ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Catiolanze 50 micrograms/mL eye drops, emulsion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 mL eye drops emulsion contains 50 micrograms of latanoprost.
A single-dose container of 0.3 mL eye drops emulsion contains 15 micrograms of latanoprost.
One drop contains approximately 1.65 micrograms latanoprost.

Excipient with known effect:

One ml of emulsion contains 0.05 mg cetalkonium chloride (see section 4.4)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops, emulsion
The emulsion is a white liquid with a pH of 4.0-5.5 and an osmolality of 250-310 mOsm/kg.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Catiolanze is indicated for the reduction of elevated intraocular pressure (IOP) in adult patients with open angle glaucoma or ocular hypertension.
Catiolanze is indicated for the reduction of elevated IOP in children from 4 years of age and adolescents with elevated IOP and paediatric glaucoma.

4.2 Posology and method of administration

Posology

Catiolanze may be used in paediatric patients from 4 years old onwards at the same posology as in adults.

Recommended therapy is one eye drop in the affected eye(s) once daily. Optimal effect is obtained if Catiolanze is administered in the evening.

The dose of Catiolanze should not exceed once daily since it has been shown that more frequent administration decreases the IOP lowering effect.

Missed dose
If one dose is missed, treatment should continue with the next dose as normal.

Paediatric population
The safety of Catiolanze in children aged less than 4 years old has not been established as no data for this formulation (emulsion) are available. Currently available safety data for the active substance latanoprost are described in sections 4.8 and 5.1.

Method of administration

Ocular use.
For single use only.

A single-dose container contains enough eye drops liquid to treat both eyes.

As with any eye drops, it is recommended that the lachrymal sac be compressed at the medial canthus (punctal occlusion) for one minute, in order to reduce possible systemic absorption. This should be performed immediately following the instillation of each drop.

Contact lenses should be removed before instillation of the eye drops and may be reinserted after 15 minutes.

If more than one topical ophthalmic medicinal product is being used, the medicinal products must be administered at least 5 minutes apart. Catiolanze should be administered last (see section 4.5).

This medicinal product is a sterile white liquid that does not contain a preservative. The liquid from one individual single-dose container is to be used immediately after opening for administration to the affected eye(s). Since sterility cannot be maintained after the individual single-dose container is opened, any remaining contents must be discarded immediately after administration.
Patients should be instructed:
- to avoid contact between the dropper tip and the eye or eyelids
- to use the eye drops emulsion immediately after first opening the single-dose container and to discard the single-dose after use.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Change in eye colour

Catiolanze may gradually change eye colour by increasing the amount of brown pigment in the iris. Before treatment is instituted, patients should be informed of the possibility of a permanent change in eye colour. Unilateral treatment can result in permanent heterochromia.

This change in eye colour has predominantly been seen with latanoprost in patients with mixed coloured irides, i.e. blue-brown, grey-brown, yellow-brown and green-brown. In studies with latanoprost, the onset of the change is usually within the first 8 months of treatment, rarely during the second or third year, and has not been seen after the fourth year of treatment. The rate of progression of iris pigmentation decreases with time and is stable for five years. The effect of increased pigmentation beyond five years has not been evaluated. In an open 5-year latanoprost safety study, 33% of patients developed iris pigmentation (see section 4.8). The iris colour change is slight in the majority of cases and often not observed clinically. The incidence in patients with mixed colour irides ranged from 7 to 85%, with yellow-brown irides having the highest incidence. In patients with

homogeneously blue eyes, no change has been observed and in patients with homogeneously grey, green or brown eyes, the change has only rarely been seen.

The colour change with latanoprost treatment is due to increased melanin content in the stromal melanocytes of the iris and not to an increase in number of melanocytes. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery in affected eyes, but the entire iris or parts of it may become more brownish. No further increase in brown iris pigment has been observed after discontinuation of latanoprost treatment. It has not been associated with any symptom or pathological changes in clinical trials to date.

Neither naevi nor freckles of the iris have been affected by latanoprost treatment. Accumulation of pigment in the trabecular meshwork or elsewhere in the anterior chamber has not been observed with latanoprost in clinical trials. Based on 5 years clinical experience with latanoprost, increased iris pigmentation has not been shown to have any negative clinical sequelae and Catiolanze can be continued if iris pigmentation ensues. However, patients should be monitored regularly and if the clinical situation warrants, Catiolanze treatment may be discontinued.

Chronic angle closure glaucoma

There is limited experience of latanoprost in chronic angle closure glaucoma, open angle glaucoma of pseudophakic patients and in pigmentary glaucoma. There is no experience of latanoprost in inflammatory and neovascular glaucoma or inflammatory ocular conditions. Latanoprost has no or little effect on the pupil, but there is no experience in acute attacks of closed angle glaucoma. Therefore, it is recommended that Catiolanze should be used with caution in these conditions until more experience is obtained.

Cataract surgery

There are limited study data on the use of latanoprost during the peri-operative period of cataract surgery. Catiolanze should be used with caution in these patients.

