

**16 October 2024**

**SUMMARY OF PRODUCT CHARACTERISTICS**

**for**

**Alendronat "Teva", tablets 10 mg**

**0. D.SP.NO.**

20651

**1. NAME OF THE MEDICINAL PRODUCT**

Alendronat "Teva"

**2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each tablet contains 10 mg alendronic acid (equivalent to 11.6 mg alendronate sodium monohydrate).

For the full list of excipients, see section 6.1.

**3. PHARMACEUTICAL FORM**

Tablets

White to off-white, round biconvex tablet, debossed with “T” on one side and “10” on the other side.

**4. CLINICAL PARTICULARS**

**4.1 Therapeutic indications**

Alendronat "Teva" is indicated in adults for the treatment of osteoporosis in post-menopausal women. Alendronate reduces the risk of vertebral and hip fractures.

**4.2 Posology and method of administration**

Posology

The recommended dosage is one 10 mg tablet once a day.

Patients should be instructed that if they miss a dose of alendronate, they should take one tablet on the morning after they remember. They should not take two tablets on the same day but should return to taking one tablet once a day, as originally scheduled.

The optimal duration of bisphosphonate treatment for osteoporosis has not been established. The need for continued treatment should be re-evaluated periodically based on the benefits and potential risks of alendronic acid on an individual patient basis, particularly after 5 or more years of use.

*Elderly*

In clinical studies there was no age-related difference in the efficacy or safety profiles of alendronate. Therefore, no dosage adjustment is necessary for the elderly.

*Renal impairment*

No dosage adjustment is necessary for patients with creatinine clearance greater than 35 ml/min. Alendronate is not recommended for patients with renal impairment where creatinine clearance is less than 35 ml/min, due to lack of experience.

*Paediatric population*

The safety and efficacy of alendronate in children less than 18 years of age has not been established. This medicinal product should not be used in children less than 18 years of age. Currently available data for alendronic acid in the paediatric population is described in section 5.1.

Method of administration

Oral use.

*To permit adequate absorption of alendronate:*

Alendronate must be taken at least 30 minutes before the first food, beverage, or medicinal product of the day with plain water only. Other beverages (including mineral water), food and some medicinal products are likely to reduce the absorption of alendronate (see section 4.5).

To facilitate delivery to the stomach and thus reduce the potential for local and oesophageal irritation/adverse experiences (see section 4.4):

* Alendronate should only be swallowed upon arising for the day with a full glass of water (not less than 200 ml).
* Patients should only swallow alendronate whole. Patients should not crush or chew the tablet or allow the tablet to dissolve in their mouths because of a potential for oropharyngeal ulceration.
* Patients should not lie down for at least 30 minutes after taking alendronate and until after the first food of the day.
* Alendronate should not be taken at bedtime or before arising for the day.

Patients should receive supplemental calcium and vitamin-D if dietary intake is inadequate (see section 4.4).

Alendronate 10 mg has not been investigated in the treatment of glucocorticoid-induced osteoporosis.

**4.3 Contraindications**

* Hypersensitivity to the active substance, other bisphosphonates, or to any of the excipients listed in section 6.1.
* Abnormalities of the oesophagus and other factors which delay oesophageal emptying such as stricture or achalasia.
* Inability to stand or sit upright for at least 30 minutes.
* Hypocalcaemia.

**4.4 Special warnings and precautions for use**

Upper gastrointestinal adverse reactions

Alendronate can cause local irritation of the upper gastrointestinal mucosa. Because there is a potential for worsening of the underlying disease, caution should be used when alendronate is given to patients with active upper gastrointestinal problems, such as dysphagia, oesophageal disease, gastritis, duodenitis, ulcers, or with a recent history (within the previous year) of major gastrointestinal disease such as peptic ulcer, or active gastrointestinal bleeding, or surgery of the upper gastrointestinal tract other than pyloroplasty (see section 4.3). In patients with known Barrett's oesophagus, prescribers should consider the benefits and potential risks of alendronate on an individual patient basis.

