead to positive urine glucose tests. Use alternative methods to monitor glycemic control.

Interference with 1,5-anhydroglucitol (1,5-AG) Assay
Monitoring glycemic control with 1,5-AG assay is not recommended as measurements of 1,5-AG are unreliable in assessing glycemic control in patients taking SGLT2 inhibitors. Use alternative methods to monitor glycemic control.

Use in Specific Populations
Pregnancy
Pregnancy
Risk Summary
Based on animal data showing adverse renal effects, Dapagliflozin is not recommended during the second and third trimesters of pregnancy.
Limited data with dapagliflozin in pregnant women are not sufficient to determine drug associated risk for major birth defects or miscarriage. There are risks to the mother and fetus associated with poorly controlled diabetes and untreated heart failure in pregnancy.
In animal studies, adverse renal pelvic and tubule dilatations, that were not fully reversible, were observed in rats when dapagliflozin was administered during a period of renal development corresponding to the late second and third trimesters of human pregnancy, at all doses tested; the lowest of which provided an exposure 15-times the 10 mg clinical dose

Lactation
Risk Summary
There is no information regarding the presence of dapagliflozin in human milk, the effects on the breastfed infant, or the effects on milk production. Dapagliflozin is present in the milk of lactating rats (see Data). However, due to species specific differences in lactation physiology, the clinical relevance of these data are not clear.
Since human kidney maturation occurs in utero and during the first 2 years of life when lactational exposure may occur, there may be risk to the developing human kidney. Because of the potential for serious adverse reactions in breastfed infants, advise women that use of dapagliflozin is not recommended while breastfeeding.

Data
Dapagliflozin was present in rat milk at a milk/plasma ratio of 0.49, indicating that dapagliflozin and its metabolites are transferred into milk at a concentration that is approximately 50% of that in maternal plasma. Juvenile rats directly exposed to dapagliflozin showed risk to the developing kidney (renal pelvic and tubular dilatations) during maturation.

Effects on Ability to Drive and Use Machines
Dapagliflozin has no or negligible influence on the ability to drive and use machines. Patients should be alerted to the risk of hypoglycaemia when dapagliflozin is used in combination with a sulphonylurea or insulin.

Undesirable Effects
Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.
Dapagliflozin has been evaluated in clinical trials in patients with type 2 diabetes mellitus, in patients with heart failure, and in patients with chronic kidney disease. The overall safety profile of dapagliflozin was consistent across the studied indications. Severe hypoglycemia and diabetic ketoacidosis (DKA) were observed only in patients with diabetes mellitus.
These adverse reactions were not present at baseline, occurred more commonly on Dapagliflozin than on placebo, and occurred in at least 2% of patients treated with either Dapagliflozin 5 mg or Dapagliflozin 10 mg.
Table - shows common adverse reactions associated with the use of Dapagliflozin

Adverse Reaction	% of Patients		
	Pool of 12 Placebo-Controlled Studies		
	Placebo N=1393	DAPAGLIFLOZIN 5 mg N=1145	DAPAGLIFLOZIN 10 mg N=1193
Female genital mycotic infections*	1.5	8.4	6.9
Nasopharyngitis	6.2	6.6	6.3
Urinary tract infections[†]	3.7	5.7	4.3
Back pain	3.2	3.1	4.2
Increased urination[‡]	1.7	2.9	3.8
Male genital mycotic infections[§]	0.3	2.8	2.7
Nausea	2.4	2.8	2.5
Influenza	2.3	2.7	2.3
Dyslipidemia	1.5	2.1	2.5
Constipation	1.5	2.2	1.9
Discomfort with urination	0.7	1.6	2.1
Pain in extremity	1.4	2.0	1.7