History of herpetic keratitis, aphakic, and pseudophakic patients

Catiolanze should be used with caution in patients with a history of herpetic keratitis, and should be avoided in cases of active herpes simplex keratitis and in patients with a history of recurrent herpetic keratitis specifically associated with prostaglandin analogues.

Macular oedema and cystoid macular oedema

Reports of macular oedema have occurred with latanoprost (see section 4.8) mainly in aphakic patients, in pseudophakic patients with torn posterior lens capsule or anterior chamber lenses, or in patients with known risk factors for cystoid macular oedema (such as diabetic retinopathy and retinal vein occlusion). Catiolanze should be used with caution in aphakic patients, in pseudophakic patients with torn posterior lens capsule or anterior chamber lenses, or in patients with known risk factors for cystoid macular oedema.

Iritis/ uveitis

Catiolanze should be used with caution in patients with known predisposing risk factors for iritis/uveitis.

Patients with asthma

There is limited experience with latanoprost in patients with asthma, but some cases of exacerbation of asthma and/or dyspnoea were reported with latanoprost in post marketing experience. Asthmatic patients should therefore be treated with caution until there is sufficient experience (see also section 4.8).

Periorbital skin discolouration

Periorbital skin discolouration has been observed with latanoprost, the majority of reports being in Japanese patients. Experience to date shows that periorbital skin discolouration is not permanent and in some cases has reversed while continuing treatment with latanoprost.

Eyelash changes

Latanoprost may gradually change eyelashes and vellus hair in the treated eye and surrounding areas; these changes include increased length, thickness, pigmentation, number of lashes or hairs and misdirected growth of eyelashes. Eyelash changes are reversible upon discontinuation of latanoprost treatment.

Other

Concomitant use of latanoprost with prostaglandins, prostaglandin analogues or prostaglandin derivatives is not recommended (see section 4.5).

Excipient with known effect

Catiolanze contains cetalkonium chloride which may cause eye irritation.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed in adults.

There have been reports of paradoxical elevations in IOP following the concomitant ophthalmic administration of two prostaglandin analogues. Therefore, the use of two or more prostaglandins, prostaglandin analogues or prostaglandin derivatives is not recommended.

Paediatric population

No interaction studies have been performed in the paediatric population.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of this medicinal product for use in human pregnancy has not been established. It has potential hazardous pharmacological effects with respect to the course of pregnancy, to the unborn or the neonate. Therefore, Catiolanze should not be used during pregnancy.

Breast-feeding

Latanoprost and its metabolites may pass into breast milk. Catiolanze should therefore not be used in breast-feeding women or breast feeding should be stopped.

Fertility

Latanoprost has not been found to have any effect on male or female fertility in animal studies (see section 5.3).

4.7 Effects on ability to drive and use machines

Catiolanze has minor influence on the ability to drive and use machines. In common with other eye preparations, instillation of Catiolanze may cause transient blurring of vision. Until this has resolved, patients should not drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

The majority of adverse reactions relate to the ocular system. In an open 5-year safety study with preserved latanoprost eye drops, solution, 33% of patients developed iris pigmentation (see section 4.4). Other ocular adverse reactions are generally transient and occur on dose administration.

Safety data specific for Catiolanze are available from 330 patients. The most common adverse reactions were ocular hyperaemia (1.6%) and conjunctival hyperaemia (1.0%). There were no serious adverse reactions during the studies specific for Catiolanze.

Long term safety data are available from a Phase 3 study in which 118 patients received Catiolanze at least for 360 days. The long term safety profile did not differ from that observed during the first 3 months of treatment. The most common ocular adverse reactions reported during long term use were ocular and conjunctival hyperaemia (4.4%), abnormal sensation in eye (2.2%) and growth of eyelashes (2.2%).

Tabulated list of adverse reactions

The table below describes adverse reactions for preserved latanoprost eye drops, solution from clinical trials and postmarketing data. Adverse reactions occurring with a different frequency observed in clinical trials with Catiolanze eye drops emulsion product are labelled in the table with ¥.
The adverse reactions are categorised by frequency as follows: 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) and very rare (<1/10 000), not known (frequency cannot be estimated from the available data).

System organ class	**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**
Infections and infestations				Herpetic keratitis*§	
Nervous system disorders			Headache*; dizziness*		

Eye disorders	Iris hyperpigmentation	Mild to moderate conjunctival hyperaemia¥ Eye irritation (burning grittiness, itching, stinging, foreign body sensation and abnormal sensation)¥; Punctate keratitis, mostly without symptoms; eye pain; Photophobia; Conjunctivitis*	Eyelid oedema¥; eyelash and vellus hair changes of the eyelid (increased length, thickness, pigmentation and number of eyelashes)¥; blepharitis¥; dry eye; keratitis*; vision blurred¥; macular oedema including cystoid macular oedema*; uveitis*	Iritis*; corneal oedema*; corneal erosion; periorbital oedema; trichiasis*; distichiasis; iris cyst*§; localised skin reaction on the eyelids; darkening of the palpebral skin of the eyelids; pseudopemphigoid of ocular conjunctiva*§	Periorbital and lid changes resulting in deepening of the eyelid sulcus
Cardiac disorders			Angina; palpitations*		Angina unstable
Respiratory, thoracic and mediastinal disorders			Asthma*; dyspnoea*	Asthma exacerbation	
Gastrointestinal disorders			Nausea*; vomiting*		
Skin and subcutaneous tissue disorder			Rash	Pruritis	
Musculoskeletal and connective tissue disorders			Myalgia*; arthralgia*		
General disorders and administration site conditions			Chest pain*		

*ADR identified post-marketing

§ADR frequency estimated using "The Rule of 3"

¥ADR frequency estimated from studies specific to Catiolanze eye drops emulsion

Description of selected adverse reactions

No information is provided.