Oesophageal reactions (sometimes severe and requiring hospitalisation), such as oesophagitis, oesophageal ulcers and oesophageal erosions, rarely followed by oesophageal stricture, have been reported in patients receiving alendronate. Physicians should therefore be alert to any signs or symptoms signalling a possible oesophageal reaction and patients should be instructed to discontinue alendronate and seek medical attention if they develop symptoms of oesophageal irritation such as dysphagia, pain on swallowing or retrosternal pain, new or worsening heartburn (see section 4.8).

The risk of severe oesophageal adverse experiences appears to be greater in patients who fail to take alendronate properly and/or who continue to take alendronate after developing symptoms suggestive of oesophageal irritation. It is very important that the full dosing instructions are provided to, and understood by the patient (see section 4.2). Patients should be informed that failure to follow these instructions may increase their risk of oesophageal problems.

While no increased risk was observed in extensive clinical trials, there have been rare (post-marketing) reports of gastric and duodenal ulcers, some severe and with complications (see section 4.8).

Osteonecrosis of the jaw

Osteonecrosis of the jaw, generally associated with tooth extraction and/or local infection (including osteomyelitis) has been reported in patients with cancer who are receiving treatment regimens including primarily intravenously administered bisphosphonates. Many of these patients were also receiving chemotherapy and corticosteroids. Osteonecrosis of the jaw has also been reported in patients with osteoporosis receiving oral bisphosphonates.

The following risk factors should be considered when evaluating an individual’s risk of developing osteonecrosis of the jaw:

* potency of the bisphosphonate (highest for zoledronic acid), route of administration (see above) and cumulative dose
* cancer, chemotherapy, radiotherapy, corticosteroids, angiogenesis inhibitors, smoking
* a history of dental disease, poor oral hygiene, periodontal disease, invasive dental procedures and poorly fitting dentures.

A dental examination with appropriate preventive dentistry should be considered prior to treatment with oral bisphosphonates in patients with poor dental status.

While on treatment, these patients should avoid invasive dental procedures if possible. For patients who develop osteonecrosis of the jaw while on bisphosphonate therapy, dental surgery may exacerbate the condition. For patients requiring dental procedures, there are no data available to suggest whether discontinuation of bisphosphonate treatment reduces the risk of osteonecrosis of the jaw. Clinical judgement of the treating physician should guide the management plan of each patient based on individual benefit/risk assessment.

During bisphosphonate treatment, all patients should be encouraged to maintain good oral hygiene, receive routine dental check-ups, and report any oral symptoms such as dental mobility, pain, or swelling.

Osteonecrosis of the external auditory canal

Osteonecrosis of the external auditory canal has been reported with bisphosphonates, mainly in association with long-term therapy. Possible risk factors for osteonecrosis of the external auditory canal include steroid use and chemotherapy and/or local risk factors such as infection or trauma. The possibility of osteonecrosis of the external auditory canal should be considered in patients receiving bisphosphonates who present with ear symptoms such as pain or discharge, or chronic ear infections.

Musculoskeletal pain

Bone, joint, and/or muscle pain has been reported in patients taking bisphosphonates. In post-marketing experience, these symptoms have rarely been severe and/or incapacitating (see section 4.8). The time to onset of symptoms varied from one day to several months after starting treatment. Most patients had relief of symptoms after stopping treatment. A subset had recurrence of symptoms when rechallenged with the same medicinal product or another bisphosphonate.

Atypical fractures of the femur

Atypical subtrochanteric and diaphyseal femoral fractures have been reported with bisphosphonate therapy, primarily in patients receiving long-term treatment for osteoporosis. These transverse or short oblique fractures can occur anywhere along the femur from just below the lesser trochanter to just above the supracondylar flare. These fractures occur after minimal or no trauma and some patients experience thigh or groin pain, often associated with imaging features of stress fractures, weeks to months before presenting with a complete femoral fracture. Fractures are often bilateral; therefore, the contralateral femur should be examined in bisphosphonate-treated patients who have sustained a femoral shaft fracture. Poor healing of these fractures has also been reported. Discontinuation of bisphosphonate therapy in patients suspected to have an atypical femur fracture should be considered pending evaluation of the patient, based on an individual benefit risk assessment.

During bisphosphonate treatment patients should be advised to report any thigh, hip or groin pain and any patient presenting with such symptoms should be evaluated for an incomplete femur fracture.

