1. NAME OF THE MEDICINAL PRODUCT

Wainua
solution for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pre-filled pen contains 45 mg eplontersen (as eplontersen sodium) in 0.8 ml of solution.

Each ml contains 56 mg eplontersen (as eplontersen sodium).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection).
Clear, colourless to yellow solution (pH of approximately 7.4 and osmolality 250 to 330 mOsm/kg).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Wainua is indicated for the treatment of hereditary transthyretin-mediated amyloidosis (ATTRv amyloidosis) in adults patients with Stage 1 and 2 polyneuropathy.

4.2 Posology and method of administration

Treatment should be prescribed and supervised by a physician experienced in the treatment of patients with hereditary transthyretin-mediated amyloidosis.

Posology

The recommended dose of eplontersen is 45 mg administered monthly.

Supplementation at the recommended daily allowance of vitamin A is advised for patients taking WAINUA. (see section 4.4).

Treatment should be initiated as early as possible after symptom onset (see section 5.1).

Missed dose

If a dose of Wainua is missed, then the next dose should be administered as soon as possible. Dosing should be resumed at monthly intervals from the date of the last dose; a double dose should not be administered.

Special populations

Elderly

No dose adjustment is required in elderly patients (≥ 65 years of age) (see section 5.2).

Renal impairment

No dose adjustment is necessary in patients with mild to moderate renal impairment (estimated glomerular filtration rate [eGFR] ≥ 45 to < 90 mL/min/1.73 m^2). Wainua has not been studied in patients with eGFR < 45 mL/min/1.73 m^2 or end-stage renal disease (see section 5.2) and should only be used in these patients if the anticipated clinical benefit outweighs the potential risk.

Hepatic impairment

No dose adjustment is necessary in patients with mild hepatic impairment. Eplontersen has not been studied in patients with moderate or severe hepatic impairment and should only be used in these patients if the anticipated clinical benefit outweighs the potential risk (see section 5.2).

Patients undergoing liver transplant

The safety and efficacy of Wainua have not been evaluated in patients undergoing liver transplant. No data are available.

Paediatric population

The safety and efficacy of Wainua in children and adolescents below 18 years of age have not been established. No data are available (see section 5.1).

Method of administration

Wainua is for subcutaneous use. Wainua is a pre-filled pen for single-use only.

The first injection administered by the patient or caregiver should be performed under the guidance of an appropriately qualified health care professional. Patients and/or caregivers should be trained in the subcutaneous administration of Wainua.

The pre-filled pen should be removed from refrigerated storage at least 30 minutes before use and allowed to reach room temperature prior to injection. Other warming methods should not be used.

Inspect solution visually before use. The solution should appear colourless to yellow. Do not use if cloudiness, particulate matter, or discolouration is observed prior to administration.

If self-administered, Wainua should be injected in the abdomen or upper thigh region. If a caregiver administers the injection, the back of the upper arm can also be used.

Wainua should not be injected into skin that is bruised, tender, red, or hard, into scars or damaged skin, the area around the navel should be avoided.

Comprehensive instructions for administration using the pre-filled pen are provided in the 'Instructions for Use'.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Vitamin A deficiency

Based on the mechanism of action, Wainua is expected to reduce serum vitamin A (retinol) below normal levels (see section 5.1). Serum vitamin A levels below the lower limit of normal should be corrected and any ocular symptoms or signs related to vitamin A deficiency should be evaluated prior to initiation of treatment with Wainua.

Supplementation at the recommended daily allowance of vitamin A is advised for patients taking WAINUA to reduce the potential risk of ocular symptoms due to vitamin A deficiency. Referral for ophthalmological assessment is recommended if patients develop ocular symptoms consistent with vitamin A deficiency, including reduced night vision or night blindness, persistent dry eyes, eye inflammation, corneal inflammation or ulceration, corneal thickening or corneal perforation.

During the first 60 days of pregnancy, both too high and too low vitamin A levels may be associated with an increased risk of foetal malformation. Therefore, pregnancy should be excluded before treatment initiation and women of childbearing potential should practise effective contraception (see section 4.6). If a woman intends to become pregnant, Wainua and vitamin A supplementation should be discontinued, and serum vitamin A levels should be monitored and have returned to normal before conception is attempted.