Paediatric population

In two short term clinical trials (≤12 weeks), involving 93 (25 and 68) paediatric patients treated with preserved latanoprost eye drops, solution, the safety profile was similar to that in adults and no new adverse events were identified.
The short-term safety profiles in the different paediatric subsets were also similar (see section 4.2 and 5.1). Adverse events seen more frequently with preserved latanoprost in the paediatric population as compared to adults were nasopharyngitis and pyrexia.

Catiolanze was not specifically studied in the paediatric population.

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 the national reporting system listed in Appendix V.

4.9 Overdose

Overdose is unlikely to occur after ocular administration. If overdose occurs, treatment should be symptomatic.

Symptoms

Apart from ocular irritation and conjunctival hyperaemia, no other ocular side effects are known if latanoprost is overdosed via the ocular route.

Treatment

If overdosage with this medicine occurs, treatment should be symptomatic.

Paediatric population

The principles described above apply to the management of overdose in the paediatric population.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals; Antiglaucoma preparations and miotics.
ATC code: S01EE01

Mechanism of action

The active substance latanoprost, a prostaglandin $F_{2\alpha}$ analogue, is a selective prostanoid FP receptor agonist which reduces the IOP by increasing the outflow of aqueous humour.

Studies indicate that the main mechanism of action is increased uveoscleral outflow, although some increase in outflow facility (decrease in outflow resistance) has been reported.

Pharmacodynamic effects

Reduction of the IOP starts about three to four hours after administration and maximum effect is reached after eight to twelve hours. Pressure reduction is maintained for at least 24 hours. Pivotal studies have demonstrated that latanoprost is effective as monotherapy. In addition, clinical trials investigating combination use have been performed. These include studies that show that latanoprost is effective in combination with beta-adrenergic antagonists (timolol). Short-term (1 or 2 weeks) studies suggest that the effect of latanoprost is additive in combination with adrenergic agonists (dipivalyl epinephrine), oral carbonic anhydrase inhibitors (acetazolamide) and at least partly additive with cholinergic agonists (pilocarpine).

Latanoprost has no significant effect on the production of aqueous humour. Latanoprost has not been found to have any effect on the blood-aqueous barrier. Latanoprost has not induced fluorescein leakage in the posterior segment of pseudophakic human eyes during short term treatment. Latanoprost in clinical doses has not been found to have any significant pharmacological effects on the cardiovascular or respiratory system.

Clinical efficacy and safety

The efficacy and safety of Catiolanze has been evaluated in one pivotal Phase 3 study.

A Phase 3, single-masked, randomised, controlled non-inferiority study evaluated the efficacy and safety of Catiolanze eye drops emulsion to benzalkonium chloride preserved latanoprost eye drops solution in 386 adults with open angle glaucoma (OAG) or ocular hypertension (OHT). Primary endpoint was the peak and trough change from baseline in IOP between treatment groups over a 12-week treatment period, with a prespecified non inferiority margin of 1.5 mmHg. Baseline demographic and disease characteristics were similar between groups, with an overall mean age (SD) of 63.1 years (11.16). The majority (61.5%) of participants were women and 96.4% were White. 75.8% (n=291) of patients had a primary OAG and 21.1% (n=81) had OHT; the remaining had a pseudo-exfoliative glaucoma (2.1%) and pigmentary glaucoma (1.0%).

Efficacy
The primary endpoint was met as the non-inferiority of Catiolanze versus the preserved latanoprost 0.005% solution was demonstrated at Week 12 (see table 1). The Least square (LS) mean treatment difference between the Catiolanze and the preserved latanoprost solution groups at the peak and trough timepoints were -0.6 (95% CI -1.2, -0.1) and -0.5 (95% CI -1.0, 0.1), respectively.

Change from baseline in corneal fluorescein staining (CFS) score at Week 12 in subjects with baseline CFS ≥1 on the modified Oxford scale was assessed as key secondary endpoint. Catiolanze demonstrated superiority versus the control in terms of improvement in CFS score at Week 12.