Alendronate is not recommended for patients with renal impairment where creatinine clearance is less than 35 ml/min (see section 4.2).

Bone and mineral metabolism

Causes of osteoporosis other than oestrogen deficiency and ageing should be considered.

Hypocalcaemia must be corrected before initiating therapy with alendronate (see section 4.3). Other disorders affecting mineral metabolism (such as vitamin D deficiencyand hypoparathyroidism) should also be effectively treated before starting this medicinal product. In patients with these conditions, serum calcium and symptoms of hypocalcaemia should be monitored during therapy with alendronate.

Due to the positive effects of alendronate in increasing bone mineral, decreases in serum calcium and phosphate may occur especially in patients taking glucocorticoids in whom calcium absorption may be decreased. These are usually small and asymptomatic. However, there have been rare reports of symptomatic hypocalcaemia, which have occasionally been severe and often occurred in patients with predisposing conditions (e.g. hypoparathyroidism, vitamin D deficiency and calcium malabsorption).

Ensuring adequate calcium and vitamin D intake is particularly important in patients receiving glucocorticoids.

In post-marketing experience, there have been rare reports of severe skin reactions including Stevens Johnson syndrome and toxic epidermal necrolysis.

Excipient

*Sodium*

This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially “sodium-free”.

**4.5 Interaction with other medicinal products and other forms of interaction**

If taken at the same time, it is likely that food and beverages (including mineral water), calcium supplements, antacids, and some oral medicinal products will interfere with absorption of alendronate. Therefore, patients must wait at least 30 minutes after taking alendronate before taking any other oral medicinal product (see sections 4.2 and 5.2).

No other interactions with medicinal products of clinical significance are anticipated. A number of patients in the clinical trials received oestrogen (intravaginal, transdermal or oral) while taking alendronate. No adverse experiences attributable to their concomitant use were identified.

Since NSAID use is associated with gastrointestinal irritation, caution should be used during concomitant use with alendronate.

Although specific interaction studies were not performed, in clinical studies alendronate was used concomitantly with a wide range of commonly prescribed medicinal products without evidence of clinical adverse interactions.

**4.6 Fertility, pregnancy and lactation**

Pregnancy

There are no or limited amount of data from the use of alendronate in pregnant women. Studies in animals have shown reproductive toxicity. Alendronate given during pregnancy in rats caused dystocia related to hypocalcaemia (see section 5.3). Alendronate should not be used during pregnancy.

Breast-feeding

It is unknown whether alendronate/metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded. Alendronate should not be used during breast-feeding.

Fertility

Bisphosphonates are incorporated into the bone matrix, from which they are gradually released over a period of years. The amount of bisphosphonate incorporated into adult bone, and hence, the amount available for release back into the systemic circulation, is directly related to the dose and duration of bisphosphonate use (see section 5.2). There are no data on foetal risk in humans. However, there is a theoretical risk of foetal harm, predominantly skeletal, if a woman becomes pregnant after completing a course of bisphosphonate therapy. The impact of variables such as time between cessation of bisphosphonate therapy to conception, the particular bisphosphonate used, and the route of administration (intravenous versus oral) on the risk has not been studied.

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

No traffic warning.

Alendronate has no or negligible direct influence on the ability to drive and use machines. Patients may experience certain adverse reactions (for example blurred vision, dizziness and severe bone muscle or joint pain (see section 4.8)) that may influence the ability to drive and use machines.

**4.8 Undesirable effects**

Summary of the safety profile

In a one-year study in postmenopausal women with osteoporosis the overall safety profiles of alendronate once weekly 70 mg (n=519) and alendronate 10 mg/day (n=370) were similar.

In two three-year studies of virtually identical design, in postmenopausal women (alendronate 10 mg: n=196, placebo: n=397) the overall safety profiles of alendronate 10 mg/day and placebo were similar.

