Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

CitraFleet oral solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each bottle (160ml) contains the following active ingredients:

Sodium picosulfate	10.0 mg
Light magnesium oxide	3.5 g
Citric acid	10.97 g

Excipients with known effect:
Each bottle contains 3.4 g sodium, 0.83g sodium metabisulfite (E 223), 0.17 g sodium methyl p-hydroxybenzoate (E 219), 0.066 g ethanol, 0.02 g sodium propyl p-hydroxybenzoate (E 217) and 0.013 g propylene glycol (E 1520).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral solution.

Transparent solution, colourless or slightly yellowish with grenadine flavour.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For bowel cleansing prior to any diagnostic procedures requiring a clean bowel e.g. colonoscopy or x-ray examination.
CitraFleet oral solution is indicated in adults (including the elderly) aged 18 years and over.

4.2 Posology and method of administration

Posology

Adults (including the elderly) aged 18 years and over.
The treatment can be administered in one of the following ways:

- Usually, one bottle on the evening prior to the procedure and the second bottle in the morning of the day of the procedure.
- Both bottles on the afternoon and evening prior to the procedure. This schedule is more suitable when the procedure is early in the morning.
- Both bottles in the morning of the day of the procedure. This regimen is only suitable when the procedure is planned in the afternoon/evening.

The time elapsed between the two bottles should be at least 5 hours.

Method of administration

Route of administration: Oral use.

A special (low fibre food) diet or only clear liquids on the day before the procedure is recommended. No solid food should be taken from the start of the course of treatment until after the procedure.

CitraFleet oral solution should not be mixed or diluted. It is ready to be drunk right from the bottle.

After a period of ten minutes following the administration of each bottle, it is recommended to drink approximately 1.5-2 litres of a variety of clear fluids at a rate of approximately 250-400 ml/h. Clear soups and/or balanced electrolyte solutions would be recommended. It is advisable not to drink clear or demineralised water alone.

The patient should be nil-by-mouth prior to the procedure (usually for at least 2 hours) in accordance with anaesthesia requirements.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1, congestive cardiac failure, severe dehydration, hypermagnesaemia, gastric retention, gastro-intestinal ulceration, toxic colitis, toxic megacolon, ileus, nausea and vomiting, ascites, acute surgical abdominal conditions such as acute appendicitis and known or suspected gastro-intestinal obstruction or perforation.

Do not use in patients with rhabdomyolysis as laxatives may induce rhabdomyolysis and may therefore exacerbate the condition.

Do not use in patients with active inflammatory bowel disease e.g. Crohn's disease, ulcerative colitis.

In patients with severely reduced renal function, accumulation of magnesium in plasma may occur. Another preparation should be used in such cases.

4.4 Special warnings and precautions for use

CitraFleet oral solution should not be used as a routine laxative.

CitraFleet oral solution could rarely lead to severe and potentially fatal cases of electrolyte disorders or impaired renal function in frail or debilitated patients. Therefore, the benefit/risk ratio of CitraFleet oral solution needs to be carefully considered before initiating treatment in this at-risk population.

Special attention should be taken when prescribing CitraFleet oral solution to any patient with regard to known contra-indications and special attention made to the importance of adequate hydration and, in at-risk populations (as defined below), to the importance of also obtaining baseline and post-treatment electrolyte levels.

Elderly and debilitated patients, and patients at risk of hypokalaemia or hyponatraemia, may need particular attention.

CitraFleet oral solution should be used with caution in patients with known disorders of water and/or electrolyte balance or on drugs that might affect water and/or electrolyte balance e.g. diuretics, corticosteroids, lithium (see 4.5).

Care should also be taken in patients who have recently undergone gastrointestinal surgery or who have renal impairment, mild to moderate dehydration, hypotension or heart disease.

The period of bowel cleansing should not exceed 24 hours because longer preparation may increase the risk of water and electrolyte imbalance.

Diarrhoea due to the evacuating effect of CitraFleet oral solution may result in fluid and electrolyte losses, hypovolemia and hypotension. Additionally, vasovagal reflex may be triggered by abdominal stimuli, e.g. pain, which may lead to low blood pressure and loss of consciousness. Adequate intake of clear liquids is required, see section 4.2.

CitraFleet oral solution may modify the absorption of regularly prescribed oral medication and should be used with caution e.g. there have been isolated reports of seizures in patients on antiepileptics, with previously controlled epilepsy (see 4.5 and 4.8).

This medicinal product contains 3.4 g sodium per bottle, equivalent to 173.6% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

This medicinal product contains sodium metabisulfite (E 223). It may rarely cause severe hypersensitivity reactions and bronchospasm.

