Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Kacital 1080 mg modified-release tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 1080 mg of potassium citrate (10 milliequivalents (mEq)), equivalent to 390 mg of potassium.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Modified-release tablet
Cream coloured to yellow, oval, biconvex, uncoated tablets (length: 18.50 mm).

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Kacital is an alkalizing agent and indicated in adults for:

- The treatment of patients with kidney stones and hypocitraturia, or chronic calcium oxalate stones.
- The treatment and prevention of recurrent uric acid lithiasis with or without calcium lithiasis and cystine lithiasis.
- The treatment of distal renal tubular acidosis with calcium nephrolithiasis.

4.2 Posology and method of administration

Posology
In patients with severe hypocitraturia (urinary citrate <150 mg/day), therapy should be initiated at a dosage of 6480 mg (60 mEq) per day (6 tablets) divided into 3 intakes per day.

In patients with mild hypocitraturia (urinary citrate >150 mg/day), therapy should be initiated at a dosage of 3240 mg (30 mEq) per day (3 tablets) divided into 3 intakes per day.

If necessary, the dosage may be increased as long as the 10800 mg (100 mEq)/day limit is not exceeded.

Renal impairment
Kacital is contraindicated in individuals with glomerular filtration rate (GFR) ≤44 mL/min/1.73 m^2 (see section 4.3). For individuals with a GFR between 45 and 59 mL/min/1.73 m^2 and plasma potassium levels in the normal range, regular monitoring of renal function parameters and blood potassium levels is recommended (see section 4.4).

Kacital is contraindicated in patients with elevated plasma potassium levels (see section 4.3 and 5.2).

It is recommended that 24-hour urinary citrate and urinary pH measurement is used to determine the adequacy of the initial dosage and to evaluate the effectiveness of any dosage change. In the case of a pH value which is higher or lower than the target range of 6.0 to 7.0, the daily dose should be adjusted in accordance with the needs of the patient. This is preferably done with the evening dose.

Hepatic impairment
Potassium citrate should be used with caution in patients with hepatic impairment (see section 4.4).

Paediatric population
The safety and efficacy of Kacital in children have not been established. No data are available.

Elderly
Dosage adjustment is not necessary for the elderly.

Method of administration
Kacital is administered orally.

The tablets should be taken with meals or within 30 minutes after meals to avoid gastrointestinal reactions.

The tablets must be swallowed whole with enough liquid and should not be taken with alcohol, crushed, chewed, or dissolved as this may result in the medicine being released too early (see also section 4.5).

The tablets should be taken in conjunction with a diet that avoids foods with high sodium content and avoids the use of table salts. Patients who take Kacital tablets should increase their fluid intake.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Renal impairment (GFR ≤ 44 mL/min/1.73 m^2)
- Active or persistent urinary tract infections
- Significant or complete obstruction of the urinary tract
- Hyperkalaemia
- Severe myocardial injury
- Uncontrolled diabetes mellitus
- Adrenal insufficiency
- Metabolic or respiratory alkalosis
- Active peptic ulcer
- Delayed gastric emptying
- Intestinal obstruction
- Patients on anticholinergic drug therapy

4.4 Special warnings and precautions for use

Hyperkalaemia and cardiotoxicity
In patients with impaired mechanisms for excreting potassium, the administration of Kacital can produce hyperkalaemia and cardiac arrest. Potentially fatal hyperkalaemia can develop rapidly and be asymptomatic.

There is an increased risk of hyperkalaemia when Kacital is administered concomitantly with other medicinal products, see section 4.5. Caution should be exercised in patients with sickle cell anaemia due to the increased risk of hyperkalaemia.

Patients with cardiovascular disease e.g., cardiac arrest, cardiac arrhythmias, may be more susceptible to life-threatening cardiac effects associated with hyper/hypokalaemia and, therefore, potassium citrate should be used with caution.

Serum electrolytes (sodium, potassium, chloride and carbon dioxide), serum creatinine, and complete blood count should be monitored prior to initiation of therapy and every three months for the duration of the therapy.

Severe hepatic impairment
There is the potential for hyperkalaemia and citrate toxicity in severe hepatic impairment though the impact of oral potassium citrate in these patients has not been studied (see section 4.2).

Renal impairment
For individuals with a GFR between 45 and 59 mL/min/1.73m^2 and plasma potassium levels in the normal ranges, regular monitoring of renal function parameters and blood potassium levels is recommended at starting dose, after new dose increase or in case of decreased GFR. Then frequency should be according to the physician's criteria, every three months.

Other Information
This medicinal product contains 390 mg potassium per tablet. To be taken into consideration by patients with reduced kidney function or patients on a controlled potassium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use should be avoided

Amphetamines	Alkalinizing agents may decrease the excretion of amphetamines. Management: Consider alternatives to using amphetamines and alkalinizing agents in combination. If these agents must be used together, patients should be monitored closely for excessive amphetamine effects. Modification of therapy should be considered.
Anticholinergic agents	May enhance the ulcerogenic effect of potassium citrate.
Potassium-sparing diuretics (i.e., amiloride, eplerenone, spironolactone, triamterene)	Potassium salts may enhance the hyperkalaemic effect of potassium-sparing diuretics. Management: This combination should only be used in cases of significant hypokalaemia, and only if serum potassium can be closely monitored. Modification of therapy should be considered.