In the event of an unplanned pregnancy, Wainua should be discontinued. Due to the long half-life of eplontersen (see section 5.2), a vitamin A deficit may even develop after cessation of treatment. No recommendation can be given whether to continue or discontinue vitamin A supplementation during the first trimester of an unplanned pregnancy. If vitamin A supplementation is continued, it should be given at the recommended daily allowance of vitamin A

It is not known whether vitamin A supplementation in pregnancy will be sufficient to prevent vitamin A deficiency if the pregnant female continues to receive Wainua. However, increasing vitamin A supplementation to above 3,000 IU per day during pregnancy is unlikely to correct serum retinol levels due to the mechanism of action of eplontersen and may be harmful to the mother and foetus.

Excipients with known effect

This medicinal product contains less than 1 mmol sodium (23 mg) per dose of 0.8 ml, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

In vitro studies indicate that eplontersen is not a substrate or inhibitor of transporters, does not interact with highly plasma protein bound medicinal products, and is not an inhibitor or inducer of CYP enzymes.

4.6 Fertility, pregnancy and lactation

Women of child-bearing potential

Wainua will reduce the plasma levels of vitamin A, which is crucial for normal foetal development. It is not known whether vitamin A supplementation will be sufficient to reduce the risk to the foetus (see section 4.4). For this reason, pregnancy should be excluded before initiation of Wainua therapy and women of child-bearing potential should practice effective contraception.

If a woman intends to become pregnant, Wainua and vitamin A supplementation should be discontinued, and serum vitamin A levels should be monitored and have returned to normal before conception is attempted (see section 4.4). Serum vitamin A levels may remain reduced for more than 15 weeks after the last dose of treatment.

Pregnancy

There are no data on the use of eplontersen in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3). Due to the potential teratogenic risk arising from unbalanced vitamin A levels, Wainua should not be used during pregnancy and in women of

childbearing potential not using contraception. In case of pregnancy, close monitoring of the foetus and vitamin A status should be carried out, especially during the first trimester (see section 4.4).

Breast-feeding

It is unknown whether eplontersen or its metabolites are excreted in human milk. A risk to the breastfed child cannot be excluded.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Wainua therapy, taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Fertility

There is no information available on the effects of eplontersen on human fertility. No impact on male or female fertility was detected in animal studies (see section 5.3).

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Summary of the safety profile

The most frequent adverse reactions during treatment with eplontersen were vitamin A decreased (97% of patients) and vomiting (9% of patients).

Tabulated list of adverse reactions

The safety data reflects exposure to Wainua in 144 patients with polyneuropathy caused by ATTRv (ATTRv-PN) randomised to eplontersen and who received at least one dose of eplontersen. 130 patients completed treatment with eplontersen through Week 85. The mean duration of treatment was 541 days (range: 57 to 582 days).

Adverse reactions are organised by MedDRA System Organ Class (SOC). Within each SOC, preferred terms are arranged by decreasing frequency and then by decreasing seriousness. Frequencies of occurrence of adverse reactions are defined as: 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) and not known (cannot be estimated from available data).

Table 1: Adverse reactions reported for Wainua

System organ class	Adverse reaction	Frequency
Gastrointestinal disorders	Vomiting	Common
General disorders and administration site conditions	Injection site erythema	Common
	Injection site pain	Common
	Injection site pruritus	Common
Investigations	Vitamin A decreased	Very common*
Renal and urinary disorders	Proteinuria	Common

* Based on laboratory findings of vitamin A below the lower limit of normal during the study.

Three serious adverse reactions of atrioventricular (AV) heart block (2%) occurred in WAINUA-treated patients, including one case of complete AV block.

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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: https://sideeffects.health.gov.il

4.9 Overdose

There is no specific treatment for an overdose with eplontersen. In the event of an overdose, supportive medical care should be provided.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other nervous system drugs, ATC code: N07XX21.

