SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

TRANSISOFT 8.5 g powder for oral solution in sachet

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains 8.5 g of macrogol 3350.

3 PHARMACEUTICAL FORM

Powder for oral solution in sachet.

White or almost white powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

TRANSISOFT 8.5 g powder for oral solution in sachet is indicated for the symptomatic treatment of chronic constipation in adults.

4.2 Posology and method of administration

Adults and the elderly: 2 sachets daily.

Do not take more than 2 sachets per day.

Paediatric population: Not recommended in children below 17 years of age.

Elderly

No dosage change is necessary for the treatment of chronic constipation in elderly.

In patients with renal impairment

No dosage adjustment is required for the treatment of chronic constipation in patients with renal impairment. (see section 5.2)

Method of administration

Each sachet should be dissolved in a ½ glass of water (100 mL) just before use.

The dissolved solution remains as clear as water.

Should be taken as a single dose, preferably in the morning.

The effect of TRANSISOFT 8.5 g powder for oral solution in sachet usually becomes apparent within 24 to 48 hours after its administration.

An organic disorder should have been ruled out before initiation of treatment. TRANSISOFT 8.5 g powder for oral solution in sachet should remain a temporary adjuvant treatment to appropriate lifestyle and dietary management of constipation. A course of treatment for chronic constipation with TRANSISOFT 8.5 g does not normally exceed 2 weeks, although this can be repeated if required. As for all laxatives, prolonged use is not usually recommended. If symptoms persist despite associated dietary measures, an underlying cause should be considered.

4.3 Contraindications

- Severe inflammatory bowel disease (such as ulcerative colitis, Crohn's disease) or toxic megacolon,

- Intestinal perforation or risk of intestinal perforation

- Constipation associated with:

  Ileus or intestinal obstruction,

  Painful abdominal syndromes of indeterminate cause,

- Hypersensitivity to macrogol (polyethylene glycol).

4.4 Special warnings and precautions for use

Warnings

The treatment of constipation with any medicinal product is only an adjuvant to a healthy lifestyle and diet, for example:

- Increased intake of liquids and dietary fibre,

- Appropriate physical activity and rehabilitation of the bowel reflex.

In case of diarrhoea, caution should be exercised in patients who are prone to a disturbance of water -electrolyte balance (e.g. the elderly, patients with impaired hepatic or renal function or patients taking diuretics) and electrolyte control should be considered.

If patients develop any symptoms indicating shifts of fluid/ electrolytes (e.g. oedema, shortness of breath, increasing fatigue, dehydration, cardiac failure) TRANSISOFT 8.5 g should be stopped immediately, electrolytes measured and any abnormality treated appropriately.

Precautions for use

Cases of hypersensitivity reactions (rash, urticaria, oedema, anaphylactic shock) have been reported with drugs containing macrogol (polyethylene glycol).

TRANSISOFT 8.5 g powder for oral solution in sachet is sugar free so it can be prescribed to diabetic patients or patients on a galactose-free diet.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed and data is limited. It is theoretically possible that intestinal absorption of other medicinal products could be reduced transiently during use with TRANSISOFT 8.5 g. There have been isolated reports of decreased efficacy with some concomitantly administered medicinal products (e.g. anti-coagulants or anti-epileptics').

4.6 Fertility, pregnancy and lactation

Pregnancy:

There are limited amount of data from the use of TRANSISOFT 8.5 g in pregnant women. Animal studies (rats and rabbits) do not indicate reproductive toxicity.

Clinically, no effects during pregnancy are anticipated, since systemic exposure to MACROGOL **3350** is negligible.

Breast-feeding:

No effects on the breast-feeding newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to MACROGOL 3350 is negligible. TRANSISOFT 8.5 g powder for oral solution in sachet can be used during breast-feeding.

Fertility:

There are no data on the effects of TRANSISOFT 8.5 g on fertility in humans. However, no effects on fertility are anticipated since systemic exposure to TRANSISOFT 8.5 g is negligible.

There were no effects on fertility in a study in male and female rats.

4.7 Effects on ability to drive and use machines

TRANSISOFT 8.5 g has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

Gastrointestinal disorders, in particular diarrhea, are the most frequent adverse reactions associated with PEG use in constipation. Other adverse effects include abdominal pain, abdominal distension, nausea, flatulence, vomiting and faecal incontinence.

Tabulated list of adverse reactions

The undesirable effects listed below have been reported during clinical trials (including 635 adult patients exposed to MACROGOL 3350) and during post-marketing use.