This medicinal product contains sodium methyl p-hydroxybenzoate (E 219) and sodium propyl p-hydroxybenzoate (E 217). It may cause allergic reactions (possibly delayed).

This medicine contains 66 mg of alcohol (ethanol) in each bottle. The amount in 160ml of this medicine is equivalent to less than 2 ml beer or 1 ml wine. The small amount of alcohol in this medicine will not have any noticeable effects.

4.5 Interaction with other medicinal products and other forms of interaction

As a purgative, CitraFleet oral solution increases the gastrointestinal transit rate. Absorption of other orally administered medicines (e.g. anti-epileptics, contraceptives, anti-diabetics, antibiotics) may therefore be modified during the treatment period (see 4.4). Tetracycline and fluoroquinolone antibiotics, and penicillamine, should be taken at least 2 hours before and not less than 6 hours after administration of CitraFleet oral solution to avoid chelation with magnesium.

The efficacy of CitraFleet oral solution is lowered by bulk-forming laxatives.

Care should be taken with patients already receiving drugs which may be associated with hypokalaemia (such as diuretics or corticosteroids, or drugs where hypokalaemia is a particular risk i.e. cardiac glycosides). Caution is also advised when CitraFleet oral solution is used in patients on NSAIDs or drugs known to induce SIADH e.g. tricyclic antidepressants, selective serotonin re-uptake inhibitors, antipsychotic drugs and carbamazepine as these drugs may increase the risk of water retention and/or electrolyte imbalance.

4.6 Fertility, pregnancy and lactation

Pregnancy

For CitraFleet oral solution neither clinical data on exposed pregnancy nor reproductive toxicity are available. As picosulfate is a stimulant laxative, for safety measure, it is preferable to avoid the use of CitraFleet oral solution during pregnancy.

Breast-feeding

There is no experience with the use of CitraFleet oral solution in nursing mothers. However, due to the pharmacokinetic properties of the active ingredients, treatment with CitraFleet oral solution may be considered for females who are breastfeeding.

4.7 Effects on ability to drive and use machines

CitraFleet oral solution may cause fatigue or dizziness, probably as a result of dehydration, and this may have a mild to moderate effect on the ability to drive or use machinery.

4.8 Undesirable effects

The most common adverse events reported in clinical trials using the combination of sodium picosulfate and magnesium citrate were related to direct effects on the bowel (abdominal pain and nausea) and the consequences of diarrhoea and dehydration (sleep disturbance, dry mouth, thirst, headache and fatigue).

Undesirable effects are presented below by MedDRA System Organ Class and Preferred Term, using the following frequency convention: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100). The frequency calculations are based on data derived from an analysis of clinical studies. Undesirable effects that were not reported in these clinical trials are described as 'Frequency not known (cannot be estimated from the available data)'.

MedDRA System Organ Class	**Very common (≥ 1/10)**	**Common (≥ 1/100 to < 1/10)**	**Uncommon (≥ 1/1,000 to < 1/100)**	**Frequency not known (cannot be estimated from the available data)**
Immune System Disorders				Anaphylactoid reaction, hypersensitivity
Metabolism and nutrition disorders				Hyponatraemia, hypokalaemia
Psychiatric		Sleep		

disorders		disorder		
Nervous system disorders		Headache	Dizziness	Epilepsy, grand mal convulsion, convulsion, confusional state
Vascular disorders			Orthostatic hypotension	
Gastrointestinal disorders	Abdominal pain	Dry mouth, nausea, abdominal distension, anal discomfort, proctalgia	Vomiting, faecal incontinence	Diarrhoea*, flatulence
Skin and subcutaneous tissue disorders				Rash (including erythematous and maculo-papular rash), urticaria, pruritus, purpura
General disorders and administration site conditions		Thirst, fatigue		Pain

* Diarrhoea is the primary clinical effect of CitraFleet.

Hyponatraemia has been reported with or without associated convulsions (see 4.4). In epileptic patients, there have been reports of seizure/grand mal convulsion without associated hyponatraemia (see 4.4 and 4.5).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 HPRA Pharmacovigilance, Website: www.hpra.ie.

4.9 Overdose

No cases of overdose with CitraFleet oral solution, or similar combinations of sodium picosulfate and magnesium citrate, have been reported. However, because of its modes of action, an overdose of CitraFleet oral solution would be expected to cause profuse diarrhoea with dehydration and electrolyte loss. Dehydration could also lead to orthostatic hypotension and dizziness. Dehydration and electrolyte imbalances should be corrected with fluid and electrolytes as necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Sodium picosulfate, combinations, ATC code: A06AB58.
The active components of CitraFleet oral solution are sodium picosulfate, a stimulant cathartic, active locally in the colon, and magnesium citrate which acts as an osmotic laxative by retaining moisture in the colon. The action is of a potent 'washing out' effect combined with peristaltic stimulation to clear the bowel prior to radiography, colonoscopy or surgery. The product is not intended for use as a routine laxative.

