SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Clensia Powder for oral solution.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Clensia is available as a powder in 2 separate sachets (A-large and B-small) to be dissolved together in water and administered as an oral solution.

Sachet **A** (large) contains the following active substances:

Macrogol 4000	52.500 g
Sodium sulphate anhydrous	3.750 g
Simeticone	0.080 g

Sachet **B** (small) contains the following active substances:

Sodium citrate	1.863 g
Citric acid anhydrous	0.813 g
Sodium chloride	0.730 g
Potassium chloride	0.370 g

The concentration of electrolyte ions when 2 sachets A and 2 sachets B are dissolved in 1 litre of water is as follows:

Sodium	168.6 mmol/l
Sulphate	52.8 mmol/l
Chloride	34.9 mmol/l
Potassium	11.2 mmol/l
Citrate	21.1 mmol/l

Excipient with known effect: sachet B contains 0.130 g of acesulfame potassium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for oral solution.

White to almost white powder in Sachet A. The dimension of Sachet A is: 130 x 165 mm
White to almost white powder with lime smell in Sachet B. The dimension of Sachet B is: 60 x 80 mm

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Bowel cleansing prior to any clinical procedures requiring a clean bowel e.g. bowel endoscopy or radiology.

Clensia is indicated for use in adults.

4.2 Posology and method of administration

Posology

Adults
A single treatment for bowel cleansing in adults consists of 4 sachets A and 4 sachets B dissolved in 2 litres of water taken orally.

Paediatric population
Clensia is not recommended for use in children below 18 years of age, as the product has not been studied in the paediatric population.

Patients with renal impairment
Clensia should be administered with caution in patients affected by severe renal insufficiency (creatinine clearance <30 ml/min) (see section 4.4).

Dosing regimen

For an adequate colon cleansing, it is necessary to drink the full amount of the solution. For a single course of treatment it is necessary that the 4 sachets A and the 4 sachets B are dissolved in 2 litres of water.

The solution should be prepared and drunk prior to the procedure in one of the two following ways:

1. Full dose regimen the day before:

On the evening before the day of the clinical procedure, the solution of Clensia should be prepared using 2 sachets A and 2 sachets B dissolved in 1 litre of water and drunk over a period of about 1.5 hours (1-2 hours), at a rate of 2 glasses (about 250 ml) every 15-20 minutes.
After one hour of rest, the remaining 2 sachets A and 2 sachets B should be dissolved again in 1 litre of water and drunk in the same way. In addition, 1 litre of an additional clear liquid (water, fruit juice, soft drink, tea/coffee without milk) should be taken during the evening.

2. Split dose regimen:

The evening before the diagnostic procedure Clensia solution should be prepared using 2 sachets A and 2 sachets B dissolved in 1 litre of water and drunk over a period of about 1.5 hours (1-2 hours) at a rate of 2 glasses (about 250 ml) every 15-20 minutes. In addition, at least 0.5 litre of additional clear liquid (water, fruit juice, soft drink, tea/coffee without milk) should be taken during the evening.
On the morning of the diagnostic procedure the remaining 2 sachets A and 2 sachets B should be dissolved again in 1 litre of water and drunk following the same way, in addition to 0.5 litre of supplementary clear liquid (water, fruit juice, soft drink, tea/coffee without milk).

No solid food should be taken from the start of the course of treatment until after the clinical procedure.

There should be at least two hours between the end of intake of fluid (Clensia or clear liquid) and the start of the clinical procedure.

For further instructions on reconstitution of the medicinal product before administration, see section 6.6.

After the procedure:
In order to replace fluid loss during the preparation of the procedure patients should be encouraged to drink plenty of fluid afterwards.

Method of administration
Oral use.

4.3 Contraindications

The product should not be used in patients with known or suspected:
- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Gastrointestinal obstruction
- Severe disorders of gastric emptying (e.g, gastroparesis)
- Ileus
- Gastrointestinal perforation
- Toxic colitis or toxic megacolon.

Do not use in unconscious patients.