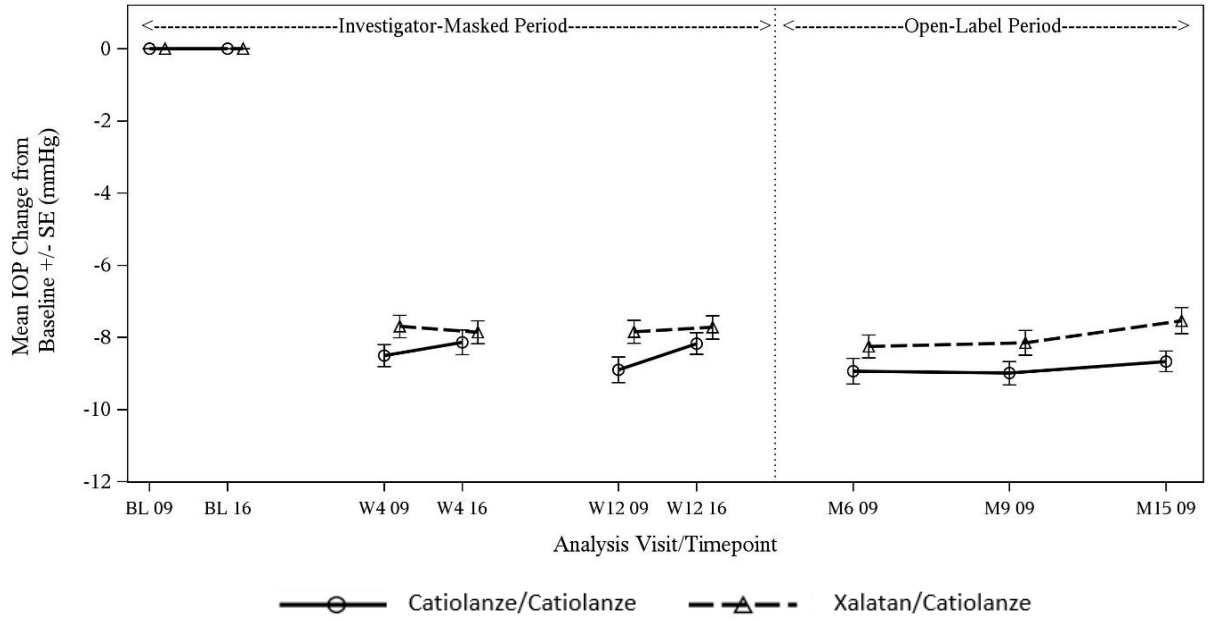
Table 1 Efficacy results: MMRM on observed cases (study Eye, full analysis set)

Endpoint (Week 12 assessment)	Outcome	Catiolanze (N=192)	Preserved latanoprost solution (N=192)
Primary Endpoint IOP Change from baseline	9 am assessment		
	N	188	189
	LS Mean (SE)	-8.8 (0.25)	-8.2 (0.26)
	95% CI of Difference	-1.2, -0.1	
	4 pm assessment		
	N	186	188
	LS Mean (SE)	-8.6 (0.24)	-8.1 (0.25)
	95% CI of Difference	-1.0, 0.1	
Key Secondary Endpoint CFS change from baseline in patients with baseline CFS score ≥ 1	N	80	86
	LS Mean (SE)	-0.71 (0.069)	-0.41 (0.077)
	95% CI of Difference	-0.46, -0.13	
	P-Value	**0.0006**	

CFS, Corneal fluorescein staining; CI, confidence interval; FAS, full analysis set; n, number of patients; LS mean, Least square mean; MMRN, mixed-effects model for repeated measures; SE, standard error.

The analysis is applied to all patients in the FAS with baseline CFS score ≥1 for CFS. Statistical significance (P≤0.05) shown in bold.

Figure Efficacy Results: IOP RAW Mean Change from Baseline with SE by Analysis Visit and Timepoint (Study Eye, Open Label Population)



09/16 = 9am/4pm; BL = Baseline; IOP = Intraocular pressure; M = Month; SE = Standard error; W = Week

Paediatric population

Catiolanze eye drops, emulsion was not specifically studied in the paediatric population.

Efficacy and safety of preserved latanoprost eye drops solution has been established in paediatric patients. The efficacy of latanoprost in paediatric patients ≤18 years of age was demonstrated in a 12-week, double-masked clinical study of latanoprost compared with timolol in 107 patients diagnosed with ocular hypertension and paediatric glaucoma. Neonates were required to be at least 36 weeks gestational age. Patients received either latanoprost 50 mcg/mL once daily or timolol 0.5% (or optionally 0.25% for subjects younger than 3 years old) twice daily. The primary efficacy endpoint was the mean reduction in IOP from baseline at Week 12 of the study. Mean IOP reductions in the latanoprost and timolol groups were similar. In all age groups studied (0 to <3 years, 3 to <12 years and 12 to 18 years of age) the mean IOP reduction at Week 12 in the latanoprost group was similar to that in the timolol group. Nevertheless, efficacy data in the age group 0 to <3 years were based on only 13 patients for latanoprost and no relevant efficacy was shown from the 4 patients representing the age group 0 to <1 year old in the clinical paediatric study. No data are available for preterm infants (less than 36 weeks gestational age).

IOP reductions among subjects in the primary congenital glaucoma (PCG) subgroup were similar between the latanoprost group and the timolol group. The non-PCG (e.g. juvenile open angle glaucoma, aphakic glaucoma) subgroup showed similar results as the PCG subgroup.

