PROFESSIONAL INFORMATION FOR

CITROGRAN

SCHEDULING STATUS

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1. NAME OF THE MEDICINE

CITROGRAN (Effervescent granules)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each medicine measures (4 g) contains:

Sodium citrate 0,613 g

Sodium bicarbonate 1,716 g

Citric acid anhydrous 0,702 g

Tartaric acid 0,858 g

Contains sugar (liquid glucose) 0,252 mL

For the full list of excipients, see **section 6.1**.

3. PHARMACEUTICAL FORM

Effervescent granules.

White to straw coloured granules with a lemon odour and a sweet/ sour slightly lemon taste.

After reconstitution with water a clear to straw coloured solution with a slight lemon odour is obtained.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

CITROGRAN is indicated as a gastric antacid and urinary alkalinising agent. As a urinary alkaliniser, CITROGRAN can be used to alleviate symptoms associated with inflammatory conditions of the bladder. CITROGRAN can be used to prevent crystalluria during sulphonamide treatment.

4.2 Posology and method of administration

Posology

Adults:

One to two 5 mL medicine measures (4 to 8 g) in half a glass of ~~cold~~ water, 3 to 4 times daily, taken on an empty stomach and followed with additional water. Drink after effervescence (see **section 4.8**).

Long-term therapy: One 5 mL (4 g) medicine measure daily.

Paediatric population

Children (6 - 12 years):

One 5 mL medicine measure (4 g) in half a glass of ~~cold~~ water, 2 or 3 times daily, taken on an empty stomach and followed with additional water. Drink after effervescence (see **section 4.8**).

Method of administration

Take on an empty stomach, followed with additional water. Drink after effervescence.

4.3 Contraindications

CITROGRAN is contraindicated in:

- Patients with known hypersensitivity to sodium bicarbonate, citric acid, sodium citrate, tartaric acid or to any of the excipients used in the formulation of CITROGRAN (see **section 6.1**).
- In patients with severe renal disease and metabolic disturbances with alkalosis, hypocalcaemia or hypochlorhydria.
- When co-administered with urinary tract antiseptics which require acid urine, such as methenamine mandelate and methenamine hippurate. (see **section 4.5**).

4.4 Special warnings and precautions for use

In patients suffering from renal insufficiency, CITROGRAN effervescent granules should be used with caution.

Alkalinising agents may temporarily relieve lower urinary tract symptoms but they do not eliminate bacteriuria.

In patients with compromised renal function, concurrent use of CITROGRAN effervescent granules with an antacid may result in the absorption of dangerously high amounts of aluminium (see **section 4.5**).

Patients that suffer from hypertension and congestive cardiac failure should not use CITROGRAN effervescent granules, except under the advice and supervision of a doctor.

To avoid the condition of metabolic alkalosis, patients with renal abnormalities and patients with peptic ulceration should use CITROGRAN with caution. To ensure that acid-base balance is maintained, patients with renal disease should have periodic determinations of serum electrolytes.

Patients on a sodium-restricted diet should not take CITROGRAN.

In patients with cirrhosis of the liver, pre-eclampsia, peripheral and pulmonary oedema caution should also be taken.

Liquid Glucose

CITROGRAN contains liquid glucose.

Patients with rare glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

CITROGRAN effervescent granules should not be administered with urinary tract antiseptics which require acid urine, such as methenamine hippurate and methenamine mandelate (see **section 4.3**).

Antacids:

Systemic alkalosis may occur with concurrent use of antacids and citrates. In patients with uric acid stones, simultaneous administration of antacids with sodium bicarbonate and sodium citrate may promote the development of calcium stones and may also cause hypernatraemia.

Concomitant use of citrate salts in CITROGRAN effervescent granules with aluminium-containing antacids, especially by patients with compromised renal function, may result in the absorption of dangerously high amounts of aluminium (see **section 4.4**).

Quinolones:

The solubility of ciprofloxacin, norfloxacin, or ofloxacin in the urine may be reduced by citrates. Patients should be monitored for signs of nephrotoxicity and crystaluria.

Salicylates:

Simultaneous use of salicylates with citrates may decrease the therapeutic effects of salicylates by increasing the urinary excretion of salicylates due to urine alkalinisation.

Tetracyclines:

Due to the increase in intragastric pH, a decrease in tetracycline absorption may occur when it is used simultaneously with sodium bicarbonate. CITROGRAN should not be taken within 1 to 2 hours of tetracyclines.