4.4 Special warnings and precautions for use

When taken according to instructions, Clensia normally induces diarrhoea. Clear rectal effluent with no residual stools normally indicates adequate bowel cleansing.

If patients develop symptoms such as severe bloating, abdominal distension, abdominal pain or any other reaction which make it difficult to continue the preparation, the intake of solution should be slowed down or temporarily stopped.

In patients with swallowing problems, who need the addition of a thickener to solutions to enhance an appropriate intake, interactions should be considered, see section 4.5.

If patients develop any symptoms indicating arrhythmia or shifts of fluid/electrolytes (e.g. oedema, shortness of breath, increasing fatigue, cardiac failure), plasma electrolytes should be measured, ECG monitored and any abnormality treated appropriately.

Significant gastrointestinal disease
If gastrointestinal obstruction or perforation is suspected, appropriate diagnostic procedures should be performed to rule out such conditions before the administration of Clensia.
Clensia l should be used with caution in patients with severe ulcerative colitis or Crohn's disease.

Risk of aspiration
Semi-conscious patients with impaired gag reflex, or prone to regurgitation or aspiration should be monitored during administration of Clensia, especially if a nasogastric tube is placed. The product should be used with caution in these patients.

Elderly/debilitated patients
Clensia should be administered with caution in fragile patients with poor general health or severe dehydration.

Dehydration
The presence of dehydration should be corrected before the use of Clensia.
Signs of mild to moderate dehydration are 1-5% reduction in body weight, thirst, dizziness, dry mouth, headache, dark and concentrated urines. Severe dehydration includes more than 5% reduction in body weight, thirst, sunken eyes, very dry mouth, skin and mucous membranes, hypotension, tachycardia, low level of consciousness.

Electrolyte disorders
In case of dehydration or whenever symptoms of suspected fluid/electrolytes abnormalities are present, the physician should consider to perform baseline and post-treatment electrolytes and renal function tests before using Clensia.

Renal impairment
Clensia should be used with caution in patients with severe renal insufficiency (creatinine clearance <30 ml/min).

Cardiac disease
Clensia should be used with caution in patients with heart failure (NYHA class III or IV), acute myocardial infarction and unstable angina.

Ischaemic Colitis
Post-marketing cases of ischaemic colitis, includinq serious, have been reported in patients treated with macroqol for bowel preparation. Macrogol should be used with caution in patients with known risk factors for ischaemic colitis or in case of concomitant use of stimulant laxatives (such as bisacodyl or sodium picosulfate). Patients presenting with sudden abdominal pain, rectal bleeding or other symptoms of ischaemic colitis should be evaluated promptly.

This medicinal product contains 3877.8 mg sodium per litre, equivalent to 194% of the WHO recommended maximum daily intake of 2 g sodium for an adult. This medicinal product contains 11.2 mmol of potassium per litre. 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

Any oral medication should not be taken within 1 hour of and during administration of Clensia as it may be flushed from the gastrointestinal tract. This may be of clinical significance with anti-hypertensive medications as a transient increase of blood pressure related to insufficient drug absorption has been observed.
Patients taking medicinal products that affect renal function (such as diuretics, ACE inhibitors, ARB or NSAIDs) are at increased risk of fluid and electrolyte abnormalities with osmotic bowel preparations. Such patients should be monitored for adequate hydration and baseline and post-treatment laboratory tests (electrolytes, creatinine, BUN) should be considered.
The therapeutic effect of medicinal products with a narrow therapeutic index such as antiepileptics, digoxin and immunosuppressive agents or short half-life may be particularly affected.
Clensia may result in a potential interactive effect if used with starch-based food thickeners. The macrogol ingredient counteracts the thickening effect of starch, effectively liquefying preparations that need to remain thick for people with swallowing problems.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are limited amount of data (less than 300 pregnancy outcomes) for the use of macrogol 4000 in pregnant women.
Studies in animals do not indicate direct or indirect harmful effects with respect to reproductive toxicity. No effects during pregnancy are anticipated, since systemic exposure to macrogol 4000 is negligible. Clensia can be used during pregnancy, if necessary.