Adverse experiences reported by the investigators as possibly, probably or definitely drug-related are presented below if they occurred in ≥1% in either treatment group in the one-year study, or in ≥1% of patients treated with alendronate 10 mg/day and at a greater incidence than in patients given placebo in the three-year studies:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **One-Year Study** | | **Three-Year Studies** | |
| Alendronate once weekly 70 mg  (n=519)  % | Alendronate  10 mg/day  (n=370)  % | Alendronate  10 mg/day  (n=196)  % | Placebo  (n=397)  % |
| *Gastrointestinal*   * Abdominal pain * Dyspepsia * Acid regurgitation * Nausea * Abdominal distention * Constipation * Diarrhoea * Dysphagia * Flatulence * Gastritis * Gastric ulcer * Oesophageal ulcer | 3.7  2.7  1.9  1.9  1.0  0.8  0.6  0.4  0.4  0.2  0.0  0.0 | 3.0  2.2  2.4  2.4  1.4  1.6  0.5  0.5  1.6  1.1  1.1  0.0 | 6.6  3.6  2.0  3.6  1.0  3.1  3.1  1.0  2.6  0.5  0.0  1.5 | 4.8  3.5  4.3  4.0  0.8  1.8  1.8  0.0  0.5  1.3  0.0  0.0 |
| *Musculoskeletal*   * Musculoskeletal (bone, muscle or joint) pain * muscle cramp | 2.9  0.2 | 3.2  1.1 | 4.1  0.0 | 2.5  1.0 |
| *Neurological*   * Headache | 0.4 | 0.3 | 2.6 | 1.5 |

**Tabulated list of adverse reactions**

The following adverse experiences have also been reported during clinical studies and/or post-marketing use:

Frequencies are defined as: Very common (≥ 1/10), common (≥ 1/100; < 1/10), uncommon (≥ 1/1,000; < 1/100), rare (≥ 1/10,000; < 1/1,000), very rare (< 1/10,000 including isolated cases).

|  |  |  |
| --- | --- | --- |
| ***System organ class*** | **Frequency** | **Adverse reactions** |
| ***Immune system disorders*** | Rare | Hypersensitivity reactions including urticaria and angioedema |
| ***Metabolism and nutrition disorders*** | Rare | Symptomatic hypocalcaemia, often in association with predisposing conditions§ |
| ***Nervous system disorders*** | Common | Headache, dizziness† |
| Uncommon | Dysgeusia† |
| ***Eye disorders*** | Uncommon | Eye inflammation (uveitis, scleritis or episcleritis) |
| ***Ear and labyrinth disorders*** | Common | Vertigo† |
| Very rare | Osteonecrosis of the external auditory canal (bisphosphonate class adverse reaction) |
| ***Gastrointestinal disorders*** | Common | Abdominal pain, dyspepsia, constipation, diarrhoea, flatulence, oesophageal ulcer\*, dysphagia\*, abdominal distension, acid regurgitation |
| Uncommon | Nausea, vomiting, gastritis, oesophagitis\*, oesophageal erosions\*, melena† |
| Rare | Oesophageal stricture\*, oropharyngeal ulceration\*, upper gastrointestinal PUBs (perforation, ulcers, bleeding)§ |
| ***Skin and subcutaneous tissue disorders*** | Common | Alopecia†, pruritus† |
| Uncommon | Rash, erythema |
| Rare | Rash with photosensitivity, severe skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis‡ |
| ***Musculoskeletal and connective tissue disorders*** | Very common | Musculoskeletal (bone, muscle or joint) pain which is sometimes severe†§ |
| Common | Joint swelling† |
| Rare | Osteonecrosis of the jaw‡§; atypical subtrochanteric and diaphyseal femoral fractures (bisphosphonate class adverse reaction) |
| ***General disorders and administration site conditions*** | Common | Asthenia†, peripheral oedema† |
| Uncommon | Transient symptoms as in an acute-phase response (myalgia, malaise and rarely, fever), typically in association with initiation of treatment† |
| §See section 4.4  †Frequency in clinical trials was similar in the medicinal product and placebo group.  \*See sections 4.2 and 4.4  ‡This adverse reaction was identified through post-marketing surveillance. The frequency of rare was estimated based on relevant clinical trials. | | |

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:

Lægemiddelstyrelsen

Axel Heides Gade 1

DK-2300 København S

Website: www.meldenbivirkning.dk

**4.9 Overdose**

Symptoms

Hypocalcaemia, hypophosphataemia and upper gastrointestinal adverse reactions, such as upset stomach, heartburn, oesophagitis, gastritis or ulcer, may result from oral overdose.