The effect on IOP was seen after the first week of treatment (see table 2) and was maintained throughout the 12 week period of study, as in adults.

Table 2: IOP Reduction (mmHg) at Week 12 by Active Treatment Group and Baseline Diagnosis				
	Latanoprost N=53		**Timolol N=54**	
Baseline Mean (SE)	27.3 (0.75)		27.8 (0.84)	
Week 12 Change from Baseline Mean† (SE)	-7.18 (0.81)		-5.72 (0.81)	
p-value vs. timolol	0.2056			
	PCG N=28	**Non-PCG N=25**	**PCG N=26**	**Non-PCG N=28**
Baseline Mean (SE)	26.5 (0.72)	28.2 (1.37)	26.3 (0.95)	29.1 (1.33)
Week 12 Change from Baseline Mean† (SE)	-5.90 (0.98)	-8.66 (1.25)	-5.34 (1.02)	-6.02 (1.18)
p-value vs. timolol	0.6957	0.1317		

SE: standard error.
†Adjusted estimate based on an analysis of covariance (ANCOVA) model

5.2 Pharmacokinetic properties

Latanoprost (mw 432.58) is an isopropyl ester prodrug which per se is inactive, but after hydrolysis to the acid of latanoprost becomes biologically active.

Absorption

The prodrug is well absorbed through the cornea and all latanoprost that enters the aqueous humour is hydrolysed during the passage through the cornea.

Distribution

Studies in man with latanoprost indicate that the peak concentration in the aqueous humour is reached about two hours after topical administration. After topical application in monkeys, latanoprost is distributed primarily in the anterior segment, the conjunctivae and the eyelids. Only minute quantities of the drug reach the posterior segment.

Biotransformation and Elimination

There is practically no metabolism of the acid of latanoprost in the eye. The main metabolism occurs in the liver. The half-life in plasma is 17 minutes in man. The main metabolites, the 1,2-dinor and 1,2,3,4-tetranor metabolites, exert no or only weak biological activity in animal studies and are excreted primarily in the urine.

Paediatric population

An open-label pharmacokinetic study of plasma latanoprost acid concentrations was undertaken in 22 adults and 25 paediatric patients (from birth to <18 years of age) with ocular hypertension and glaucoma. All age groups were treated with latanoprost 50 mcg/mL, one drop daily in each eye for a minimum of 2 weeks. Latanoprost acid systemic exposure was approximately 2-fold higher in 3 to <12 year olds and 6-fold higher in children <3 years old compared with adults, but a wide safety margin for systemic adverse effects was maintained (see section 4.9). Median time to reach peak plasma concentration was 5 minutes post-dose across all age groups. The median plasma elimination half-life was short (<20 minutes), similar for paediatric and adult patients, and resulted in no accumulation of latanoprost acid in the systemic circulation under steady-state conditions.

5.3 Preclinical safety data

The ocular as well as systemic toxicity of latanoprost has been investigated in several animal species. Generally, latanoprost is well tolerated with a safety margin between clinical ocular dose and systemic toxicity of at least 1 000 times. High doses of latanoprost, approximately 100 times the clinical dose/kg body weight, administered intravenously to unanaesthetised monkeys have been shown to increase the respiration rate probably reflecting bronchoconstriction of short duration. In animal studies, latanoprost has not been found to have sensitising properties.

In the eye, no toxic effects have been detected with latanoprost doses of up to 100 micrograms/eye/day in rabbits or monkeys (clinical dose is approximately 1.5 micrograms/eye/day). In monkeys, however, latanoprost has been shown to induce increased pigmentation of the iris. The mechanism of increased pigmentation seems to be stimulation of melanin production in melanocytes of the iris with no proliferative changes observed. The change in iris colour may be permanent.

In chronic ocular toxicity studies with latanoprost, administration of latanoprost 6 micrograms/eye/day has also been shown to induce increased palpebral fissure. This effect is reversible and occurs at doses above the clinical dose level. The effect has not been seen in humans.

In a 28-day ocular toxicity study, administration of Catiolanze two times a day for 28 days did not reveal any significant local or systemic toxic effects in rabbits. Plasma concentrations of latanoprost acid were negligible at 15 minutes after the final instillation of Catiolanze.

Latanoprost was found to be negative in reverse mutation tests in bacteria, gene mutation in mouse lymphoma and mouse micronucleus test. Chromosome aberrations were observed *in vitro* with human lymphocytes. Similar effects were observed with prostaglandin $F_{2\alpha}$, a naturally occurring prostaglandin, and indicates that this is a class effect.

Additional mutagenicity studies on *in vitro/in vivo* unscheduled DNA synthesis in rats were negative and indicate that latanoprost does not have mutagenic potency. Carcinogenicity studies in mice and rats were negative.

Latanoprost has not been found to have any effect on male or female fertility in animal studies. In the embryotoxicity study in rats, no embryotoxicity was observed at intravenous doses (5, 50 and 250 micrograms/kg/day) of latanoprost. However, latanoprost induced embryolethal effects in rabbits at doses of 5 micrograms/kg/day and above.