Concomitant use requires monitoring

ACE inhibitors	May enhance the hyperkalaemic effect of potassium salts.
Aliskiren	Potassium salts may enhance the hyperkalaemic effect of aliskiren.
Alpha-/beta-agonists (indirect-acting)	Alkalinizing agents may increase the serum concentration of alpha-/beta-agonists (indirect-acting).
Aluminium hydroxide	Citric acid derivatives may increase the absorption of aluminium hydroxide.
Amantadine	Alkalinizing agents may increase the serum concentration of amantadine.
Angiotensin II receptor blockers	Potassium salts may enhance the hyperkalaemic effect of angiotensin II receptor blockers.
Antibiotics (e.g., amoxicillin, sulfamethoxaxole + trimethoprim, or ciprofloxacin)	Alkalizing agents may cause crystalluria in the renal system due to the alkalisation of urine
Beta-blockers	May enhance the hyperkalaemic effect of potassium salts.
Digoxin and other cardiac glycosides	May enhance the hyperkalaemic effect of potassium salts and affect how these heart medications work. This may lead to serious or life-threatening heart rhythm problems such as bradycardia or arrhythmias.
Drospirenone-containing products	May enhance the hyperkalaemic effect of potassium salts.
Finerenone	Potassium salts may enhance the hyperkalaemic effect of finerenone.
Heparins (unfractionated and low-molecular weight)	May enhance the hyperkalaemic effect of potassium salts.
Mecamylamine	Alkalinizing agents may increase the serum concentration of mecamylamine.

Memantine	Alkalinizing agents may increase the serum concentration of memantine.
Nicorandil	May enhance the hyperkalaemic effect of potassium salts.
Nonsteroidal anti-inflammatory agents (NSAIDs) (e.g., indomethacin)	May enhance the hyperkalaemic effect of potassium salts.
Quinine	Alkalinizing agents may increase the serum concentration of quinine.

Interaction with alcohol
When Kacital is mixed with alcohol the rate of dissolution may be increased. This can lead to a loss of the modified-release effect (see section 4.2).

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no data from the use of Kacital in pregnant women. Animal reproduction studies with potassium citrate or citric acid do not indicate direct or indirect harmful effects with respect to reproductive toxicity.

Kacital should only be used during pregnancy if the expected benefits outweigh the potential risks.

Hyperkalaemic and hypokalaemic serum levels may lead to impaired maternal and foetal cardiac function. Therefore, the mother's electrolyte levels should be checked regularly.

Breast-feeding
Potassium is excreted into breast milk. However, as long as maternal electrolyte levels of the mother remain within physiological limits, no effects on the breastfed newborns/infants are anticipated and Kacital can be used during breast-feeding.

Fertility
It is unknown whether potassium citrate affects fertility in human. Animal studies with citric acid did not affect fertility.

4.7 Effects on ability to drive and use machines

Kacital has no influence on the ability to drive and use machines.

4.8 Undesirable effects

The following adverse drug reactions and incidences have been reported in patients treated with potassium citrate. The main risks are based upon ingestion of potassium and the risk around induced hyperkalaemia. Severe hyperkalaemia may lead to muscle weakness/paralysis and cardiac conduction abnormalities (e.g., heart block, ventricular arrhythmias, asystole).

The other documented adverse reaction relates to the formulation and potassium products causing gastro-intestinal upset including nausea, vomiting, diarrhoea, abdominal pain, discomfort and can potentially lead to gastro-intestinal ulceration, bleeding, perforation and/or obstruction.

Adverse reactions are listed according to MedDRA organ classes and frequency. Frequencies are defined as: Very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1 000 to <1/100), rare (≥1/10 000 to <1/1 000), very rare (<1/10 000), not known (cannot be estimated from the available data).

System organ class/frequency	**MedDRA preferred term**
Gastrointestinal disorders	
Very common	Abdominal pain, mild nausea
Common	Abdominal pain upper, diarrhoea, dyspepsia, gastrointestinal pain, dysphagia, oesophagitis, vomiting

Not known	Gastrointestinal mucosal damage, gastrointestinal bleeding or obstruction
Metabolism and nutrition disorders	
Not known	Hyperkalaemia
Skin	
Common	Rash

In patients with rapid gastrointestinal transit time, the tablet wax matrix may be present in their faeces.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system:
HPRA Pharmacovigilance
Website: www.hpra.ie