* Genital mycotic infections include the following adverse reactions, listed in order of frequency reported for females: vulvovaginal mycotic infection, vaginal infection, vulvovaginal candidiasis, vulvovaginitis, genital infection, genital candidiasis, fungal genital infection, vulvitis, genitourinary tract infection, vulval abscess, and vaginitis bacterial. (N for females: Placebo = 677, DAPAGLIFLOZIN 5 mg = 581, DAPAGLIFLOZIN 10 mg = 5 9 8).
† Urinary tract infections include the following adverse reactions, listed in order of frequency reported: urinary tract infection, cystitis, *Escherichia* urinary tract infection, genitourinary tract infection, pyelonephritis, trigonitis, urethritis, kidney infection, and prostatitis.
‡ Increased urination includes the following adverse reactions, listed in order of frequency reported: pollakiuria, polyuria, and urine output increased.
§ Genital mycotic infections include the following adverse reactions, listed in order of frequency reported for males: balanitis, fungal genital infection, balanitis candida, genital candidiasis, genital infection male, penile infection, balanoposthitis, balanoposthitis infective, genital infection, and posthitis. (N for males: Placebo=716, DAPAGLIFLOZIN 5 mg=564, DAPAGLIFLOZIN 10 mg=595).

Volume Depletion
Dapagliflozin causes an osmotic diuresis, which may lead to a reduction in intravascular volume. Adverse reactions related to volume depletion (including reports of dehydration, hypovolemia, orthostatic hypotension, or hypotension) in patients with type 2 diabetes mellitus.

Hypoglycemia
Hypoglycemia was more frequent when dapagliflozin was added to sulfonylurea or insulin.

Genital Mycotic Infections
In the glycemic control trials, genital mycotic infections were more frequent with dapagliflozin treatment.
Infections were more frequently reported in females than in males. The most frequently reported genital mycotic infections were vulvovaginal mycotic infections in females and balanitis in males. Genital mycotic infections that caused study drug discontinuation were reported in 0.9% of patients treated with dapagliflozin and <0.1% of patients treated with placebo.

Hypersensitivity Reactions
Hypersensitivity reactions (e.g., angioedema, urticaria, hypersensitivity) were reported with dapagliflozin treatment. In glycemic control studies, serious anaphylactic reactions and severe cutaneous adverse reactions and angioedema were reported in 0.2% of comparator-treated patients and 0.3% of dapagliflozin-treated patients. If hypersensitivity reactions occur, discontinue use of Dapagliflozin; treat per standard of care and monitor until signs and symptoms resolve.

Ketoacidosis in Patients with Diabetes Mellitus
In the DECLARE study, events of diabetic ketoacidosis (DKA) were reported in 27 out of 8574 patients in the dapagliflozin-treated group and 12 out of 8569 patients in the placebo group. The events were evenly distributed over the study period.

Laboratory Tests
Increases in Serum Creatinine and Decreases in eGFR
Initiation of SGLT2 inhibitors, including dapagliflozin causes a small increase in serum creatinine and decrease in eGFR. In patients with normal or mildly impaired renal function at baseline, these changes in serum creatinine and eGFR generally occur within weeks of starting therapy and then stabilize.

Increase in Hematocrit
In the pool of 13 placebo-controlled studies of glycemic control, increases from baseline in mean hematocrit values were observed in dapagliflozin-treated patients starting at Week 1 and continuing up to Week 16, when the maximum mean difference from baseline was observed. At Week 24, the mean changes from baseline in hematocrit were −0.33% in the placebo group and 2.30% in the dapagliflozin 10 mg group. By Week 24, hematocrit values >55% were reported in 0.4% of placebo-treated patients and 1.3% of dapagliflozin 10 mg-treated patients.

Increase in Low-Density Lipoprotein Cholesterol
In the pool of 13 placebo-controlled studies of glycemic control, changes from baseline in mean lipid values were reported in dapagliflozin-treated patients compared to placebo-treated patients. Mean percent changes from baseline at Week 24 were 0.0% versus 2.5% for total cholesterol, and -1.0% versus 2.9% for LDL cholesterol in the placebo and dapagliflozin 10 mg groups, respectively. In the DECLARE study, mean changes from baseline after 4 years were 0.4 mg/dL versus - 4.1 mg/dL for total cholesterol, and -2.5 mg/dL versus -4.4 mg/dL for LDL cholesterol, in dapagliflozin treated and the placebo groups, respectively.

Decrease in Serum Bicarbonate
In a study of concomitant therapy of dapagliflozin 10 mg with exenatide extended-release (on a background of metformin), four patients (1.7%) on concomitant therapy had a serum bicarbonate value of less than or equal to 13 mEq/L compared to one each (0.4%) in the dapagliflozin and exenatide-extended release treatment groups.

