SUMMARY OF THE PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Actonel Wekelijks MSR 35 mg, maagsapresistente tabletten

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gastro-resistant tablet contains 35 mg risedronate sodium (equivalent to 32.5 mg risedronic acid).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gastro-resistant tablet.
Oval, yellow, gastro-resistant tablet with “EC 35” engraved on one side.
The dimensions of the tablet are as follows: width 13 mm, length 6 mm.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of osteoporosis in postmenopausal women at increased risk of fractures (see section 5.1).

4.2 Posology and method of administration

Posology

The recommended dose in adults is one Actonel Wekelijks 35 mg gastro-resistant tablet orally once a week. The tablet should be taken on the same day each week.
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 risedronate on an individual patient basis, particularly after 5 or more years of use.

Special populations

Elderly
Of the patients receiving risedronate 35 mg gastro-resistant tablets in postmenopausal osteoporosis studies, 59% were 65 and over, while 13 % were 75 and over. No overall differences in safety and effectiveness were observed between these patients and younger patients.

Patients with renal impairment
No dosage adjustment is required for those patients with mild to moderate renal impairment. The use of risedronate sodium is contraindicated in patients with severe renal impairment (creatinine clearance lower than 30 ml/min) (see sections 4.3 and 5.2).

Paediatric population
Risedronate sodium is not recommended for use in children below age 18 due to insufficient data on safety and efficacy (also see section 5.1).

Method of administration

Actonel Wekelijks 35 mg gastro-resistant tablets should be taken orally in the morning immediately after breakfast. Administration under fasting conditions may lead to an increased risk of upper abdominal pain (see section 4.8 and 5.2).

The tablet must be swallowed whole and not sucked or chewed. To aid delivery of the tablet to the stomach, it is to be taken while in an upright position with a glass of plain water (≥120 ml). Patients should not lie down for 30 minutes after taking the tablet (see section 4.4).

Supplemental calcium and vitamin D should be considered if the dietary intake is inadequate.

Patients should be instructed that if a dose is missed, it should be taken on the day that the tablet is remembered. Patients should then return to taking one tablet once a week on the day the tablet is normally taken. Two tablets should not be taken on the same day.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Hypocalcaemia (see section 4.4).
Pregnancy and lactation.
Severe renal impairment (creatinine clearance <30 ml/min).

4.4 Special warnings and precautions for use

Medicinal products containing polyvalent cations (such as calcium, magnesium, iron and aluminium) interfere with the absorption of bisphosphonates and should be taken at a different time of day to risedronate tablets (see section 4.5). In order to achieve the intended efficacy, strict adherence to dosing recommendations is necessary (see section 4.2).

Efficacy of bisphosphonates in the treatment of osteoporosis is related to the presence of low bone mineral density and/or prevalent fracture.
High age or clinical risk factors for fracture alone are not sufficient reasons to initiate treatment of osteoporosis with a bisphosphonate.
The evidence to support efficacy of bisphosphonates including risedronate in the very elderly (>80 years) is limited (see section 5.1).

Hypocalcaemia should be treated before starting risedronate therapy. Other disturbances of bone and mineral metabolism (i.e. parathyroid dysfunction, hypovitaminosis D) should be treated at the time of starting risedronate therapy.

Upper gastrointestinal adverse reactions
Bisphosphonates have been associated with oesophagitis, gastritis, oesophageal ulcerations and gastroduodenal ulcerations. Thus, caution should be used:

- In patients who have a history of oesophageal disorders which delay oesophageal transit or emptying e.g. stricture or achalasia.
- In patients who are unable to stay in the upright position for at least 30 minutes after taking the tablet.
- If risedronate is given to patients with active or recent oesophageal or upper gastrointestinal problems (including known Barrett's oesophagus).

Prescribers should emphasise to patients the importance of paying attention to the dosing instructions and be alert to any signs and symptoms of possible oesophageal reaction. The patients should be instructed to seek timely medical attention if they develop symptoms of oesophageal irritation such as dysphagia, pain on swallowing, retrosternal pain or new/worsened heartburn.

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 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.

A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates in patients with concomitant risk factors (e.g. cancer, chemotherapy, radiotherapy, corticosteroids, poor oral hygiene).

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.

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 including chronic ear infections.

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 completed 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.

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

4.5 Interaction with other medicinal products and other forms of interaction

Medicinal products containing polyvalent cations (such as calcium, magnesium, iron and aluminium) interfere with the absorption of bisphosphonates and should be taken at a different time of day to risedronate tablets (see section 4.4).