Mechanism of action

Eplontersen is a N-acetylgalactosamine (GalNAc)-conjugated 2′-*O*-2-methoxyethyl-modified chimeric gapmer antisense oligonucleotide (ASO) with a mixed backbone of phosphorothioate and phosphate diester internucleotide linkages. The GalNAc conjugate enables targeted delivery of the ASO to hepatocytes. The selective binding of eplontersen to the transthyretin (TTR) messenger RNA (mRNA) within the hepatocytes causes the degradation of both mutant and wild type (normal) TTR mRNA. This prevents the synthesis of TTR protein in the liver, resulting in significant reductions in the levels of mutated and wild type TTR protein secreted by the liver into the circulation.

Pharmacodynamic effects

In the clinical study in patients with ATTRv-PN receiving eplontersen, a decrease in serum TTR concentrations was observed at the first assessment (Week 5) and TTR concentrations continued to decrease through Week 35. A sustained reduction of TTR concentration was observed throughout the duration of the treatment (85 weeks). Mean (SD) for serum TTR percent reduction from baseline was 82.1% (11.7) at Week 35, 83.0% (10.4) at Week 65 and 81.8% (13.4) at Week 85 when treated with eplontersen. Similar reduction from baseline in serum TTR concentrations was observed regardless of sex, race, age, region, body weight, cardiomyopathy status, previous treatment, Val30Met mutation status, disease stage, and familial amyloid cardiomyopathy clinical diagnosis at baseline.

TTR is a carrier protein for retinol binding protein 4, which is the principal carrier of vitamin A (retinol). Therefore, a reduction in plasma TTR is expected to result in the reduction of plasma retinol levels to below the lower limit of normal.

Clinical efficacy and safety

The efficacy and safety of eplontersen was evaluated in a randomised, multicentre, open-label, trial (NEURO-TTRansform) that included a total of 168 adult patients with ATTRv-PN. Patients were randomised in a 6:1 ratio to receive subcutaneous injection of eplontersen 45 mg every 4 weeks (N=144) or inotersen 284 mg weekly (N=24) as a reference group. Of the 144 patients randomised to eplontersen, 140 (97.2 %) patients completed treatment through Week 35, 135 (93.8%) completed treatment through Week 65.

An external placebo control consisted of a placebo cohort of patients from the inotersen pivotal study (NEURO-TTR): randomised, double-blind, placebo-controlled, multicentre clinical trial in adult

patients with ATTRv-PN. That cohort received subcutaneous injections of placebo once weekly. Both studies employed identical eligibility criteria.

The characteristics of the eplontersen and external placebo groups were generally similar, and potential imbalances in key baseline characteristics (Val30Met mutation status, disease stage, and previous treatment) were accounted for in the prespecified statistical analysis.

Of the 144 patients randomised to eplontersen, the median patient age at baseline was 51.5 years (range 24 to 82), 30.6% were ≥ 65 years old, and 69.4% of patients were male. Twenty (20) different TTR variants were represented: Val30Met (59.0%), Phe64Leu (3.5%), Leu58His (2.8%), Thr60Ala (2.8%), Val122Ile (2.8%), Ser77Tyr (2.1%), Ser50Arg (1.4%), Thr49Ala (0.7%), Glu89Gln (0.7%), and Other (24.3%, includes Ala97Ser (15%)). At baseline, 79.9% of patients had stage 1 disease (unimpaired ambulation; mild sensory, motor, and autonomic neuropathy in the lower limbs), 20.1% had stage 2 disease (assistance with ambulation required; moderate impairment of the lower limbs, upper limbs, and trunk), and there were no patients with stage 3 disease. 69.4% of patients had prior treatment with either tafamidis or diflunisal.

At Week 66 analysis, the co-primary endpoints included percent change from baseline in serum TTR concentration at Week 65, change from baseline in mNIS+7 score and change from baseline in Norfolk QoL-DN total score at Week 66, all when eplontersen was compared to placebo.

The mNIS+7 is an objective assessment of neuropathy and comprises the NIS and Modified +7 composite scores. In the version of the mNIS+7 used in the trial, the NIS objectively measures deficits in cranial nerve function, muscle strength, reflexes, and sensations, and the Modified +7 assesses heart rate response to deep breathing, quantitative sensory testing (touch-pressure and heat-pain), and peripheral nerve electrophysiology. The validated version of the mNIS+7 score used in the trial had a range of -22.3 to 346.3 points, with higher scores representing a greater severity of disease.