DAPA-HF Heart Failure Study
No new adverse reactions were identified in the DAPA-HF heart failure study.

DAPA-CKD Chronic Kidney Disease Study
No new adverse reactions were identified in the DAPA-CKD study in patients with chronic kidney disease.

Post-marketing Experience
Additional adverse reactions have been identified during post approval use of dapagliflozin in patients with diabetes mellitus. Because these reactions are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.
Ketoacidosis
Acute Kidney Injury
Urosepsis and Pyelonephritis
Necrotizing Fasciitis of the Perineum (Fournier's Gangrene)
Rash

PHARMACOLOGICAL PROPERTIES
Pharmacodynamics:
Pharmacotherapeutic group: Drugs used in diabetes, sodium-glucose co-transporter 2 (SGLT2) inhibitors, ATC code: A10BK01
Mechanism of action
Sodium-glucose cotransporter 2 (SGLT2), expressed in the proximal renal tubules, is responsible for the majority of the reabsorption of filtered glucose from the tubular lumen. Dapagliflozin is an inhibitor of SGLT2. By inhibiting SGLT2, dapagliflozin reduces reabsorption of filtered glucose and thereby promotes urinary glucose excretion.

Dapagliflozin also reduces sodium reabsorption and increases the delivery of sodium to the distal tubule. This may influence several physiological functions including, but not restricted to, lowering both pre- and afterload of the heart and downregulation of sympathetic activity, and decreased intraglomerular pressure which is believed to be mediated by increased tubuloglomerular feedback.

Mechanism of Action
Sodium-glucose cotransporter 2 (SGLT2), expressed in the proximal renal tubules, is responsible for the majority of the reabsorption of filtered glucose from the tubular lumen. Dapagliflozin is an inhibitor of SGLT2. By inhibiting SGLT2, Dapagliflozin reduces reabsorption of filtered glucose and lowers the renal threshold for glucose, and thereby increases urinary glucose excretion. Dapagliflozin also reduces sodium reabsorption and increases the delivery of sodium to the distal tubule. This may influence several physiological functions including, but not restricted to, lowering both pre- and afterload of the heart and downregulation of sympathetic activity.

Pharmacokinetic Properties
Absorption
Following oral administration of dapagliflozin, the maximum plasma concentration (Cmax) is usually attained within 2 hours under fasting state. The Cmax and AUC values increase dose proportionally with increase in dapagliflozin dose in the therapeutic dose range. The absolute oral bioavailability of dapagliflozin following the administration of a 10 mg dose is 78%. Administration of dapagliflozin with a high-fat meal decreases its Cmax by up to 50% and prolongs Tmax by approximately 1 hour, but does not alter AUC as compared with the fasted state. These changes are not considered to be clinically meaningful and dapagliflozin can be administered with or without food.

Distribution
Dapagliflozin is approximately 91% protein bound. Protein binding is not altered in patients with renal or hepatic impairment.

Metabolism
The metabolism of dapagliflozin is primarily mediated by UGT1A9; CYP-mediated metabolism is a minor clearance pathway in humans. Dapagliflozin is extensively metabolized, primarily to yield dapagliflozin 3-O-glucuronide, which is an inactive metabolite. Dapagliflozin 3-O-glucuronide accounted for 61% of a 50 mg [14C]-dapagliflozin dose and is the predominant drug-related component in human plasma.
Elimination
Dapagliflozin and related metabolites are primarily eliminated via the renal pathway.

Following a single 50 mg dose of [14C]-dapagliflozin, 75% and 21% total radioactivity is excreted in urine and feces, respectively. In urine, less than 2% of the dose is excreted as parent drug. In feces, approximately 15% of the dose is excreted as parent drug.

Back

The mean plasma terminal half-life (t½) for dapagliflozin is approximately 12.9 hours following a single oral dose of dapagliflozin 10 mg.