Ketoconazole:

Simultaneous use with sodium bicarbonate may result in a marked reduction in absorption of ketoconazole due to the increased gastrointestinal pH caused by sodium bicarbonate. Patients should take CITROGRAN at least 2 hours after ketoconazole.

Methenamine:

Sodium bicarbonate and citrates alkalinises the urine, which may inhibit the conversion of methenamine to formaldehyde, resulting in a reduction of efficacy; simultaneous use with CITROGRAN is therefore not recommended.

4.6 Fertility, pregnancy and lactation

Pregnancy:

Safety of citrates, and therefore CITROGRAN in pregnancy has not been established.

Breastfeeding:

Caution should be exercised when administered to a breastfeeding mother.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Summary of adverse reactions

The following adverse reactions have been classified according to the following categories, frequent, less frequent and frequency unknown.

Metabolism and nutrition disorders:

Less frequent: Increased thirst. Hypernatraemia (fast heartbeat, dizziness, high blood pressure, muscle twitching, irritability, seizures,

	restlessness, swelling of feet or lower legs, weakness) may occur.
Frequency unknown:	Metabolic alkalosis (muscle weakness, shortness of breath and mental disturbances such as restlessness, convulsions and coma) may occur especially in patients with renal impairment. Excessive doses may lead to sodium overloading and hyperosmolality.

Gastrointestinal disorders:

Less frequent:	Stomach cramps and laxative effect (loose bowel movements or diarrhoea) may occur.
Frequency unknown:	Abdominal distension, belching, flatulence and nausea may occur if CITROGRAN is taken before effervescence is complete.

Musculoskeletal, connective tissue and bone disorders:

Frequency unknown:	Muscle hypertonicity, twitching and tetany may develop, especially in hypocalcaemic patients.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reactions Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8 and to Cipla Medpro (Pty) Ltd at drugsafetysa@cipla.com or telephone 080 222 6662 (toll free).

4.9 Overdose

Overdosage may result in hypernatraemia and metabolic alkalosis (see **section 4.8**).

Treatment is symptomatic and supportive and consists mainly of correction of fluid and electrolyte balance with complete withdrawal of the preparation. A doctor should be consulted in known cases of overdosage.

Electrolyte estimations should be taken regularly and the necessary treatment provided.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 18.3 Medicines acting on genito-urinary system (ion exchange preparations).

CITROGRAN effervescent granules have urinary alkalising as well as gastric antacid properties.

Urinary alkaliniser:

Sodium bicarbonate raises the urinary pH, by increasing the excretion of free bicarbonate ions in the urine. The actual dissolution of uric acid stones may be accomplished by maintaining an alkaline urine. Citrates (citric acid and sodium citrate) are metabolised to bicarbonates (see above).

Gastric antacid:

Sodium bicarbonate, citric acid and sodium citrate react chemically to neutralise or buffer existing quantities of gastric hydrochloric acid but have no direct effect on its output. This action results in an increased pH value of stomach contents, thus providing relief of hyperacidity symptoms.

5.2 Pharmacokinetic properties

Sodium bicarbonate:

Sodium bicarbonate undergoes renal elimination. The carbon dioxide (CO_2) that is formed is eliminated via the lungs.

Sodium citrate and citric acid:

In the body, citrates are oxidised to form sodium bicarbonate, which is eliminated via the urine. Less than 5 % is excreted unchanged.

Tartaric acid:

Tartaric acid is absorbed from the gastrointestinal tract but of an ingested dose up to 80 % is probably destroyed in the lumen of the intestine by micro-organisms before absorption occurs. Absorbed tartaric acid is excreted unchanged in the urine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Flav Lemon permaseal 60301-71
- Liquid glucose

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

- Store in a cool dry place at or below 25 °C.
- Do not refrigerate or freeze.
- Keep the bottle tightly closed.
- Keep the bottle in the outer carton.

6.5 Nature and contents of container

CITROGRAN effervescent granules are available in round clear glass bottles with a white screw cap and a dosage measure, packed in an outer carton.

CITROGRAN is packed in 60 g or 120 g effervescent granules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

After reconstitution with water a clear to straw coloured solution with a slight lemon odour is obtained.

7. HOLDER OF CERTIFICATE OF REGISTRATION

CIPLA MEDPRO (PTY) LTD.

Building 9

Parc du Cap

Mispel Street

Bellville

7530

Customer Care: 080 222 6662

8. REGISTRATION NUMBER(S)

45/18.3/0182

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30 September 2016

10. DATE OF REVISION OF THE TEXT

18 November 2022