Management

No specific information is available on the treatment of overdose with alendronate. Milk or antacids should be given to bind alendronate. Owing to the risk of oesophageal irritation, vomiting should not be induced, and the patient should remain fully upright.

**4.10 Legal status**

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**5. PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Drugs for treatment of bone diseases, bisphosphonates

ATC code*:* M05BA04.

Mechanism of action

Alendronate is an amino-bisphosphonate, which in animal studies was deposited among the osteoclasts in areas with bone resorption. It inhibits bone resorption with no direct effect on bone formation. Since bone resorption and bone formation are coupled, bone formation is also reduced, but to a lesser extent than resorption, resulting in a progressive increase in bone mass, with normal bone structure. Alendronate is stored in the bone matrix, where it is pharmacologically inactive.

In rats the lowest dose of alendronate which influenced bone mineralisation (leading to osteomalacia) was 6000 times greater than the antiresorptive dose. This data indicates that alendronate administered in therapeutic doses is most unlikely to induce osteomalacia.

Clinical efficacy and safety

*Osteoporosis in postmenopausal women*

Alendronate treatment of postmenopausal women produces biochemical changes which indicate dose-dependent inhibition of bone resorption.

In investigations lasting up to 5 years, 10 mg/day alendronate for 3-6 months, reduced the biochemical markers for bone resorption by approx. 50-70% to a level corresponding to that seen in healthy pre-menopausal women. The markers of bone formation were similarly reduced by 25-50% after 6-12 months. The new plateau for bone resorption and bone formation was maintained for the rest of the period of alendronate treatment.

*Effect on bone mineral density*

In clinical studies, 10 mg alendronate once a day for 3 years produced an increase in bone mineral density (BMD) in postmenopausal women with osteoporosis. After three years treatment with 10 mg alendronate once a day there was an increase (compared with placebo) in BMD of approx. 8.8% in the lumbar spine, 5.9% in the femoral neck, 7.8% in the trochanter, 2.2% in the forearm and 2.5% in the whole body. In the 2-year extension of these studies, treatment with 10 mg alendronate once a day lead to continued increase in BMD in the spinal column and trochanter (further absolute increase between years 3 and 5: spinal column, 0.94%, trochanter 0.88%,). BMD in the femoral neck, forearm and whole body was maintained.

The effect of alendronate was the same regardless of age, race, initial rate of bone turnover, kidney function and use together with a wide-ranging assortment of other medicinal products.

After withdrawal of alendronate after 1-2 years’ therapy, neither further increase in bone mass, nor accelerated bone loss was observed. This data indicates that daily treatment with alendronate has to be continued in order to produce progressive increase in bone mass.

*Effect on incidence of fracture*

Alendronate produced the same reduction of incidence in both vertebral and non-vertebral fractures in patients who have had no previous fractures and those with previous vertebral fractures.

Analysis of 3 years’ pooled data from the two largest treatment studies in which various doses of alendronate were administered to postmenopausal women, yielded the following results: 48% reduction in the proportion of patients who experienced one or several vertebral fractures (alendronate 3.2% v. placebo 6.2%). In patients who did have vertebral fracture, the loss in height was less in those who were treated with alendronate (5.9mm v. 23.3mm). Pooled data from 5 studies of 2-3 years’ duration showed 29% reduction in the number of non-vertebral fractures (alendronate 9.0% v. placebo 12.6%).

Three years’ treatment with alendronate (5 mg/day for the first 2 years, 10 mg/day for the 3rd year) in postmenopausal women with osteoporosis (who had had at least one crush fracture of the spinal vertebrae) led to reduction of incidence of fracture as follows:

Ratio of patients who experienced at least one new vertebral fracture (alendronate 8.0% v. placebo 15.0%, a reduction of 47%); at least two new vertebral fractures (0.5% v. 4.9%, a reduction of 90%); any clinical (i.e. painful) fracture (13.7% v. 18.3%, a reduction of 28%); hip fracture (1.1% v. 2.2%, a reduction of 51%); and wrist (forearm) fracture (2.2% v. 4.1%, a reduction of 48%).