The dose of 5 micrograms/kg/day (approximately 100 times the clinical dose) caused significant embryofoetal toxicity characterised by increased incidence of late resorption and abortion and by reduced foetal weight.

No teratogenic potential has been detected.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Medium chain triglycerides
Cetalkonium chloride
Polysorbate 80
Glycerol
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years
This medicinal product is a sterile white liquid that does not contain a preservative. Sterility cannot be maintained after the individual single-dose container is opened.
Discard any opened individual single-dose container immediately after use.

6.4 Special precautions for storage

Store below 30°C.

After opening of the aluminium pouch, the single-dose containers should be kept in the pouch in order to avoid evaporation and protect from light.

6.5 Nature and contents of container

Low density polyethylene single-dose containers in a sealed aluminium-polyethylene foil pouch.

Each single-dose container contains 0.3 mL. One pouch contains 5 single-dose containers.

Pack sizes: 30, 60, 90 or 120 single-dose containers.

Not all pack sizes may be marketed.

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. MARKETING AUTHORISATION HOLDER

Santen Oy
Niittyhaankatu 20
33720 Tampere
Finland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1763/001
EU/1/23/1763/002
EU/1/23/1763/003
EU/1/23/1763/004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15 November 2023

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

Santen Oy
Kelloportinkatu 1
33100 Tampere
Finland

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON CONTAINING POUCH(ES) WITH SINGLE-DOSE CONTAINERS

1. NAME OF THE MEDICINAL PRODUCT

Catiolanze 50 micrograms/mL eye drops, emulsion
latanoprost

2. STATEMENT OF ACTIVE SUBSTANCE(S)

A single-dose container of 0.3 mL eye drops emulsion contains 15 micrograms of latanoprost.

3. LIST OF EXCIPIENTS

Medium chain triglycerides, cetalkonium chloride, polysorbate 80, glycerol, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Eye drops, emulsion
30 single-dose containers
60 single-dose containers
90 single-dose containers
120 single-dose containers

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Ocular use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP
Discard any opened individual single-dose container immeadiately after use.

9. SPECIAL STORAGE CONDITIONS

Store below 30°C.
After opening the foil pouch, single-dose containers should be kept in the pouch to avoid evaporation and protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Santen Oy
Niittyhaankatu 20
33720 Tampere
Finland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1763/001
EU/1/23/1763/002
EU/1/23/1763/003
EU/1/23/1763/004

13. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

catiolanze

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

POUCH FOR SINGLE-DOSE CONTAINERS

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Catiolanze 50 micrograms/mL eye drops, emulsion
latanoprost

2. METHOD OF ADMINISTRATION

Ocular use

3. EXPIRY DATE

EXP
Discard any opened individual single-dose container immediately after use.

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

5 × 0.3 mL single-dose container

6. OTHER

After opening the foil pouch, single-dose containers should be kept in the pouch to avoid evaporation and protect from light.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SINGLE-DOSE CONTAINER LABEL

1. NAME OF THE MEDICINAL PRODUCT

Catiolanze 50 mcg/mL
Eye drops
latanoprost
Ocular use

2. NAME OF THE MARKETING AUTHORISATION HOLDER

3. EXPIRY DATE

EXP [engraved]

4. BATCH NUMBER

Lot [engraved]

5. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Catiolanze 50 micrograms/mL eye drops, emulsion
latanoprost

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or the doctor treating your child or pharmacist.
- This medicine has been prescribed for you or for your child only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or the doctor treating your child or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Catiolanze is and what it is used for

Catiolanze contains the active ingredient latanoprost, which belongs to a group of medicines known as prostaglandin analogues. It works by increasing the natural outflow of fluid from inside the eye into the bloodstream.

This medicine is used to treat conditions known as open angle glaucoma (damage to the optic nerve caused by high pressure in the eye) or ocular hypertension (raised pressure in the eye) in adults. Both of these conditions are linked with an increase in the pressure within your eye due to clogging of fluid drainage canals, eventually affecting your eyesight.

Catiolanze is also used to treat increased eye pressure and glaucoma in children from 4 years of age and adolescents.

2. What you need to know before you use Catiolanze

Do not use Catiolanze
- If you are allergic (hypersensitive) to latanoprost or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor or the doctor treating your child or pharmacist before using Catiolanze, or before you give Catiolanze to your child if you think any of the following apply to you or your child:
- If you or your child are about to have or have had eye surgery (including cataract surgery).
- If you or your child suffer from eye problems (such as eye pain, irritation or inflammation, blurred vision).
- If you or your child have severe asthma or the asthma is not well controlled.

- If you or your child wear contact lenses. You can still use Catiolanze, but follow the instruction for contact lens wearers in section 3.
- If you have suffered or are currently suffering from a viral infection of the eye caused by the herpes simplex virus (HSV).

Other medicines and Catiolanze
Catiolanze may interact with other medicines. Please tell your doctor, the doctor treating your child or pharmacist if you or your child are using or have used any other medicines, including those medicines (or eye drops) obtained without a prescription.
In particular, speak to your doctor or pharmacist if you know that you or your child are using prostaglandins, prostaglandin analogues or prostaglandin derivatives.