In a randomized, multicentre, rater-blinded study in adults, bowel cleansing prior to colonoscopy using two different regimens of CitraFleet was compared with that following Klean-Prep (each sachet containing 59 g polyethylene glycol 3350, 5.685 g anhydrous sodium sulfate, 1.685 g sodium bicarbonate, 1.465 g sodium chloride and 0.7425 g potassium chloride; to be dissolved in 1 litre of water). The treatment groups were: late prior-day CitraFleet (2 sachets, 5 hours apart during the afternoon and evening the day before colonoscopy, n=229); late prior-day Klean-Prep (4 sachets administered during the afternoon and evening the day before colonoscopy, n=227); same-morning CitraFleet (2 sachets, 3 hours apart on the morning before colonoscopy, n=56). Bowel cleansing was assessed using a categorical scale (excellent, good, fair and poor). Good/excellent cleansing was reported in 68.1% of patients on the late prior-day CitraFleet regimen (not statistically different from Klean-Prep), while a significantly higher proportion of patients had good/excellent cleansing with same-morning CitraFleet compared with either late prior-day regimen ($p<0.05$). Both CitraFleet regimens were rated as significantly easier to complete by patients than Klean-Prep ($p<0.001$). All regimens were well tolerated, with only 2.2% of patients on the late prior-day CitraFleet regimen having adverse drug reactions. There were no serious adverse drug reactions.

In a randomized, multicentre, rater-blinded study in adults, bowel cleansing prior to colonoscopy was compared using two different regimens of CitraFleet: split-dose (1 sachet in the evening the day before colonoscopy, and another sachet on the morning before colonoscopy, n=159); early prior-day regimen (1 sachet before 0800h the day before colonoscopy and another sachet 6-8 hours later, n=156). Bowel cleansing was assessed using a categorical scale (excellent, good, fair and poor). A significantly higher proportion of patients on the split-dose regimen had good/excellent cleansing (79.9% vs 30.8% for early prior-day, p<0.0001). Over 93% of patients in both groups rated the regimens as 'easy' or 'very easy' to take. Both regimens were well tolerated, with 1.9% and 2.5% of patients having adverse drug reactions in the split-dose and early prior-day groups, respectively. More patients in the split-dose group than in the early prior-day group reported nausea (23.3% vs 13.5%) and overall physical discomfort (29.6% vs 17.3%), while more patients in the early prior-day group reported hunger (46.2% vs 32.1% with split-dose). There were no serious adverse drug reactions. Overall, changes in electrolyte levels and other laboratory parameters were minor in both groups.

5.2 Pharmacokinetic properties

Both active components are locally active in the colon, and neither is absorbed in any detectable amounts.

In patients with severely reduced renal function, accumulation of magnesium in plasma may occur.

5.3 Preclinical safety data

Prenatal developmental studies in rats and rabbits did not reveal any teratogenic potential after oral dosing of sodium picosulfate up to 100 mg/kg/d, but embryotoxicity had been observed in both species at this dose level. In rats, daily doses of 10mg/kg during late gestation (fetal development) and lactation reduced body weights and survival of the offspring. Male and female fertility was not affected by oral doses of sodium picosulfate up to 100 mg/kg.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Malic acid
Sodium metabisulfite (E 223)
Sodium methyl p-hydroxybenzoate (E 219)
Sodium propyl p-hydroxybenzoate (E 217)
Sucralose
Masking flavour (modulator sweet)
Grenadine flavour (contains ethanol and propylene glycol (E 1520))
Sodium hydroxide (for pH-adjustment)
Purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Unopened bottles: 24 months.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Bottles are packaged in cartons containing:

- 2, 20, 40 or 80 bottles, or
- multipacks containing 20 (10x2), 40 (20x2) or 80 (40x2) bottles.

The bottles contain a single dose of 160ml. The white bottle is composed polyethylene terephthalate (PET) with screw cap of propylene (PP).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Casen Recordati, S.L.
Autovia de Logrono, Km 13,300
50180 Utebo - Zaragoza
Spain

8 MARKETING AUTHORISATION NUMBER

PA2028/002/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 3rd March 2023

10 DATE OF REVISION OF THE TEXT