Breast-feeding
There is no documented experience with the use of macrogol during lactation. No effects on the breast fed newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to macrogol 4000 is negligible. For this reason Clensia can be used during breast-feeding, if necessary.

Fertility
There are no data on the effects of Clensia on fertility. However, since macrogol 4000 is hardly resorbed, no effect on fertility is anticipated

4.7 Effects on ability to drive and use machines

Clensia has no influence on the ability to drive or use machines.

4.8 Undesirable effects

Patients undergoing bowel cleansing with mixtures of macrogols and electrolytes commonly have gastrointestinal discomfort such as abdominal cramps, bloating, nausea, and anal irritation. These adverse reactions are generally mild and typically subside rapidly if the rate of administration is slowed down or the intake of the product temporarily discontinued. Diarrhoea is an expected outcome of bowel preparation.
Hypersensitivity reactions (such as pruritus, rash, angioedema, urticaria, dyspnoea, anaphylactic shock) have been very rarely reported.

During controlled clinical trials, a population of 442 adult subjects treated with Clensia have been compared to other PEG 4000/3350 preparations.
All adverse reactions that occurred in subjects treated with Clensia during these studies as well as adverse drug reactions reported in the post-marketing experience with the use of other PEG 4000/3350 preparations are summarised in the following table, grouped by system organ class and frequency categories defined using the following convention:
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).

MedDRA System Organ Class	**Frequency**			
	Very common	**Common**	**Uncommon**	**Not known**
Immune system disorders				Anaphylactic shock Hypersensitivity
Metabolism and nutrition disorders				Dehydration
Nervous system disorders		Headache		Presyncope Dizziness
Ear and labyrinth disorders				Vertigo
Cardiac disorders				Arrhythmia
Respiratory, thoracic, and mediastinal disorders				Dyspnoea
Gastrointestinal Disorders	Nausea Abdominal pain Abdominal distension	Vomiting Anal irritation	Abdominal pain upper Disgeusia Dry mouth	
Skin and subcutaneous tissue disorders				Rash Erythema Urticaria Pruritus Angioedema
General disorders and administration site conditions			Chills	Asthenia Malaise
Investigations			Blood potassium decreased Transient blood pressure increase	Electrolytes disturbances

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 the national reporting system listed in Appendix V.

4.9 Overdose

No cases of overdose with Clensia have been reported.
Intentional or accidental ingestion of more than the recommended dose of Clensia may lead to severe diarrhoea and electrolyte imbalance, including hyponatraemia and hypokalaemia, as well as dehydration and hypovolaemia with related signs and symptoms. In such a case, the patient should be monitored and generous amounts of fluid - especially fruit juices - should be provided. In the rare case of overdosing associated with provoking severe metabolic derangement, intravenous rehydration may be used.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Osmotically acting laxative, ATC code: A06AD65.

Mechanism of action
The primary mechanism of action of Clensia is the osmotic action of macrogol 4000 (polyethylene glycol), sodium sulphate and the citrates which cause water to be retained in the colon. This enhances transportation of the solid faecal material, induces a laxative effect leading to colon cleansing.
Simeticone has anti-gas and anti-foam activities which is postulated to improve mucosal visibility during colonic examination. However, improved visibility could not be demonstrated in the clinical trials conducted with Clensia compared to other bowel cleansing solutions without simeticone (see below).
Clensia is a low volume bowel preparation. As it is mildly hyperosmotic, it may cause more fluid and electrolyte shift from plasma into the gastrointestinal tract. Therefore it is recommended that additional clear liquid (e.g. water, fruit juice, soft drink, tea, etc. but no milk) is taken after the bowel preparation in order to avoid loss of fluid and electrolytes from the body.
The electrolytes present in the formulation to adjust osmolarity (sodium chloride, potassium chloride) as well as the supplementary clear liquid intake usually do not result in any clinically significant variations of sodium, potassium or water and minimise the risk of dehydration.