The Norfolk QoL-DN scale is a patient-reported assessment that evaluates the subjective experience of neuropathy in the following domains: physical functioning/large fibre neuropathy, activities of daily living, symptoms, small fibre neuropathy, and autonomic neuropathy. The version of the Norfolk QoL-DN that was used in the trial had a range from -4 to 136 points, with higher scores representing greater impairment.

Other secondary endpoints were formally tested hierarchically at Week 66 analysis and included change from baseline in neuropathy symptoms and change score, in the physical component summary score of short form 36-item health survey (version 2), in polyneuropathy disability score and in nutritional status (modified body mass index).

Treatment with eplontersen in NEURO-TTRansform study demonstrated statistically significant improvements in all endpoints at both Week 35 and Week 66 (see Table 2) compared to the external placebo group (all $p < 0.0001$).

Table 2: Summary of clinical efficacy results from NEURO-TTRansform Study

Analysis/ Endpoint	Mean (SD)		LSM Change/Percent Change from Baseline, (Estimate SE) [95% CI]		Eplontersen-Placebo* Difference in LSM [95% CI]	p-value
	Placebo*	Eplontersen	Placebo*	Eplontersen		
Safety analysis set	**N = 60**	**N = 144**	**N = 60**	**N = 144**		
Serum TTR, g/L [1]						
Baseline	0.15 (0.04)	0.23 (0.08)				
Week 35			-14.7% (2.2) [-18.96, -10.44]	-81.3% (1.8) [-84.83, -77.71]	-66.6% [-71.61, -61.53]	p < 0.0001
Week 65	0.14 (0.04)	0.04 (0.02)	-10.2% (2.2) [-14.43, -5.87]	-80.2% (1.8) [-83.75, -76.72]	-70.1% [-75.02, -65.15]	p < 0.0001
mNIS+7 composite score [1]						
Baseline	74.1 (39.0)	79.8 (42.3)				
Week 35			9.9 (1.9) [6.29, 13.56]	1.1 (1.8) [-2.47, 4.77]	-8.8 [-13.21, -4.34]	p = 0.0001
Week 66	96.6 (50.2)	79.7 (44.9)	26.3 (2.6) [21.32, 31.38]	3.2 (2.5) [-1.75, 8.18]	-23.1 [-29.26, -17.01]	p < 0.0001
Norfolk QOL-DN total score [1]						
Baseline	48.6 (27.0)	43.3 (26.2)				
Week 35			8.4 (2.1) [4.30, 12.58]	-2.8 (2.1) [-6.87, 1.19]	-11.3 [-16.26, -6.30]	p < 0.0001
Week 66	58.9 (32.0)	35.6 (26.3)	13.7 (2.4) [8.92, 18.50]	-5.5 (2.4) [-10.19, -0.91]	-19.3 [-24.99, -13.53]	p < 0.0001
Full analysis set	**N = 59**	**N = 141**	**N = 59**	**N = 141**		
Neuropathy symptom and change score, Week 66 [2]			8.2 [6.24, 10.12]	-0.0 [-1.92, 1.86]	-8.2 [-10.65, -5.76]	p < 0.0001
Physical component score of short form 36 item health survey, Week 65 [2]			-4.46 [-6.139, -2.770]	0.85 [-0.711, 2.412]	5.31 [3.195, 7.416]	p < 0.0001
Modified body mass index, Week 65 [2]			-90.8 [-112.84, -68.69]	-8.1 [-28.55, 12.42]	82.7 [54.64, 110.76]	p < 0.0001

***** External placebo group from another randomised controlled trial (NEURO-TTR).

[1] Based on an ANCOVA with a reference-based multiple imputation approach for missing data, adjusted by propensity score weights with fixed categorical effects for treatment, time, treatment-by-time interaction, disease stage, Val30M mutation, previous treatment, fixed covariates for the baseline value and the baseline-by-time interaction. In the reference-based imputation approach, missing data in the placebo group and missing data in eplontersen treatment group while on treatment, is imputed under a within treatment arm missing at random assumption. For a patient in eplontersen treatment group who discontinued, missing data were imputed based on the placebo group.