Preclinical Safety Data

Carcinogenesis, Mutagenesis, Impairment of Fertility

Dapagliflozin did not induce tumors in either mice or rats at any of the doses evaluated in 2-year carcinogenicity studies. Oral doses in mice consisted of 5, 15, and 40 mg/kg/day in males and 2, 10, and 20 mg/kg/day in females, and oral doses in rats were 0.5, 2, and 10 mg/kg/day for both males and females. The highest doses evaluated in mice were approximately 72-times (males) and 105-times (females) the clinical dose of 10 mg per day, based on AUC exposure. In rats, the highest dose was approximately 131-times (males) and 186-times (females) the clinical dose of 10 mg per day, based on AUC exposure.

Dapagliflozin was negative in the Ames mutagenicity assay and was positive in a series of in vitro clastogenicity assays in the presence of S9 activation and at concentrations greater than or equal to 100 µg/mL. Dapagliflozin was negative for clastogenicity in a series of in vivo studies evaluating micronuclei or DNA repair in rats at exposure multiples greater than 2100-times the clinical dose.

There was no carcinogenicity or mutagenicity signal in animal studies, suggesting that dapagliflozin does not represent a genotoxic risk to humans. Dapagliflozin had no effects on mating, fertility, or early embryonic development in treated male or female rats at exposure multiples less than or equal to 1708-times and 998-times the maximum recommended human dose in males and females, respectively.

PHARMACEUTICAL PARTICULARS:

INCOMPATIBILITY
Not applicable.

SHELF-LIFE:
24 months

STORAGE CONDITION
Store below 30°C.

NATURE AND CONTENTS OF CONTAINER
10 tablets in Alu-Alu blister pack, 3 such blisters in a printed carton along with Pack Insert.

VERSION No.: 00

LAST REVISION DATE:
Sep 30, 2021

Manufacturing Authorization Holder	Manufacturer
Ajanta Pharma Limited Ajanta House, Charkop Kandivli (West) Mumbai - 400 067, India. Tel : 022-6913 2111/2112 Fax : 022-6913 2070 Email : info@ajantapharma.com	Ajanta Pharma Limited Z/103/A, Dahej SEZ II, Bharuch – 392 130 Gujarat State, India

DIAZAC

Dapagliflozin Tablets

PATIENT INFORMATION LEAFLET

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet:

1. What DIAZAC tablet is and what it is used for
2. What you need to know before you take DIAZAC tablet
3. How to take DIAZAC tablet
4. Possible side effects
5. How to store DIAZAC tablet
6. Contents of the pack and other information

1. What DIAZAC tablet is and what it is used for

DIAZAC contains the active substance dapagliflozin. It belongs to a group of medicines called "sodium glucose co-transporter-2 (SGLT2) inhibitors". They work by blocking the SGLT2 protein in your kidney. By blocking this protein, blood sugar (glucose), salt (sodium) and water are removed from your body via the urine.
DIAZAC is a prescription medicine used:

- along with diet and exercise to improve blood sugar (glucose) control in adults with type 2 diabetes
- to reduce the risk of hospitalization for heart failure in adults with type 2 diabetes who also have known cardiovascular disease or multiple cardiovascular risk factors
- to reduce the risk of cardiovascular death, hospitalization for heart failure in adult patients with heart failure, when the heart is weak and cannot pump enough blood to the rest of your body
- to reduce the risk of further worsening of your kidney disease, end-stage kidney disease (ESKD), death due to cardiovascular disease, and hospitalization for heart failure in adults with chronic kidney disease.

DIAZAC is not for people with type 1 diabetes. DIAZAC may increase the risk of diabetic ketoacidosis (increased ketones in your blood or urine) in people with type 1 diabetes.

DIAZAC is not for use to improve blood sugar (glucose) control in adults with type 2 diabetes who have moderate to severe kidney problems, because it may not work.

DIAZAC is not for people with certain genetic forms of polycystic kidney disease, or who are taking or have recently received immunosuppressive therapy to treat kidney disease. DIAZAC is not expected to work if you have these conditions.

It is not known if DIAZAC is safe and effective in children younger than 18 years of age.

2. What you need to know before you take DIAZAC tablet

Do not take DIAZAC if you:

- Are allergic to dapagliflozin or any of the ingredients in DIAZAC.