Risedronate sodium is not systemically metabolised, does not induce cytochrome P450 enzymes, and has low protein binding.

Co-administration of risedronate 35 mg gastro-resistant tablets with the proton pump inhibitor esomeprazole increased the risedronate bioavailability. The maximum plasma concentration (Cmax) and the area under the plasma concentration time curve (AUC) were increased by 60% and 22% respectively, but the clinical implications measured by body mass density changes were not statistically significant.

If considered appropriate risedronate sodium may be used concomitantly with oestrogen supplementation.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no adequate data from the use of risedronate sodium in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3). The potential risk for humans is unknown.

Breast-feeding
Studies in animal indicate that a small amount of risedronate sodium pass into breast milk. Risedronate sodium must not be used during pregnancy or by breast-feeding women.

Fertility
There are no adequate data on the effects of risedronate on human fertility. Animal studies showed adverse effects at exposures considerably above that in humans (see section 5.3).

4.7 Effects on ability to drive and use machines

Risedronate sodium has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most commonly reported side effects with risedronate tablets are gastrointestinal disorders including abdominal pain, diarrhoea, dyspepsia, nausea, constipation; musculoskeletal pain and headache.

Tabulated list of adverse reactions from clinical studies

Risedronate sodium has been studied in phase III clinical studies involving more than 15,000 patients. The majority of undesirable effects observed in clinical studies was mild to moderate in severity and usually did not require cessation of therapy.

Adverse experiences reported in phase III clinical studies in postmenopausal women with osteoporosis and considered possibly or probably related to risedronate sodium are listed below 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).
Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Table 1

MedDRA System Organ Class	Common	Uncommon	Rare
Infections and infestations		Influenza	
Blood and lymphatic system disorders		Leukopenia, neutropenia	
Immune system disorders		Hypersensitivity	
Endocrine disorders		Hyperparathyroidism secondary	
Metabolism and nutrition disorders		Hypercalcaemia	
Psychiatric disorders		Depression	
Nervous system disorders	Headache	Dizziness, paresthesia, hypoaestesia	
Eye disorders		Iritis*, ocular	

		hyperaemia, conjunctivitis, vision blurred	
Ear and labyrinth disorders		Vertigo	
Vascular disorders		Hot flush, hypotension	
Respiratory, thoracic and mediastinal disorders		Cough	
Gastrointestinal disorders	Abdominal pain including abdominal pain upper and abdominal pain lower, constipation, dyspepsia, nausea, diarrhoea, vomiting	Gastritis, Helicobacter gastritis, oesophagitis, dysphagia, duodenitis, oesophageal ulcer, abdominal discomfort, abdominal distension, erosive esophagitis, gastritis erosive, haematochezia, hyperchlorhydria, eructation, flatulence, gastritis atrophic, gastroesophageal reflux disease, gingivitis, haemorrhoids, hiatus hernia, melaena, abdominal tenderness, aphtous stomatitis, colitis, dry mouth, faecal incontinence, gastric mucosal hypertrophy, gastrointestinal inflammation, gastrointestinal pain, hypoaesthesia oral, lip swelling, odynophagia, swollen tongue	Oesophageal stricture, glossitis
Hepatobiliary disorders			Abnormal liver function tests*
Skin and subcutaneous tissue disorders		Erythema, Henoch-Schonlein purpura, urticarial, dermatitis allergic, pruritus, rash	
Musculoskeletal and connective tissues disorders	Musculoskeletal pain	Arthralgia, back pain, muscle spasm, myalgia, pain in extremity, bone pain, muscle fatigue, muscular weakness, neck pain, pain in jaw	
Renal and Urinary disorders		Nephrolithiasis	
Reproductive system and breast disorders		Ovarian cyst	
General disorders and		Asthenia, chills,	

administration site conditions		fatigue, influenza like illness, chest discomfort, chest pain, face oedema, oedema, oedema peripheral, pain, pyrexia	
Investigations		Blood calcium and phosphate decreased, heart rate irregular, urine analysis abnormal, transaminases increased blood alkaline phosphatase increased, blood parathyroid hormone increased, occult blood, platelet count decreased	

* No relevant incidences from Phase III osteoporosis studies; frequency based on adverse event/laboratory/rechallenge findings in earlier clinical studies.