4.9 Overdose

Reports of a laxative effect after excessive oral doses of individual alkalising salts have occurred. An acute massive intake of potassium can cause hyperkalaemia resulting in nausea, vomiting, and diarrhoea and in severe cases paraesthesia, muscular weakness, mental confusion, electrocardiographic abnormalities (large and symmetric T waves), arrhythmia, atrioventricular block and heart failure. Hyperkalaemia is a particular concern in patients with underlying renal insufficiency.
In case of severe hyperkalaemia, patients should be monitored (mostly plasma potassium level and ECG) and the appropriate symptomatic and supportive therapy instituted in specialised care units, where emergency treatments leading to rapid elimination of potassium such as ion exchange resin, combination of insulin-dextrose or β2 mimetics (salbutamol) or haemodialysis will be implemented.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: mineral supplements, potassium
ATC code: A12BA02

Administration of the medicinal product increases urinary pH and raises urinary citrate. During long-term administration the daily excreted amounts of potassium largely correlate with the daily given dose and an accumulation of potassium is unlikely in the case of intact renal and hepatic function. In some patients, a transient decrease of urinary calcium can occur.

As a result of the alkalizing effect of Kacital, the tendency for calcium oxalate and uric acid to crystallize is significantly decreased, with subsequent decreased tendency for development of renal lithiasis from these salts. Evidence is based but not limited to the following studies. During a long-term therapy (1 to 4.33 years) in 89 patients potassium citrate (usually 20 mEq three times a day) caused a sustained increase in urinary pH and potassium and restored urinary citrate to normal levels - pH 5.65 ± 0.40 to 6.43 ± 0.42 after 4 months remaining at same level until 24 months. The treatment produced clinical improvement, since individual stone formation decreased in 97.8% of the patients, remission was obtained in 79.8% and the need for surgical treatment of newly formed stones was eliminated.
In 18 patients receiving potassium citrate for 3 years stone formation significantly declined after treatment from 1.2 ± 0.6 to 0.1 ± 0.2 per patient year ($p<0.0001$), in 13 patients (72%) the disease was in remission and all patients showed a reduced stone formation rate individually. In contrast 20 patients taking placebo medication for 3 years showed no significant change in stone formation rate (1.1 ± 0.4 to 1.1 ± 0.3 per patient year) and in only 4 patients (20%) was the disease in remission.

Furthermore, the increase in urine citrate content favours its combination with calcium salts, decreasing calcium ion activity and thus the saturation of calcium oxalate. Evidence is based but not limited to the following studies. During potassium citrate therapy in 5 patients, urinary calcium significantly declined from 154 mg/day to 99 mg/day and the urinary saturation of calcium oxalate decreased. The increase in urinary pH, both decreases the calcium ion activity to make its combination with dissociated anions easier and contributes to increase the ionization of uric acid.

In another study urinary pH increased from low (5.30 ± 0.31) to normal (6.19 to 6.46) during long-term treatment (2.78 years) in 18 patients (six with uric acid stones alone and 12 with both uric acid and calcium stones). Urinary content of undissociated uric acid decreased from 204 to the normal range (64 – 108 mg/day) following treatment. Urinary citrate rose from 503 mg/day to a range 852 – 998 mg/day. Urinary saturation of calcium oxalate and stone formation significantly declined. Remission was experienced in 94.4% of patients.

Kacital does not alter the urinary saturation of calcium phosphate, since the effect of increased citrate complexation of calcium is opposed by the rise in the pH-dependent dissociation of phosphate. Calcium phosphate stones are more stable in alkaline urine.

5.2 Pharmacokinetic properties

Kacital is almost completely absorbed from the upper part of the gastrointestinal tract within 3 hours.

In patients with normal renal function, a rise in urinary citrate is observed within the first hour after administering Kacital at a 20 mEq dose and lasts approximately 12 hours. With multiple doses, the rise in citrate excretion reaches its peak by the third day. Kacital averts the normally wide circadian fluctuation in urinary citrate, thus maintaining urinary citrate at a higher, more constant level throughout the day.

When the treatment with Kacital is withdrawn, urinary citrate begins to return to pre-treatment levels.

The rise in citrate excretion is directly dependant on the dose of Kacital. Following long-term treatment, administering 60 mEq/day increases urinary citrate and pH by approximately 400 mg/day and 0.7 units, respectively.

5.3 Preclinical safety data

Non-clinical data reveals no special hazard for humans based on studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Carnauba Wax (E 903)
Magnesium stearate (E 470b)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store in the original package in order to protect from moisture. This medicinal product does not require any special temperature storage conditions.

6.5 Nature and contents of container

This medicinal product is packed in a polyethylene (HDPE) bottle closed with a tamper evident cap with an aluminium PE / PP / Al insert. The bottle is labelled and packed into a unit carton.

Pack size: 100 modified-release tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

XGX Pharma ApS
Frederiksgade 11, st. th
1265 Copenhagen
Denmark

8 MARKETING AUTHORISATION NUMBER

PA23382/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 2nd August 2024

10 DATE OF REVISION OF THE TEXT

October 2025