Pregnancy and breast-feeding
Do not use this medicine if you are pregnant or breast-feeding unless your doctor considers it necessary. If you are pregnant or breast-feeding, think you may be pregnant, or are planning to have a baby, ask your doctor for advice before using this medicine**.**

Driving and using machines
This medicine can cause blurred vision, for a short time. If this happens to you, do not drive or use any tools or machines until your vision becomes clear again.

Catiolanze contains cetalkonium chloride
Cetalkonium chloride may cause eye irritation.

3. How to use Catiolanze

Always use this medicine exactly as your doctor or the doctor treating your child has told you. You should check with your doctor or the doctor treating your child or pharmacist if you are not sure.

The recommended dose for adults and children is one drop once a day in the affected eye(s). The best time to do this is in the evening.

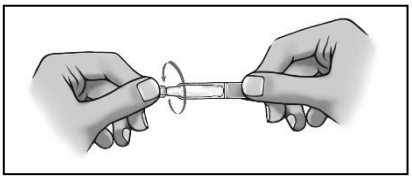
Do not use Catiolanze more than once a day, because the effectiveness of the treatment can be reduced if you administer it more often.

Use Catiolanze as instructed by your doctor or by the doctor treating your child until they tell you to stop.

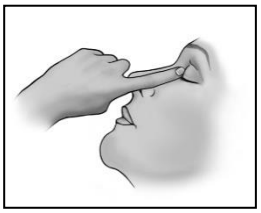
Contact lens wearers
If you or your child wear contact lenses, these should be removed before using Catiolanze. After using this medicine you should wait 15 minutes before putting the contact lenses back into the eyes.

Instructions for use
- For single use only.
- Use the liquid from one individual single-dose container immediately after opening and administer one drop to the affected eye(s). Any remaining contents must be discarded immediately after use.
- After using Catiolanze, press a finger lightly on the inner corner of the affected eye by the nose. Hold for 1 minute whilst keeping the eye closed, see step 11 and picture 3.
- Contact between the dropper tip and eye/eye lids must be avoided.

Follow these instructions carefully and ask your doctor or pharmacist if there is anything you do not understand.

1 

 **2**

3 

1. Wash your hands and sit or stand comfortably.
2. Open the aluminium pouch, which contains 5 single-dose containers.
3. Take 1 single-dose container from the aluminium pouch, leaving the remaining containers in the pouch.
4. Gently shake the single-dose container.
5. Twist off the cap **(picture 1).**
6. Use your finger to gently pull down the lower eyelid of your affected eye **(picture 2)**.
7. Tilt your head back and look up at the ceiling.
8. Place the tip of the single-dose container close to, but not touching, your eye.
9. Gently squeeze one drop of the medicine onto your eye, then release the lower eyelid.
10. Blink a few times so that the medicine spreads across your eye.
11. After using Catiolanze, press a finger lightly on the inner corner of the affected eye by the nose. Hold for 1 minute whilst keeping the eye closed **(picture 3)**.
    A small duct that drains tears away from your eye and into your nose is located here. By pressing at this point, you close down the opening of this drainage duct. This helps to stop Catiolanze getting into the rest of the body.
12. Repeat steps 6-11 in your other eye if your doctor has told you to use drops in both eyes.
13. Discard the single-dose container after use. Do not keep it to use it again.

If you use Catiolanze with other eye drops
Use Catiolanze at least 5 minutes after using the other eye drops.

If you use more Catiolanze than you should
If you put too many drops into the eye, it may lead to some minor irritation in the eye and the eyes may water and turn red. This should pass, but if you are worried contact your doctor or the doctor treating your child for advice.

Contact your doctor as soon as possible if you or your child swallows Catiolanze accidentally.

If you forget to use Catiolanze
Carry on with the usual dosage at the usual time. Do not use a double dose to make up for the dose you have forgotten. If you are unsure about anything talk to your doctor or pharmacist.

If you stop using Catiolanze
You should speak to your doctor or the doctor treating your child if you or your child want to stop using this medicine.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following are known side effects of using Catiolanze:

Very common (may affect more than 1 in 10 people):
- A gradual change in your eye colour by increasing the amount of brown pigment in the coloured part of the eye known as the iris. If you have mixed-colour eyes (blue-brown, grey-brown, yellow-brown or green-brown) you are more likely to see this change than if you have eyes of one colour (blue, grey, green or brown eyes). Any changes in your eye colour may take years to develop although it is normally seen within 8 months of treatment. The colour change may be permanent and may be more noticeable if you use this medicine in only one eye. There appears to be no problems associated with the change in eye colour. The eye colour change does not continue after Catiolanze treatment is stopped.

Common (may affect up to 1 in 10 people):
- Redness of the eye (conjunctival hyperaemia).
- Eye irritation (a feeling of burning, grittiness, itching, stinging or the sensation of a foreign body in the eye, abnormal sensation in the eye). If you experience eye irritation severe enough to make your eyes water excessively, or make you consider stopping this medicine, talk to your doctor, pharmacist or nurse promptly. You may need your treatment to be reviewed to ensure you keep receiving appropriate treatment for your condition.
- Irritation or disruption to the surface of the eye, eye pain, light sensitivity (photophobia), conjunctivitis.