Description of selected adverse events

Gastrointestinal disorders

In the Phase III study, comparing risedronate 35 mg gastro-resistant tablets and risedronate sodium 5 mg daily (immediate-release) more patients that used NSAID/aspirin reported upper gastrointestinal treatment-emergent adverse events than non-users.
The frequency of patients that reported such events were:
- 22.0% in NSAID/aspirin users vs 15.7% in the NSAID/aspirin non-users in the 35 mg immediately-following-breakfast group
- 29.8% in NSAID/aspirin users vs 15.3% in the NSAID/aspirin non-users in the 35 mg 30 minutes- before-breakfast group
- 22.4% in NSAID/aspirin users vs 13.4% in the NSAID/aspirin non-users in the 5 mg immediate-release before-breakfast group

A higher incidence of upper abdominal pain was seen when risedronate 35 mg gastro-resistant tablets were taken in a fasted state 30 minutes before breakfast.

The frequency of lower gastrointestinal treatment-emergent adverse events were 22.1% in the 35 mg immediately-following-breakfast group, 20.1% in the 35 mg 30 minutes- before-breakfast group and 15.6% in the 5 mg immediate-release group.

During post marketing experience the following reactions have been reported

Rare: Atypical subtrochanteric and diaphyseal femoral fractures (bisphosphonate class adverse reaction).

Very rare: Osteonecrosis of the external auditory canal (bisphosphonate class adverse reaction).

Frequency not known (cannot be estimated from available data)

Eye disorders
Iritis, uveitis, orbital inflammation

Musculoskeletal and connective tissues disorders

Osteonecrosis of the jaw

Skin and subcutaneous tissue disorders
Hypersensitivity and skin reactions, including angioedema, and bullous skin reactions, some severe including isolated reports of Stevens Johnson syndrome, toxic epidermal necrolysis and leukocytoclastic vasculitis.
Hair loss

Immune system disorders
Anaphylactic reaction

Hepatobiliary disorders
Serious hepatic disorders. In most of the reported cases the patients were also treated with other products known to cause hepatic disorders.

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 het Nederlands Bijwerkingen Centrum Lareb
Website: www.lareb.nl

4.9 Overdose

No specific information is available on the treatment of overdose with risedronate sodium.

Decreases in serum calcium following substantial overdose may be expected. Signs and symptoms of hypocalcaemia may also occur in some of these patients.

Milk or antacids containing magnesium, calcium or aluminium should be given to bind risedronate and reduce absorption of the drug.

The impact of this intervention for Actonel Wekelijks 35 mg gastro-resistant tablets has not been evaluated. The Actonel Wekelijks 35 mg gastro-resistant formulation is less sensitive to the binding effects of divalent cations. Standard procedures that are effective for treating hypocalcaemia, including the administration of calcium intravenously, would be expected to restore physiologic amounts of ionised calcium and to relieve signs and symptoms of hypocalcaemia.

In cases of substantial overdose, gastric lavage may be considered to remove unabsorbed drug if performed within 30 minutes of ingestion.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs for treatment of bone diseases, Drugs affecting bone structure and mineralization, Bisphosphonates, ATC Code: M05BA07.

Mechanism of action
Risedronate sodium is a pyridinyl bisphosphonate that binds to bone hydroxyapatite and inhibits osteoclast-mediated bone resorption. The bone turnover is reduced while the osteoblast activity and bone mineralisation is preserved.

Pharmacodynamic effects
In preclinical studies risedronate sodium demonstrated potent anti-osteoclast and anti-resorptive activity, and dose dependently increased bone mass and biomechanical skeletal strength. The activity of risedronate sodium was confirmed by measuring biochemical markers for bone turnover during

pharmacodynamic and clinical studies. In studies of postmenopausal women, decreases in biochemical markers of bone turnover were observed at month 3 and at subsequent timepoints. Decreases in biochemical markers of bone turnover were similar with risedronate 35 mg gastro-resistant weekly tablets and risedronate 5 mg daily at all-time points.

Clinical efficacy and safety

Treatment of Postmenopausal Osteoporosis

Based on effects on mean change in lumbar spine BMD, risedronate 35 mg gastro-resistant tablets (n=307 following breakfast and n=308 before breakfast) was shown to be equivalent to risedronate 5 mg daily tablets (n=307) in a two-year, double-blind, multicentre study of postmenopausal women with osteoporosis.

Risedronate 35 mg gastro-resistant tablets administered either before or after breakfast was shown to be therapeutically equivalent to risedronate 5 mg daily (immediate-release formulation) in a 2-year, double-blind, multicentre study of postmenopausal women with osteoporosis. The primary efficacy endpoint of percent change from baseline in lumbar spine BMD (LS) at week 52 was met. Secondary efficacy endpoints included percent change from baseline in lumbar spine BMD at week 104; non-vertebral fractures at week 104 which were consistent with the primary outcome measure; and change in bone turnover markers. Table 2 presents the primary efficacy analysis at 1 year (Primary Analysis Population), as well as the 2 year results (Week 104 Endpoint Population).

