

VI.2 Elements for a Public Summary

T1565 [Softacort] is a preservative free eye drop solution that contains the active substance hydrocortisone.

VI.2.1 Overview of disease epidemiology

T1565 [Softacort] is indicated for the treatment of mild allergic or inflammation conditions of the superficial of your eye(s) (conjunctives). Inflammation of the conjunctives could be caused by several causes such as trauma , irritation or allergies and could affect people of all ages and sex ⁸⁴. Mild allergic or inflammation conditions when they are not treated could lead to loss of corneal cell, clouding of the cornea (corneal opacification) and, sometimes, to corneal perforations ⁸⁵.

VI.2.2 Summary of treatment benefits

The company provided data from the published literature on hydrocortisone, already authorised in the European Union (EU) with a large experience which had shown the benefit of treatment with Hydrocortisone by decreasing the symptoms of inflammation or allergies of the outer part of your eye(s) (conjunctives).

Allergic conjunctivitis

Based on two published well-designed, controlled, randomised, double-blind trials^{86,87}, where a total of 408 patients have received a treatment with hydrocortisone, it can be stated that hydrocortisone eye drops are effective in treating allergic conjunctivitis.

Other ocular surface inflammations

⁸⁴ Sheppard, J. and Bartlett, J. (2011). "Loteprednol Etabonate in Ocular Inflammation". US ophthalmic review: 57-62.

⁸⁵ Kruse, F. E. (2002). Classification of ocular surface disease. Ocular surface disease. Medical and surgical management. . E. J. Holland and M. J. Mannis. New York, Springer-Verlag. 2: 16-36.

⁸⁶ Ciprandi, G., S. Buscaglia, et al. (1992). "Topical anti-inflammatory drugs in the treatment of allergic pollinosis conjunctivitis: a comparative double-blind study." J Investig Allergol Clin Immunol 2(5): 248-252.

⁸⁷ Sergiyenko, N., L. Sukhina, et al. (2014). "Hydrocortisone concentration influences time to clinically significant healing of acute inflammation of the ocular surface and adnexa - results from a double-blind randomized controlled trial." BMC Ophthalmol 14: 64.

Similarly, efficacy of hydrocortisone has been published in case reports in other ocular surface inflammations. In these published case series a lesser number of patients were involved^{88, 89, 90, 91, 92, 93}.

VI.2.3 Unknowns relating to treatment benefits

The use in lactating women was not studied.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Viral eye infection (herpes)	Anti-inflammatory may induce reactivation of infection with Herpes virus.	<p>Routine</p> <p>It must not be used in patients who have or are thought to have ocular herpes infections unless the infection is being treated with an anti-infective treatment and close monitoring of the eyes is required.</p> <p>Prescription only medicine</p>
Ocular infection (bacterial or fungal)	<p>Developing a bacterial or a fungal infection of the eye has been reported as a possible side-effect with hydrocortisone or corticosteroids</p> <p>The use of corticosteroids can cause opportunistic ocular infections. In addition, topical ocular corticosteroids may promote, aggravate or mask signs and symptoms of opportunistic eye infections.</p>	<p>Routine</p> <p>It must not be used in patients who have or are thought to have ocular or periocular infections (infections in or around the eyes)</p>
Prolonged use or overdosage: increase of pressure inside	Corticosteroids, when not used adequately, e.g. not exactly as	Routine

⁸⁸ McDonald, P. R., I. H. Leopold, et al. (1953). "Hydrocortisone (compound F) in ophthalmology; clinical and experimental studies." *AMA Arch Ophthalmol* 49(4): 400-412.

⁸⁹ Begue, H. and L. Negre (1954). "[Hydrocortisone acetate in ophthalmology]." *Presse Med* 62(11): 226-227.

⁹⁰ Gordon, D. M., J. M. McLean, et al. (1953). "Present status of corticotropin; ACTH, cortisone, and hydrocortisone in ophthalmology." *Br J Ophthalmol* 37(2): 85-98.

⁹¹ Gordon, D. M. (1955). "Ocular therapy with the topical application of hydrocortisone." *Ann N Y Acad Sci* 61(2): 549-560.

⁹² Kreft, W. W. (1957). "Soluble hydrocortisone and prednisolone in ophthalmology." *Ill Med J* 112(3): 109-110.

⁹³ Raj, A., G. P. Williams, et al. (2012). "Ulcerative keratitis following particulate elemental gold deposition." *J Ocul Pharmacol Ther* 28(3): 323-325.

Risk	What is known	Preventability
the eye (ocular hypertension, glaucoma)	described in the leaflet or as your doctor told you, may cause problems. For example, a continuous application for more than 14 days may induce increase of pressure inside the eye (ocular hypertension, glaucoma).	It must not be used in patients who have high pressure inside the eye (ocular hypertension) known to be due to glucosteroids (family of corticosteroids) or to other causes. In case where continuous application for more than 14 days is needed, close regular monitoring of eyes is required Prescription only medicine
Cloudy patches of the cornea (corneal calcifications)	T1565 [Softacort] contains phosphates. Some patients with severe damage to the clear layer at the front of the eye (the cornea) have developed cloudy patches on the cornea due to calcium build-up during treatment	Routine Use with caution in patients with severe damage to the clear layer at the front of the eye (the cornea) Prescription only medicine