Adverse Drug Reactions are listed under headings of frequency using the following categories: 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). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System Organ Class	Frequency	Adverse Reaction
Blood and lymphatic system disorders	Uncommon	Anemia, decreased hematocrit
Cardiac disorders	Uncommon	tachycardia
Endocrine disorders	Uncommon	hypothyroidism, increased blood glucose
Gastrointestinal disorders	Very Common	diarrhoea
	Common	abdominal distension, abdominal pain, flatulence, nausea, vomiting
General disorders and administrations site	Uncommon	fatigue, pain, peripheral oedema
Hepatobiliary disorders	Common	abnormal liver function tests
Immune System Disorders	Uncommon	hypersensitivity reactions (anaphylactic shock, face oedema, pruritus, Quincke's oedema, rash, urticaria)
Infections and infestations	Uncommon	intestinal abscess, viral gastroenteritis
Investigations	Uncommon	increased blood amylase, increased blood CPK, increased red blood cell sedimentation rate
Metabolism and nutrition disorders	Uncommon	appetite disorder, dehydration, electrolytes disorders

		(hypokalaemia, hyponatraemia), hypoglycaemia
Musculoskeletal and connective tissue disorders	Uncommon	local swelling, muscle twitching
Nervous system disorders	Uncommon	dizziness, dysgeusia, migraine, neuritis
Reproductive system and breast disorders	Uncommon	pelvic pain
Respiratory, thoracic and mediastinal disorders	Uncommon	hiccups, sinus congestion
Skin and subcutaneous tissue disorders	Uncommon	acne, rash, urticaria
Vascular disorders	Uncommon	arterial hypertension

Description of selected adverse reactions

Diarrhoea was the single most common adverse event in all the clinical studies. Diarrhoea occurred at a rate up to 17.2% during the clinical trials. In most cases diarrhoea was mild to moderate in severity and was easily treated by dose reduction or medication withdrawal.

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 Yellow Card Scheme.

Website: www.mhra.gov.uk/yellowcard

4.9 Overdose

Overdose leads to diarrhoea which disappears when treatment is temporarily interrupted or the dosage is reduced.

Excessive fluid loss by diarrhoea or vomiting may require correction of electrolyte disturbances.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Osmotically acting laxatives

ATC code: A06AD15

High molecular weight macrogols are long linear polymers which retain water molecules by means of hydrogen bonds. When administered by the oral route, they lead to an increase in volume of intestinal fluids.

The volume of unabsorbed intestinal fluid accounts for the laxative properties of the solution.

5.2 Pharmacokinetic properties

Studies showed that MACROGOL is negligibly absorbed and predominantly eliminated via faeces (93% of the dose in one study).

In healthy adult volunteers after oral dosing with 17 g, MACROGOL 3350 was detected in plasma as early as 30 minutes, reached maximum levels (mean Cmax ranging from 353 – 1111 ng/ ml) within a mean of 2.0 – 5.4 hours and fell, in most subjects, to undetectable levels by 18 – 24 hours.

The half was variable with a range of 3.6 to 8 hours. The small amount of MACROGOL absorbed systemically is excreted in the urine. Excretion is prolonged with MACROGOL 3350 detected at 60 hours post dose in urine and 96 hours post dose in faeces.

Patients with end stage renal disease (ESRD) have significantly higher exposure to MACROGOL 3350 than healthy adults. Orally administered MACROGOL 3350 is excreted primarily in faeces. Healthy adult volunteers clear absorbed MACROGOL 3350 rapidly via urinary excretion; these data suggest that, in the absence of renal function, PEG 3350 plasma levels are higher in ESRD patients and that the rate of clearance is slower. Dialysis may reduce MACROGOL 3350 levels but several dialysis sessions may be needed to clear PEG 3350 from plasma. The plasma level of PEG 3350 was similar 24 hours after 4, 6 or 7 daily doses, suggesting that PEG 3350 does not accumulate in plasma of ESRD patients dosed repeatedly for up to 7 days.

There were no adverse events associated with these levels of exposure in ESRD patients. Although the extent of exposure in ESRD patients was greater than in healthy adult volunteers, the Cmax was less than 1/10 those observed in rodents receiving daily oral doses of PEG for 6 months while the AUC (O-tau) was about 3 times lower.

5.3 Preclinical safety data

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

Reconstituted solution: use immediately.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Paper/Polyethylene, Low Density/Aluminum Foil/Polyethylene, Low Density unit-dose sachet.

Pack sizes of 14 or 28 sachets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

7 MARKETING AUTHORISATION HOLDER

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78401 CHATOU CEDEX – France

8 MARKETING AUTHORISATION NUMBER(S)

PL 19549/0006

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