Table 2 Lumbar Spine BMD (LS) - Percent Change from Baseline at 1 yr and 2 yr Endpoints [a]

	Risedronate 5 mg Daily immediate-release N=307	Risedronate 35 mg Once a Week gastro-resistant Following Breakfast N=307	Risedronate 35 mg Once a Week gastro-resistant Before Breakfast N=308
Primary Efficacy (LOCF), at 1 year [c]			
n	270	261	271
LS Mean (95% CI)	3.1* (2.7, 3.5)	3.3* (2.9, 3.7)	3.4* (3.0, 3.8)
LS Mean Difference [b] (95% CI)		-0.2 (-0.8, 0.3)	-0.3 (-0.9, 0.3)
2 year-endpoint [d]			
n	274	265	273
LS Mean (95% CI)	4.1 (3.7, 4.6)	5.2 (4.7, 5.7)	5.1 (4.6,5.6)
LS Mean Difference[b] (95% CI)		-1.1 (-1.8, -0.4)	-0.9 (-1.6, -0.2)

N = number of intent-to-treat patients within specified treatment; n = number of patients with values at baseline and at the visit.
* Indicates a statistically significant difference from baseline determined from 95% CI unadjusted for multiple comparisons.
[a] at 1 year and 2 year LOCF
[b] LS Mean Difference is 5 mg daily minus 35 mg weekly treatment.
[c] Based on PE Population (all ITT patients who had analyzable lumbar spine BMD data at both baseline and Week 52 LOCF Endpoint)
[d] Based on **Week 104-Endpoint population(**all ITT patients who had analyzable lumbar spine BMD data at both baseline and Week 104 LOCF Endpoint)

The clinical programme for risedronate sodium administered once daily studied the effect of risedronate sodium on the risk of hip and vertebral fractures and contained early and late postmenopausal women with and without fracture. Daily doses of 2.5 mg and 5 mg were studied and all groups, including the control groups, received calcium and vitamin D (if baseline levels were low). The absolute and relative risk of new vertebral and hip fractures was estimated by use of a time-to-first event analysis.

- Two placebo-controlled studies (n=3661) enrolled postmenopausal women under 85 years with vertebral fractures at baseline. Risedronate sodium 5 mg daily given for 3 years reduced the risk of new vertebral fractures relative to the control group. In women with respectively at least 2 or at least 1 vertebral fractures, the relative risk reduction was 49% and 41% respectively (incidence of new vertebral fractures with risedronate sodium 18.1% and 11.3%, with placebo 29.0% and 16.3%, respectively).

- Two further placebo controlled studies enrolled postmenopausal women above 70 years with or without vertebral fractures at baseline. Women 70-79 years were enrolled with femoral neck BMD T-score <-3 SD (manufacturer's range, i.e. -2.5 SD using NHANES III (National Health and Nutrition Examination Survey)) and at least one additional risk factor. Women >80 years could be enrolled on the basis of at least one non-skeletal risk factor for hip fracture or low bone mineral density at the femoral neck. Statistical significance of the efficacy of risedronate versus placebo is only reached when the two treatment groups 2.5 mg and 5 mg are pooled. The following results are only based on *a-posteriori* analysis of subgroups defined by clinical practise and current definitions of osteoporosis:

    - In the subgroup of patients with femoral neck BMD T-score ≤-2.5 SD (NHANES III) and at least one vertebral fracture at baseline, risedronate sodium given for 3 years reduced the risk of hip fractures by 46% relative to the control group (incidence of hip fractures in combined risedronate sodium 2.5 mg and 5 mg groups 3.8%, placebo 7.4%);

Paediatric population
The safety and efficacy of risedronate sodium has been investigated in a 3-year study (a randomized, double-blind, placebo-controlled, multicenter, parallel group study of one year duration followed by 2 years of open-label treatment) in paediatric patients aged 4 to less than 16 years with mild to moderate osteogenesis imperfecta. In this study, patients weighing 10-30 kg received risedronate 2.5 mg daily and patients weighing more than 30 kg received risedronate 5 mg daily.

After completion of its one-year randomized, double-blind, placebo-controlled phase, a statistically significant increase in lumbar spine BMD in the risedronate group versus placebo group was demonstrated; however an increased number of patients with at least 1 new morphometric (identified by x-ray) vertebral fracture was found in the risedronate group compared to placebo. During the one-year double-blind period, the percentage of patients who reported clinical fractures was 30.9% in the risedronate group and 49.0% in the placebo group. In the open-label period when all patients received risedronate (month 12 to month 36), clinical fractures were reported by 65.3% of patients initially randomized to the placebo group and by 52.9% of patients initially randomized to the risedronate group.

