**SCHEDULING STATUS**

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## 1. NAME OF THE MEDICINE

MOLATIVE ORANGE, (powder for oral solution)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each MOLATIVE ORANGE sachets contains:

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|---|---|
| Macrogol 3350 | 13,125 g |
| Sodium chloride | 350,7 mg |
| Sodium hydrogen carbonate | 178,5 mg |
| Potassium chloride | 46,6 mg |

The content of electrolyte ions per sachet when diluted to 125 ml of solution is as follows:

| | |
|---|---|
| Sodium | 65 mmol/l |
| Chloride | 53 mmol/l |
| Hydrogen carbonate (bicarbonate) | 17 mmol/l |
| Potassium | 5,4 mmol/l |

*Excipient with known effect:*

Contains sweetener (Acesulfame Potassium 10,05 mg per sachet).

Sugar free.

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Powder for oral solution.

Single-dose sachets, containing free-flowing white powder with an orange odour, for oral solution.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

MOLATIVE ORANGE is indicated in adults and adolescents for the treatment of chronic constipation.

### 4.2 Posology and method of administration

**Posology**

***Adults, adolescents and the elderly***: 1 to 3 sachets daily in divided doses, according to individual response, each sachet reconstituted in 125 ml water and taken orally.

No dosage change is needed to be made for patients with renal insufficiency.

A course of treatment with MOLATIVE ORANGE does not normally exceed two weeks, although this can be repeated if required.

Extended use may be necessary in the care of patients with severe chronic or resistant constipation, secondary to multiple sclerosis or Parkinson's disease, or induced by regular constipating medication, in particular opioids and antimuscarinics.

For extended use, the dose can be adjusted down to 1 or 2 sachets daily, in divided doses, each reconstituted with 125 ml water and taken orally.

**Paediatric population**

Not recommended for use in children under 12 years of age (see section 4.3)

**Method of administration**

For oral administration.

Each sachet should be dissolved in 125 ml water.

### 4.3 Contraindications

- Hypersensitivity to macrogol (PEG), sodium hydrogen carbonate, sodium chloride, potassium chloride or to

any of the excipients of MOLATIVE ORANGE listed in section 6.1.

- Intestinal perforation or obstruction due to structural or functional disorder of the gut wall, ileus, gastric retention, peptic ulceration, and severe inflammatory conditions of the intestinal tract, such as Crohn's disease, ulcerative colitis and toxic megacolon.
- Children under 12 years of age.

**4.4 Special warnings and precautions for use**

The fluid content of MOLATIVE ORANGE when re-constituted with water does not replace regular fluid intake and adequate fluid intake must be maintained.

MOLATIVE ORANGE should not be used in the presence of abdominal pain, nausea or vomiting.
MOLATIVE ORANGE should not be used continuously unless directed by a doctor. Frequent or prolonged use of laxatives may result in dependence and loss of normal bowel function.

Mild adverse drug reactions are possible as indicated in section 4.8. If patients develop any symptoms indicating shifts of fluids/electrolytes (e.g. oedema, shortness of breath, increasing fatigue, dehydration, cardiac failure) MOLATIVE ORANGE should be stopped immediately and electrolytes measured, and any abnormality should be treated appropriately.

If there is a sudden change in bowel habits that has persisted for a period greater than 2 weeks, a medical practitioner should be consulted.
Rectal bleeding or failure to have a bowel movement after use of MOLATIVE ORANGE may indicate a serious condition. MOLATIVE ORANGE should be discontinued, and medical advice obtained.

The absorption of other medicines could transiently be reduced due to an increase in gastrointestinal transit rate induced by MOLATIVE ORANGE (see section 4.5).

Reactions related to the gastrointestinal tract occur most commonly. These reactions may occur as a consequence

of expansion of the contents of the gastrointestinal tract, and an increase in motility due to the pharmacologic effects of MOLATIVE ORANGE (see section 4.8). Diarrhoea usually responds to dose reduction.

MOLATIVE ORANGE contains 187 mg of sodium per sachet, equivalent to approximately 9 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.
When used to treat chronic constipation the maximum daily dose of this product is equivalent to approximately 28 % of the WHO recommended maximum daily intake for sodium.
MOLATIVE ORANGE is considered high in sodium. This should be particularly taken into account for those on a low salt diet.

**4.5 Interaction with other medicines and other forms of interaction**

Macrogol 3350 raises the solubility of medicines that are soluble in alcohol and mainly insoluble in water. There is a possibility that the absorption of other medicines could be transiently reduced during use with MOLATIVE ORANGE (see section 4.4). There have been reports of decreased efficacy with some concomitantly administered medicines, e.g. anti-epileptics.