*Bone histology*

Bone histology in 270 postmenopausal women with osteoporosis treated with alendronate at doses from 1-20 mg/day for 1-3 years showed normal mineralisation and structure as well as the expected decrease in bone turnover relative to placebo.

*Laboratory test findings*

In clinical studies, asymptomatic, mild and transient decreases in serum calcium and phosphate were observed in approximately 18 and 10%, respectively, of patients taking alendronate 10 mg/day versus approximately 12 and 3% of those taking placebo. However, the incidences of decreases in serum calcium to <8.0 mg/dl (2.0 mmol/l) and serum phosphate to ≤2.0 mg/dl (0.65 mmol/l) were similar in both treatment groups.

*Paediatric population*

Alendronate sodium has been studied in a small number of patients with osteogenesis imperfecta under the age of 18 years. Results are insufficient to support the use of alendronate sodium in paediatric patients with osteogenesis imperfecta.

**5.2 Pharmacokinetic properties**

Absorption

Oral bioavailability of alendronate in women is 0,7% for doses ranging from 5 to 40 mg, when administered after an overnight fast and two hours before a standardised breakfast. Oral bioavailability in men (0.6%) was approx. the same as in women. Bioavailability is reduced by approx. 40%, when alendronate was administered ½ hour to 1 hour before a standardised breakfast. Bioavailability was negligible if alendronate was taken with or up to two hours after a standard breakfast. Coffee and orange juice reduced bioavailability by approx. 60% (see section 4.2).

In healthy test subjects, oral prednisone (20 mg 3 times daily for 5 days) did not significantly affect the oral bioavailability of alendronate (average increase 20-44%).

Distribution

Protein binding is approx. 78%. Preclinical investigation shows that alendronate is distributed to the soft tissues and then is rapidly redistributed to the bones, where is binds or is eliminated in the urine. The steady-state distribution volume in the soft areas of the body are at least 28 litres (22-35 litres). Plasma concentrations of the active substance after administration of an oral therapeutic dose are below the level of detection (<5 ng/ml).

Biotransformation

Alendronate has no known metabolites.

Elimination

Approx. 50% of 14C-tagged alendronate is excreted in the urine within 72 hours. Very little or no radioactivity was recovered in the faeces. The remainder is deposited in bone tissue, where it is inactive. Renal clearance was 71 ml/minute after a single I.V. dose of 10 mg. Within 6 hours the plasma concentration fell by more than 95% after I.V. administration. This is followed by a slow release of alendronate from the skeleton. The estimated half-life is thus > 10 years.

Renal impairment

Preclinical investigations show that the active substance, which is not deposited in the bones, is rapidly excreted in the urine. After chronic dosage with cumulative doses I.V., up to 35 mg/kg in animals, no saturation of bone uptake was observed. In animals, elimination of alendronate via the kidneys was reduced in impaired renal function. There is no corresponding information in man, but greater accumulation of alendronate in bone should be anticipated in people with impaired renal function (see section 4.2).

**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 and carcinogenic potential. Studies in rats have shown that treatment with alendronate during pregnancy was associated with dystocia in dams during parturition which was related to hypocalcaemia. In studies, rats given high doses showed an increased incidence of incomplete foetal ossification. The relevance to humans is unknown.

**6. PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

Low-substituted hydroxypropylcellulose

Hydroxypropylcellulose

Precipitated silicon dioxide

Sodium stearyl fumarate

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

3 years.

**6.4 Special precautions for storage**

This medicinal product does not require any special storage conditions.

**6.5 Nature and contents of container**

PVC/PVdC/Aluminium blisters PVC/PVdC blister pack. containing 14, 28, 30, 50, 56, 84, 90, 98, 112, 140 tablets, 28 tablets in calendar pack, 50 × 1 (individual blisters)

Not all pack sizes may be marketed.

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

No special requirements.

**7. MARKETING AUTHORISATION HOLDER**

Teva B.V.

Swensweg 5

2031 GA Haarlem

Holland

**Representative**

Teva Denmark A/S

Vandtårnsvej 83a

2860 Søborg

**8. MARKETING AUTHORISATION NUMBER(S)**

31649

**9. DATE OF FIRST AUTHORISATION**

7 June 2002

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

16 October 2024