Overall, results do not support the use of risedronate sodium in paediatric patients with mild to moderate osteogenesis imperfecta.

5.2 Pharmacokinetic properties

Absorption
The time to peak concentration (Tmax) for risedronate 35 mg gastro-resistant tablet is ~3 hours when administered in the morning 4 hours prior to a meal. The relative bioavailability of the risedronate 35 mg gastro-resistant tablets administered after a high-fat breakfast was 2 to 4-fold higher than the corresponding immediate-release formulation administered 30 minutes prior to a high-fat breakfast.

Food Effect
The presence of food did not appreciably affect the bioavailability of the gastro-resistant tablets.

Distribution
The mean steady state volume of distribution is 6.3 L/kg in humans. Plasma protein binding is about 24%.

Biotransformation
There is no evidence of systemic metabolism of risedronate sodium.

Elimination
Approximately half of the absorbed dose is excreted in urine within 24 hours, and 85% of an intravenous dose is recovered in the urine after 28 days. Mean renal clearance is 105 ml/min and mean total clearance is 122 ml/min, with the difference probably attributed to clearance due to adsorption to bone. The renal clearance is not concentration dependent, and there is a linear relationship between renal clearance and creatinine clearance. Unabsorbed risedronate sodium is eliminated unchanged in faeces. After oral administration the concentration-time profile shows three elimination phases with a terminal half-life of 480 hours.

Special Populations

Elderly
No dosage adjustment is necessary.

Acetyl salicylic acid/NSAID users
Among regular acetyl salicylic acid or NSAID users (3 or more days per week) the incidence of upper gastrointestinal adverse events in risedronate sodium treated patients was similar to that in control patients (see section 4.5).

5.3 Preclinical safety data

Repeat-dose toxicity
In toxicological studies in rat and dog, dose dependent liver toxic effects of risedronate sodium were seen, primarily as enzyme increases with histological changes in rat. The clinical relevance of these observations is unknown. Testicular toxicity occurred in rat and dog at exposures considered in excess of the human therapeutic exposure. Dose related incidences of upper airway irritation were frequently noted in rodents. Similar effects have been seen with other bisphosphonates. Lower respiratory tract effects were also seen in longer term studies in rodents, although the clinical significance of these findings is unclear.

The results of a 13-week repeat-dose toxicity study in dogs comparing the gastro-resistant risedronate formulation with conventional risedronate showed a similar toxicity profile for the two formulations.

Reproductive toxicity
A fertility study in male and female rats showed no adverse effects at oral doses up to 16 mg/kg/day, corresponding to systemic exposure (serum AUC 0-24h) about 30 times higher than that in humans dosed at 30 mg/day. At higher dose levels, systemic toxicity, testicular atrophy and reduced fertility were seen in male rats, but these effects are unlikely to have clinical relevance.

In reproduction toxicity studies at exposures close to clinical exposure ossification changes were seen in sternum and/or skull of foetuses from treated rats and hypocalcemia and mortality in pregnant females allowed to deliver. There was no evidence of teratogenesis at 3.2 mg/kg/day in rat and 10 mg/kg/day in rabbit, although data are only available on a small number of rabbits. Maternal toxicity prevented testing of higher doses.

Studies on genotoxicity and carcinogenesis did not show any particular risks for humans.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Microcrystalline cellulose (E460)
Silica, colloidal anhydrous
Disodium edetate
Sodium starch glycolate
Stearic acid
Magnesium stearate (E470b)

Enteric coating:
Methacrylic acid – ethyl acrylate copolymer (1:1)
Triethyl citrate (E1505)
Talc (E553b)
Iron oxide yellow E172
Simeticone
Polysorbate 80 (E433)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Clear PVC/aluminium foil blisters in a cardboard carton.
Blisters in packs containing 1, 2, 4, 10, 12, or 16 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Theramex Ireland Limited
3rd Floor, Kilmore House
Park Lane, Spencer Dock
Dublin 1
D01 YE64
Ierland

8. MARKETING AUTHORISATION NUMBER(S)

Actonel Wekelijks MSR 35 mg: RVG 118208

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Datum van eerste verlening van de vergunning: 7 februari 2017
Datum van laatste verlenging: 12 oktober 2021

10. DATE OF REVISION OF THE TEXT

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