**4.6 Fertility, pregnancy and lactation**

**Pregnancy**

There is limited amount of data from the use of MOLATIVE ORANGE in pregnant women. Clinically, no effects during pregnancy are anticipated since systemic exposure to macrogol 3350 is negligible.

MOLATIVE ORANGE can be used during pregnancy.

**Breastfeeding**

No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breastfeeding woman to macrogol 3350 is negligible.

MOLATIVE ORANGE can be used during breastfeeding.

**Fertility**

There are no data on the effects of MOLATIVE ORANGE on fertility in humans. There were no effects on fertility in studies in male and female rats.

**4.7 Effects on ability to drive and use machines**

MOLATIVE ORANGE has no influence on the ability to drive and use machines.

Patients should not drive, use machinery or perform any tasks that require concentration until they are certain that MOLATIVE ORANGE does not adversely affect their ability to do so safely (see section 4.8).

**4.8 Undesirable effects**

Reactions related to the gastrointestinal tract occur most commonly.

These reactions may occur as a consequence of expansion of the contents of the gastrointestinal tract, and an increase in motility due to the pharmacologic effects of MOLATIVE ORANGE. Mild diarrhoea usually responds to dose reduction.

The frequency of the adverse effects is not known as it cannot be estimated from the available data.

| **System Organ Class** | **Adverse Event** |
|---|---|
| **Immune system disorders** | Allergic reactions, including anaphylaxis, angioedema, dyspnoea, rash, urticaria and pruritus |
| **Skin and subcutaneous tissue disorders** | Erythema. |
| **Metabolism and nutrition disorders** | Electrolyte disturbances, particularly hyperkalaemia and hypokalaemia. |
| **Nervous system disorders** | Headache. |
| **Gastrointestinal disorders** | Abdominal pain, diarrhoea, vomiting, nausea, dyspepsia, abdominal distension, |

| | |
|---|---|
| | borborygmi, flatulence, anorectal discomfort. |
| **General disorders and administration site conditions** | Peripheral oedema. |

*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. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

**4.9 Overdose**

Severe abdominal pain or distension can be treated using nasogastric aspiration. Extensive fluid loss by diarrhoea or vomiting may require correction of electrolyte disturbances.

**5. PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

A 11.5 Medicines acting on the gastrointestinal tract. Laxatives

Pharmacotherapeutic group: ATC code: A06A D65 Osmotically acting laxatives.

Macrogol 3350 acts by virtue of its osmotic action in the gut, which induces a laxative effect. Macrogol 3350 increases the stool volume, which triggers colon motility via neuromuscular pathways. The physiological consequence is an improved propulsive colonic transportation of the softened stools and a facilitation of the defecation. Electrolytes combined with macrogol 3350 are exchanged across the intestinal barrier (mucosa) with serum electrolytes and excreted in faecal water without net gain or loss of sodium, potassium and water.

Clinical studies using the listed active substances for the treatment of chronic constipation have shown that the dose required to produce normally formed stools tends to decrease over time. Many patients respond to between

1 and 2 sachets per day, but this dose should be adjusted depending on individual response.

**5.2 Pharmacokinetic properties**

**Absorption**

Macrogol 3350 is unchanged along the gut. It is virtually unabsorbed from the gastrointestinal tract. The laxative action of polyethylene glycol has a time course which will vary according to the severity of the constipation being treated.

**Elimination**

Any macrogol 3350 that is absorbed is excreted via the urine.

**6. Pharmaceutical particulars**

**6.1 List of excipients**

Acesulfame Potassium (E950) (sweetener)

Orange Flavour (flavouring)

(Orange flavour contains the following constituents: natural flavouring substances and preparations, maltodextrin and propylene glycol (E1520))

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

Sachet: 2 years

Reconstituted solution: Six hours.

**6.4 Special precautions for storage**

Store at or below 25 °C in its original container.

Reconstituted solution: Store covered in a refrigerator at 2 – 8 °C. Discard any solution not used within 6 hours

after reconstitution.

**6.5 Nature and contents of container**

MOLATIVE ORANGE powder for oral solution are packed in a sachet foil composed of paper, low density polyethylene and aluminium.

Available pack sizes 2, 8, 10, 20, 30, 50 or 100 sachets packed in outer carton container. Not all pack sizes to be marketed.

**6.6 Special precautions for disposal and other handling**

Not applicable

**7. HOLDER OF CERTIFICATE OF REGISTRATION**

Equity Pharmaceuticals (Pty) Ltd

100 Sovereign Drive

Route 21 Corporate Park

Nellmapius Drive, Irene

Pretoria

**8. REGISTRATION NUMBER(S)**

48/11.5/0086

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

19 April 2022

**10. DATE OF REVISION OF THE TEXT**