[2] Based on a MMRM adjusted by propensity score weights with fixed categorical effects for treatment, time, treatment-by-time interaction, disease stage, Val30M mutation, previous treatment, fixed covariates for the baseline value and the baseline-by-time interaction.

ANCOVA = analysis of covariance; CI = confidence interval; LSM = least squares mean; MMRM = mixed effects model with repeated measures; mNIS+7 = modified neuropathy impairment score +7; N = number of

participants in group; Norfolk QoL-DN = Norfolk quality of life – diabetic neuropathy questionnaire; SD = standard deviation; SE = standard error; TTR = transthyretin.

The secondary endpoint of change from baseline in PND score at Week 65 was statistically significant in favor of eplontersen (p= 0.02). More patients in the eplontersen group experienced improvement from baseline in PND score than in the external placebo group (5.7% vs 3.4%) and fewer patients in the eplontersen group experienced a worsening from baseline than in the external placebo group (12.8% vs. 22.0%).

Patients receiving eplontersen experienced similar improvements relative to placebo in the reduction of serum TTR concentration, mNIS+7 composite and Norfolk QoL-DN total scores across all subgroups including age, sex, race, region, Val30Met mutation status, cardiomyopathy status, familial amyloid cardiomyopathy clinical diagnosis at baseline and disease stage.

Through the end of treatment with eplontersen at Week 85, reduction of TTR concentration and the observed effect in mNIS+7 composite score were sustained, and the mean Norfolk QoL-DN total score remained stable.

Immunogenicity

In the clinical study in patients with ATTRv-PN, after an 84-week treatment period (median treatment duration of 561 days (80 weeks), range: 57 to 582 days), 58 patients (40.3%) developed treatment-emergent anti-drug antibodies (ADAs). ADA to eplontersen tended to be persistent with a late onset (median onset 223 days) and low titer (median peak titer 200). In the patients who tested positive for anti-eplontersen antibodies, there was no clinically meaningful impact on the efficacy, safety, pharmacokinetics, or pharmacodynamics of eplontersen.

5.2 Pharmacokinetic properties

The pharmacokinetic properties of Wainua were evaluated by measuring plasma concentrations of eplontersen following subcutaneous administration of single and multiple doses (once every 4 weeks) in healthy subjects and multiple doses (once every 4 weeks) in patients with ATTRv-PN.

Absorption

Following subcutaneous administration, eplontersen is absorbed rapidly into the systemic circulation with the time to maximum plasma concentrations of approximately 2 hours, based on population estimates. Population estimates of steady state maximum concentrations (C_{max}), trough concentrations (C_{trough}), and area under the curve (AUC_{τ}) were 0.218 µg/ml, 0.0002 µg/ml, and 1.95 µg h/ml, respectively, following 45 mg once every 4 weeks dosing in patients with ATTRv-PN. No accumulation of eplontersen C_{max} and AUC was observed in plasma after repeated dosing (once every 4 weeks). Accumulation was observed in C_{trough}, and steady-state was reached after approximately 17 weeks.

Distribution

Eplontersen is highly bound to human plasma proteins (> 98%). The population estimates for the apparent central volume of distribution is 12.9 l and the apparent peripheral volume of distribution is 11 100 l. Eplontersen is expected to distribute primarily to the liver and kidney cortex after subcutaneous dosing.

Biotransformation

Eplontersen is metabolised by endo- and exonucleases into short oligonucleotide fragments of varying sizes primarily within the liver. There were no major circulating metabolites in humans. Oligonucleotide therapeutics, including eplontersen, are not metabolised by CYP enzymes.

Elimination

Eplontersen is primarily eliminated by metabolism followed by renal excretion of the short oligonucleotide metabolites. The mean fraction of unchanged ASO eliminated in urine was less than 1% of the administered dose within 24 hours. The terminal elimination half-life is approximately 3 weeks based on population estimates.

Linearity/non-linearity

Eplontersen C_{max} and AUC showed a slightly greater than dose-proportional increase following single subcutaneous doses ranging from 45 to 120 mg (i.e. 1 to 2.7 times the recommended dose) in healthy volunteers.

