Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

CitraFleet, Powder for oral solution in sachet

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet (15.08 g) 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 sachet also contains 5 mmol (or 195 mg) potassium and sodium (see section 4.4).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for oral solution, in sachet

White crystalline powder with a lemon 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 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 sachet on the evening prior to the procedure and the second sachet in the morning of the day of the procedure.
- One sachet in the afternoon and the second sachet in the evening prior to the procedure. This schedule is more suitable when the procedure is early in the morning.
- Both sachets 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 sachets should be at least 5 hours.

Method of administration

Route of administration: Oral use.
For instructions on reconstitution of the medicinal product before administration, see section 6.6.

A low residue 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.

Because the osmolarity of the product needs to be maintained in order to obtain the desired effect, each sachet should be reconstituted in a cup of water. Do not further dilute the product by drinking liquid immediately after the intake of each sachet.
After a period of ten minutes following the administration of each reconstituted sachet, 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 should not be used as a routine laxative.

CitraFleet 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 needs to be carefully considered before initiating treatment in this at-risk population.

Special attention should be taken when prescribing CitraFleet 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 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 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 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).

CitraFleet may induce aphtoid ulcers of the colonic mucosa and there have been reports of serious cases of colitis (including ischaemic colitis) requiring hospitalisation. As a result, this diagnosis should be considered in case of severe and/or persistent abdominal pain, with or without rectal bleeding, after the administration of CitraFleet.

This medicine contains 5 mmol (or 195 mg) potassium per sachet. This should be taken into consideration by patients with reduced kidney function or patients on a controlled potassium diet.

This medicine contains less than 1 mmol sodium (23 mg) per sachet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

As a purgative, CitraFleet 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 pencillamine, should be taken at least 2 hours before and not less than 6 hours after the administration of CitraFleet to avoid chelation with magnesium.

The efficacy of CitraFleet 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 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 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 during pregnancy.

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

4.7 Effects on ability to drive and use machines

CitraFleet may cause fatigue or dizziness, probably as a result of dehydration, and this may have a mild or 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)'.

Immune system disorders
Not known: Anaphylactoid reaction, hypersensitivity.

Metabolism and nutrition disorders
Not known: Hyponatraemia.
Not known: Hypokalaemia.

Psychiatric disorders
Common: Sleep disorder.

Nervous system disorders
Common: Headache.
Uncommon: Dizziness.
Not known: Epilepsy, grand mal convulsion, convulsion, confusional state.

Vascular disorders
Uncommon: Orthostatic hypotension.

Gastrointestinal disorders
Very common: Abdominal pain.
Common: Dry mouth, nausea, abdominal distension, anal discomfort, proctalgia.
Uncommon: Vomiting, faecal incontinence.
Not known: Diarrhoea*, flatulence.
* Diarrhoea is the primary clinical effect of CitraFleet.

Skin and subcutaneous tissue disorders
Not known: Rash (including erythematous and maculo-papular rash), urticaria, pruritus, purpura.

General disordersand administration site conditions
Common: Thirst, fatigue.
Not known: Pain.

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, or similar combinations of sodium picosulfate and magnesium citrate, have been reported. However, because of its modes of action, an overdose of CitraFleet 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: A06A B58.

The active components of CitraFleet 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 sodiumpicosulfate up to 100 mg/kg/d, but embryotoxicity had been observed in both species at this dose level. In rats daily doses of 10 mg/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

Potassium hydrogen carbonate.

Saccharin sodium.

Lemon Flavour (lemon flavour, maltodextrin, tocopherol E307).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Unopened sachets: 36 months.
Use immediately after reconstitution.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

The powder for oral solution is supplied in unit dose sachets. Sachets are packaged in cartons of 2, 50, 50 (25x2), 100, 100 (50x2), 200, 200 (100x2), 500, 500 (250x2), 1000 sachets or 50 and 50 sachets (25x2) (hospital pack). The sachets contain white powder crystals with single dose of 15.08g. The sachet is a complex formed by a polyester layer, an intermediate aluminium layer and an internal polyethylene layer.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Directions for reconstitution:

Reconstitute the contents of one sachet in a cup of water (approximately 150 ml). Stir for 2-3 minutes. If it becomes hot when you stir it, wait until it has cooled down before drinking the whole solution. Once the solution is ready, drink it immediately. The solution will appear cloudy.

7 MARKETING AUTHORISATION HOLDER

Casen-Recordati S.L.
Autovia De Logrono, km. 13,300
50180 Utebo (Zaragoza)
Spain

8 MARKETING AUTHORISATION NUMBER

PA2028/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18th April 2008
Date of last renewal: 22nd June 2026

10 DATE OF REVISION OF THE TEXT

January 2024