Uncommon (may affect up to 1 in 100 people):
- Eyelid swelling, dryness of the eye, inflammation or irritation of the surface of the eye (keratitis), blurred vision, inflammation of the coloured part of the eye (uveitis), swelling of the retina (macular oedema), eyelid inflammation (blepharitis).
- A gradual change to eyelashes of the treated eye and the fine hairs around the treated eye, seen mostly in people of Japanese origin. These changes involve an increase of the colour (darkening), length, thickness and number of your eye lashes.
- Skin rash.
- Chest pain (angina), awareness of heart rhythm (palpitations).
- Asthma, shortness of breath (dyspnoea).
- Chest pain.
- Headache, dizziness.
- Muscle pain, joint pain.
- Nausea, vomiting.

Rare (may affect up to 1 in 1000 people):
- Inflammation of the iris (iritis), symptoms of swelling or scratching/damage to the surface of the eye, swelling around the eye (periorbital oedema), misdirected eyelashes or an extra row of eyelashes, scarring of the surface of the eye, fluid filled area within the coloured part of the eye (iris cyst).
- Skin reactions on the eyelids, darkening of the skin of the eyelids.
- Worsening of asthma.
- Severe itching of the skin.
- Developing a viral infection of the eye caused by the herpes simplex virus (HSV).

Very rare (may affect up to 1 in 10,000 people):
- Worsening of angina in patients who also have heart disease, sunken eye appearance (eye sulcus deepening).

Side effects seen more often **in children** compared to adults are runny itchy nose and fever.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Catiolanze

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton, pouch and single dose container after "EXP". The expiry date refers to the last day of that month.

Store below 30°C.

After opening the aluminium pouch, the single dose containers should be kept in the pouch in order to protect from light and avoid evaporation. Discard any opened individual single-dose container immediately after use.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Content of the pack and other information

What Catiolanze contains
- The active substance is latanoprost. One millilitre of emulsion contains 50 micrograms of latanoprost. Each single-dose container of 0.3 mL of eye drops, emulsion contains 15 micrograms of latanoprost. One drop contains approximately 1.65 micrograms latanoprost.
- The other ingredients are: medium chain triglycerides, cetalkonium chloride, polysorbate 80, glycerol and water for injections.

What Catiolanze looks like and contents of the pack
Catiolanze 50 micrograms/mL eye drops, emulsion is a white liquid.

One pouch contains 5 single-dose containers. Available in pack sizes of 30, 60, 90 or 120 single-dose containers.
Not all pack sizes may be marketed.

Marketing Authorisation Holder:
Santen Oy
Niittyhaankatu 20
33720 Tampere
Finland

Manufacturer:
Santen Oy
Kelloportinkatu 1
33100 Tampere
Finland

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
Santen Oy
Tél/Tel: +32 (0) 24019172

България
Santen Oy
Тел.: +359 (0) 888 755 393

Česká republika
Santen Oy
Tel: +358 (0) 3 284 8111

Danmark
Santen Oy
Tlf: +45 898 713 35

Deutschland
Santen GmbH
Tel: +49 (0) 3030809610

Eesti
Santen Oy
Tel: +372 5067559

Ελλάδα
Santen Oy
Τηλ: +358 (0) 3 284 8111

España
Santen Pharmaceutical Spain S.L.
Tel: +34 914 142 485

France
Santen
Tél: +33 (0) 1 70 75 26 84

Hrvatska
Santen Oy
Tel: +358 (0) 3 284 8111

Ireland
Santen Oy
Tel: +353 (0) 16950008

Ísland
Santen Oy
Sími: +358 (0) 3 284 8111

Italia
Santen Italy S.r.l.
Tel: +39 0236009983

Lietuva
Santen Oy
Tel: +370 37 366628

Luxembourg/Luxemburg
Santen Oy
Tél/Tel: +352 (0) 27862006

Magyarország
Santen Oy
Tel: +358 (0) 3 284 8111

Malta
Santen Oy
Tel: +358 (0) 3 284 8111

Nederland
Santen Oy
Tel: +31 (0) 207139206

Norge
Santen Oy
Tlf: +47 21939612

Österreich
Santen Oy
Tel: +43 (0) 720116199

Polska
Santen Oy
Tel.: +48(0) 221042096

Portugal
Santen Oy
Tel: +351 308 805 912

România
Santen Oy
Tel: +358 (0) 3 284 8111

Slovenija
Santen Oy
Tel: +358 (0) 3 284 8111

Slovenská republika
Santen Oy
Tel: +358 (0) 3 284 8111

Suomi/Finland
Santen Oy
Puh/Tel: +358 (0) 974790211

Κύπρος
Santen Oy
Τηλ: +358 (0) 3 284 8111

Latvija
Santen Oy
Tel: +371 677 917 80

Sverige
Santen Oy
Tel: +46 (0) 850598833

United Kingdom (Northern Ireland)
Santen Oy
Tel: +353 (0) 16950008
(UK Tel: +44 (0) 345 075 4863)

This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.