Symptoms of a serious allergic reaction to DIAZAC may include:

- skin rash
- raised red patches on your skin (hives)
- swelling of the face, lips, tongue, and throat that may cause difficulty in breathing or swallowing

If you have any of these symptoms, stop taking DIAZAC and contact your healthcare provider or go to the nearest hospital emergency room right away.

- Are on dialysis.

Before you take DIAZAC, tell your healthcare provider if you:

- have type 1 diabetes or have had diabetic ketoacidosis.
- have liver problems.
- have a history of urinary tract infections or problems urinating.
- are going to have surgery. Your doctor may stop your DIAZAC before you have surgery. Talk to your doctor if you are having surgery about when to stop taking DIAZAC and when to start it again.
- are eating less or there is a change in your diet.
- have or have had problems with your pancreas, including pancreatitis or surgery on your pancreas.
- drink alcohol very often or drink a lot of alcohol in the short term ("binge" drinking).
- are pregnant or plan to become pregnant. DIAZAC may harm your unborn baby. If you become pregnant while taking DIAZAC, your healthcare provider may switch you to a different medicine to control your blood sugar. Talk to your healthcare provider about the best way to control your blood sugar if you plan to become pregnant or while you are pregnant.
- are breastfeeding or plan to breastfeed. It is not known if DIAZAC passes into your breast milk. You should not breastfeed if you take DIAZAC.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

3. How to take DIAZAC tablet

- Take DIAZAC exactly as your healthcare provider tells you to take it.
- Do not change your dose of DIAZAC without talking to your healthcare provider.
- Take DIAZAC by mouth 1 time each day, with or without food.
- Stay on your prescribed diet and exercise program while taking DIAZAC.
- DIAZAC will cause your urine to test positive for glucose.
- Your healthcare provider may do certain blood tests before you start DIAZAC and during your treatment.
- If you have diabetes
  - When your body is under some types of stress, such as fever, trauma (such as a car accident), infection, or surgery, the amount of diabetes medicine you need may change. Tell your healthcare provider right away if you have any of these conditions and follow your healthcare provider's instructions.
  - Your healthcare provider will check your diabetes with regular blood tests, including your blood sugar levels and your HbA1c.
  - Follow your healthcare provider's instructions for treating low blood sugar (hypoglycemia). Talk to your healthcare provider if low blood sugar is a problem for you.

If you miss a dose, take it as soon as you remember. If it is almost time for your next dose, skip the missed dose and take the medicine at the next regularly scheduled time. Do not take 2 doses of DIAZAC at the same time.

If you take too much DIAZAC, call your healthcare provider or go to the nearest emergency room right away.

If you have diabetes

- When your body is under some types of stress, such as fever, trauma (such as a car accident), infection, or surgery, the amount of diabetes medicine you need may change. Tell your healthcare provider right away if you have any of these conditions and follow your healthcare provider's instructions.
- Your healthcare provider will check your diabetes with regular blood tests, including your blood sugar levels and your HbA1c.
- Follow your healthcare provider's instructions for treating low blood sugar (hypoglycemia). Talk to your healthcare provider if low blood sugar is a problem for you.

4. Possible side effects

DIAZAC can cause serious side effects, including:

Dehydration

DIAZAC can cause some people to become dehydrated (the loss of body water and salt). Dehydration may cause you to feel dizzy, faint, lightheaded, or weak, especially when you stand up (orthostatic hypotension). There have been reports of sudden kidney injury in people with Type 2 diabetes who are taking DIAZAC. You may be at a higher risk of dehydration if you:

- take medicines to lower your blood pressure, including water pills (diuretics)
- are 65 years of age or older
- are on a low salt diet
- have kidney problems

Talk to your healthcare provider about what you can do to prevent dehydration including how much fluid you should drink on a daily basis. Call your healthcare provider right away if you reduce the amount of food or liquid you drink, for example if you cannot eat or you start to lose liquids from your body, for example from vomiting, diarrhea, or being in the sun too long.