Clinical efficacy and safety

The efficacy and safety of Clensia were evaluated in two randomised, active-controlled, investigator-blinded, phase 3 trials in patients undergoing elective colonoscopy.
In the first study, 422 patients randomly received Clensia or PEG-ES (macrogol plus electrolytes) 4 litres gold standard preparation. Primary efficacy endpoint was the proportion of patients with excellent or good colon cleansing as evaluated by the physician performing the procedure, unaware of the preparation used. The evaluation was made according the validated Ottawa bowel preparation scale.
In the intention-to-treat analysis, 421 patients were included. Of these, successful bowel cleansing was obtained in 68.1% and 69.2% of patients treated with Clensia and PEG-ES respectively (Table 1). Mean difference in success rate was 1.2% (95% CI -10.0 up to 7.7%). Similar results have been obtained with respect to the per-protocol population (n=392) (successful colon cleansing: 73.6% and 72.3% for Clensia and PEG-ES patients, respectively; mean difference 1.3% [95% CI -7.5 up to 10.1%]). No serious adverse reactions occurred during the study.
In the second study 389 patients randomly received Clensia or PEG-ASC (macrogol ascorbate) 2 litres plus one litre of additional fluid. Primary efficacy endpoint was the proportion of patients with excellent or good colon cleansing as evaluated by a physician. 385 Patients have been included in the

intention-to-treat analysis. Of these, successful bowel cleansing was obtained in 78.8% and 74.5% of patients treated with Clensia and PEG-ASC respectively (Table 1). Mean difference in success rate was 4.3% (95% CI -13 up to 4%). Similar results have been obtained in the per-protocol population (n= 367) (successful colon cleansing: 78.3% and 74.3% for Clensia and PEG-ASC patients respectively; mean difference 4% [95% CI: -13 up to 5%]). No serious adverse reactions occurred during the study.

Table 1. Proportion of patients with good to excellent bowel cleansing in clinical studies (intention-to-treat analysis)

	Study 1			Study 2		
	Clensia	PEG-ES	Total	Clensia	PEG-ASC	Total
$N_{\text{intention-to-treat}}$	213	208	421	193	192	385
Good-excellent bowel cleansing	68.1%	69.2%	68.6%	78.8%	74.5%	76.6%
Mean difference	-1.2% (95% CI -10.0 up to 7.7%)			4.3% (95% CI -4.2 up to 12.7%)		

5.2 Pharmacokinetic properties

Absorption
Macrogol 4000 passes unchanged along the gut. It is virtually not absorbed from the gastrointestinal tract and has no known pharmacological activity.
Citric acid is absorbed mainly in the small intestine through a saturable transport mechanism. After oral ingestion of Clensia, its absorption is negligible since the urinary excretion of citric acid is not different from that of controls.
Simeticone is not absorbed from the gastrointestinal tract.

Elimination
If absorbed, macrogol 4000 and citric acid are excreted via the urine.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans. This information is based on conventional studies on acute toxicity, repeated dose toxicity, genotoxicity and reproduction toxicity.
Because of the short-term use, no carcinogenicity studies have been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acesulfame potassium (E950)
Lime flavour (containing flavouring preparations, natural flavouring substance, icing sugar with maize starch, arabic gum (E414), maltodextrin).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Sachets:

3 years.

Reconstituted solution:
Store below 25°C.
The solution can be stored for up to 24 hours and may be refrigerated (2°C-8°C).

6.4 Special precautions for storage

Sachets:
Store below 30°C.

Reconstituted solution:
For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

A paper/polyethylene/aluminium sachet containing the powder.
One pack of Clensia contains a single treatment of 8 sachets (4 sachets A large + 4 sachets B small).

6.6 Special precautions for disposal and other handling

Clensia solution is prepared by dissolving the content of two sachets A and two sachets B with water in a 1 litre bottle and shaking well to ensure that the ingredients are dissolved. The solution is more palatable if chilled before administration.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

8. MARKETING AUTHORISATION NUMBER(S)

<[To be completed nationally]>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22 june 2016
Date of latest renewal: 22 june 2021

10. DATE OF REVISION OF THE TEXT

25/02/2022