Special populations

Based on the population pharmacokinetic, body weight, sex, race, and Val30Met mutation status are unlikely to have a clinically meaningful effect on eplontersen exposure. Definitive assessments were limited in some cases as covariates were limited by the overall low numbers.

Elderly population

No overall differences in pharmacokinetics were observed between adult and elderly (≥ 65 years of age) patients.

Renal impairment

No formal clinical studies have been conducted to investigate the effect of renal impairment on eplontersen pharmacokinetics. A population pharmacokinetic and pharmacodynamic analysis showed no clinically meaningful differences in the pharmacokinetics or pharmacodynamics of eplontersen based on mild and moderate renal impairment (eGFR ≥ 45 to < 90 ml/min). Eplontersen has not been studied in patients with eGFR < 45 ml/min /1.73 m^2 or in patients with end-stage renal disease.

Hepatic impairment

No formal clinical studies have been conducted to investigate the effect of hepatic impairment on eplontersen. A population pharmacokinetic and pharmacodynamic analysis showed no clinically meaningful differences in the pharmacokinetics or pharmacodynamics of eplontersen based on mild hepatic impairment (total bilirubin ≤ 1 × ULN and AST > 1 × ULN, or total bilirubin > 1.0 to 1.5 × ULN and any AST). Eplontersen has not been studied in patients with moderate hepatic impairment (total bilirubin > 1.5 to 3 × ULN and any AST) or severe hepatic impairment (total bilirubin > 3 to 10 × ULN and any AST) or in patients with prior liver transplant.

5.3 Preclinical safety data

General toxicology

Repeated administration of eplontersen at 24 mg/kg/week for 13 weeks or 25 mg/kg/month for 9 months in monkeys reduced TTR protein in plasma by 69% and 52%, respectively. There were no toxicologically relevant findings related to this pharmacologic inhibition of TTR expression.

Most of the findings observed after repeated subcutaneous dosing for up to 6 months in mice and 9 months in monkeys were non-adverse and related to the uptake and accumulation of eplontersen by various cell types in multiple organs of all tested animal species including monocytes/macrophages,

kidney proximal tubular epithelia, Kupffer cells of the liver, and histiocytic cell infiltrates in lymph nodes and injection sites.

In a single monkey in the 13 week toxicity study, severely decreased platelet counts associated with spontaneous haemorrhage, presented as haematoma and petechiae, were observed at the highest dose tested (24 mg/kg/week). Similar findings were not observed at the NOAEL of 6 mg/kg/week in monkeys, which corresponds to more than 70-fold the human AUC at the recommended therapeutic eplontersen dose.

Genotoxicity/Carcinogenicity

Eplontersen did not exhibit genotoxic potential *in vitro* and *in vivo* and was not carcinogenic in ras.H2 transgenic mice.

Reproductive toxicity

Eplontersen had no effects on fertility or embryo-foetal development in mice up to 38-fold (based on human equivalent dose) to the recommended human monthly dose of 45 mg. Eplontersen is not pharmacologically active in mice. Consequently, only effects related to the chemistry of eplontersen could be captured in this study. However, no effect on fertility or embryo-foetal development was noted with a mouse-specific analogue of eplontersen in mice, which was associated with > 90% inhibition of TTR mRNA expression.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injection
Sodium chloride
Disodium hydrogen phosphate anhydrous
Sodium dihydrogen phosphate dihydrate
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

If necessary, Wainua may be stored outside the refrigerator at a

temperature below 30°C for up to 6 weeks in the original package.

Dispose of unrefrigerated Wainua if it is not used within 6 weeks.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C). Do not freeze.

Store in the original package in order to protect from light.

6.5 Nature and contents of container

0.8 ml sterile solution for injection in a single-use, type I glass syringe with a staked 27-gauge ½ inch (12.7 mm) stainless steel needle, rigid needle shield, and siliconised chlorobutyl elastomer stopper in a pre-filled pen.

Pack size of one single-use pre-filled pen.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. REGISTRATION NUMER

38025

8. MANUFACTURER

AstraZeneca AB
Södertälje
Sweden

9. LICENSE HOLDER AND IMPORTER

Astrazeneca (Israel) Ltd.,
1 Atirei Yeda St.,
Kfar Saba 4464301.

Approved in Septmeber 2025 according to MoH guideline.