Vaginal yeast infection

Women who take DIAZAC may get vaginal yeast infections. Symptoms of a vaginal yeast infection include:

- vaginal odor
- white or yellowish vaginal discharge (discharge may be lumpy or look like cottage cheese)
- vaginal itching

Yeast infection of the penis (balanitis)

Men who take DIAZAC may get a yeast infection of the skin around the penis. Certain men who are not circumcised may have swelling of the penis that makes it difficult to pull back the skin around the tip of the penis. Other symptoms of yeast infection of the penis include:

- redness, itching, or swelling of the penis
- rash of the penis
- foul smelling discharge from the penis
- pain in the skin around the penis

Talk to your healthcare provider about what to do if you get symptoms of a yeast infection of the vagina or penis. Your healthcare provider may suggest you use an over-the-counter antifungal medicine. Talk to your healthcare provider right away if you use an over-the-counter antifungal medication and your symptoms do not go away.

Ketoacidosis in people with diabetes mellitus (increased ketones in your blood or urine) - Ketoacidosis has happened in people who have type 1 diabetes or type 2 diabetes, during treatment with DIAZAC. Ketoacidosis has also happened in people with diabetes who were sick or who had surgery during treatment with DIAZAC. Ketoacidosis is a serious condition, which may need to be treated in a hospital. Ketoacidosis may lead to death.

Ketoacidosis can happen with DIAZAC even if your blood sugar is less than 250 mg/dL. Stop taking DIAZAC and call your healthcare provider right away if you get any of the following symptoms:

- nausea o tiredness
- vomiting o trouble breathing
- stomach area (abdominal) pain

If you get any of these symptoms during treatment with DIAZAC, if possible, check for ketones in your urine, even if your blood sugar is less than 250 mg/dL.

Serious urinary tract infections

Hospitalization have happened in people who are taking DIAZAC.

Tell your healthcare provider if you have any signs or symptoms of a urinary tract infection such as a burning feeling when passing urine, a need to urinate often, the need to urinate right away, pain in the lower part of your stomach (pelvis), or blood in the urine. Sometimes people also may have a fever, back pain, nausea or vomiting.

Low blood sugar (hypoglycemia) in patients with diabetes mellitus. If you take DIAZAC with another medicine that can cause low blood sugar, such as a sulfonylurea or insulin, your risk of getting low blood sugar is higher. The dose of your sulfonylurea medicine or insulin may need to be lowered while you take DIAZAC. Signs and symptoms of low blood sugar may include:

- headache
- weakness
- confusion
- shaking or feeling jittery
- drowsiness
- dizziness
- irritability
- sweating
- hunger
- fast heartbeat

A rare but serious bacterial infection that causes damage to the tissue under the skin (necrotizing fasciitis) in the area between and around the anus and genitals (perineum). Necrotizing fasciitis of the perineum has happened in women and men with diabetes mellitus who take DIAZAC. Necrotizing fasciitis of the perineum may lead to hospitalization, may require multiple surgeries, and may lead to death. Seek medical attention immediately if you have fever or you are feeling very weak, tired, or uncomfortable (malaise) and you develop any of the following symptoms in the area between and around the anus and genitals:

- pain or tenderness
- swelling
- redness of skin (erythema)

The most common side effects of DIAZAC include:

- vaginal yeast infections and yeast infections of the penis
- stuffy or runny nose and sore throat
- changes in urination, including urgent need to urinate more often, in larger amounts, or at night

These are not all the possible side effects of DIAZAC. For more information, ask your healthcare provider or pharmacist. Call your doctor for medical advice about side effects.

5. How to store DIAZAC

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date, which is stated on the blister or carton after 'EXP'. The expiry date refers to the last day of that month.
- This medicine does not require any special storage conditions.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the package and other information

What DIAZAC contains:

DIAZAC 5: Each film-coated tablet contains Dapagliflozin 5 mg

DIAZAC 10: Each film-coated tablet contains Dapagliflozin 10 mg

Other Ingredients:

Microcrystalline Cellulose, Anhydrous Lactose, Polyoxyl 40 Hydrogenated Castor Oil, Isopropyl Alcohol, Colloidal Silicon Dioxide, Crospovidone, Magnesium Stearate, Methylene Chloride, Opadry Yellow 03B22227.

What DIAZAC looks like and contents of the pack:

Film-coated tablets

The tablets are provided in Alu-Alu blister pack. 10 tablets are packed in a Alu-Alu blister, 3 such blisters are packed in a printed carton along with Pack Insert.

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Manufacturing Authorization Holder	Manufacturer
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