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Prolonged use: clouding of the lens in the eye (posterior capsular cataract)	Corticosteroids, when not used adequately, e.g. not exactly as described in the leaflet or as your doctor told you, may cause problems. For example, clouding of the lens in the eye (cataract).
Delayed wound healing	Corticosteroids are known to induce delayed wound healing
Changes in the thickness of the front of the eye (cornea)	Patient with a disease that causes thinning of the outer part of the eye (cornea and sclera), may be at higher risk of perforation due to the use of topical corticosteroids applied to the eye.
Risk of inhibition of fetal adrenal cortex, intrauterine growth delay associated with the use during pregnancy	The use of this medicine during pregnancy and early childhood is not recommended except when judged necessary by your doctor and under strict supervision.
Risk of adrenal suppression, increase of pressure inside the eye or clouding of the lens in the eye associated with	There is no data on safety and efficacy in children. Continual, long-term treatment may produce adrenal suppression. The increase of the eye pressure in children occurs more

Risk	What is known (Including reason why it is considered a potential risk)
use in children	frequently, more severely, and more rapidly than that reported in adults
Risk of increase of pressure inside the eye or clouding of the lens in the eye associated with the use in elderly	Prolonged use of corticosteroids has shown to cause an increase of the pressure inside the eye and of the onset of glaucoma, especially in patients who already suffer from high intraocular pressure or who are to be at risk of developing such condition with local steroid treatment (see Possible side effects) and to cause a clouding of the lens in the eye (cataract), in particular in children and elderly population..
Risk of inhibition of the function of the adrenal cortex in breastfed infant	It is not known whether this medicine passes into breast milk. However, no effects are anticipated in breastfed infants at therapeutic doses. Your doctor will decide if you can use this medicine during breast-feeding or not.

Missing information

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

The Summary of Product Characteristics and the Package leaflet for T1565 [Softacort] can be found in the X's EPAR page

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

No additional post authorisation development plan.

VI.2.7 Summary of changes to the Risk Management Plan over time

Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
1	30 September 2014	<u>Identified Risks</u> Allergic reaction (Hypersensitivity) Viral eye infection (herpes) Other ocular infection <u>Potential Risks</u> Prolonged use: increase of pressure inside the eye (ocular hypertension, glaucoma), clouding of the lens in the eye (cataract)	First version of the RMP

Version	Date	Safety Concerns	Comment
		<p>Delayed wound healing Cloudy patches of the cornea (corneal calcifications)</p> <p><u>Missing information</u> Use in Pregnant or breast-feeding and fertility Use in children Use in Elderly</p>	
1.1	25 April 2016	<p><u>Identified Risks</u> Allergic reaction (Hypersensitivity) Viral eye infection (herpes) Ocular infections (bacterial or fungal) Cloudy patches of the cornea (corneal calcifications)</p> <p><u>Potential Risks</u> Prolonged use or overdosage: increase of pressure inside the eye (ocular hypertension, glaucoma) Prolonged use: clouding of the lens in the eye (cataract) Delayed wound healing Changes in the thickness of the front of the eye (cornea) Risk associated with the use in Pregnant women Risk associated with the use in children Risk associated with the use in Elderly</p> <p><u>Missing information</u> Use in lactating women</p>	Update in accordance with D106 comments
1.2	06 October 2016	<p><u>Identified Risks</u> Allergic reaction (Hypersensitivity) Viral eye infection (herpes) Ocular infections (bacterial or fungal) Prolonged use or overdosage: increase of pressure inside the eye (ocular hypertension, glaucoma) Cloudy patches of the cornea (corneal calcifications)</p> <p><u>Potential Risks</u> Prolonged use: clouding of the lens in the eye (cataract) Delayed wound healing Changes in the thickness of the front of the</p>	Update of SPC and PIL following availability of results regarding storage conditions (Section 6.5 of SPC and Section 2 of PIL) and typo correction in Section 2 of PIL

Version	Date	Safety Concerns	Comment
		<p>eye (cornea) Risk associated with the use in Pregnant women Risk associated with the use in children Risk associated with the use in Elderly</p> <p><u>Missing information</u> <u>Use in lactating women</u></p>	
1.3	16 January 2017	<p><u>Identified Risks</u> Viral eye infection (herpes) Ocular infections (bacterial or fungal) Prolonged use or overdosage: increase of pressure inside the eye (ocular hypertension, glaucoma) Cloudy patches of the cornea (corneal calcifications)</p> <p><u>Potential Risks</u> Prolonged use: clouding of the lens in the eye (cataract) Delayed wound healing Changes in the thickness of the front of the eye (cornea) Risk of inhibition of fetal adrenal cortex, intrauterine growth delay associated with the use during pregnancy Risk of adrenal suppression, increase of pressure inside the eye or clouding of the lens in the eye associated with use in children Risk of increase of pressure inside the eye or clouding of the lens in the eye associated with the use in elderly Risk of inhibition of the function of the adrenal cortex in breastfed infant</p> <p><u>Missing information</u></p>	Update in accordance with D120 and D145 comments
1.4	23 February 2017	<p><u>Identified Risks</u> Viral eye infection (herpes) Ocular infections (bacterial or fungal) Prolonged use or overdosage: increase of pressure inside the eye (ocular hypertension, glaucoma) Cloudy patches of the cornea (corneal calcifications)</p>	Update in accordance with D180 comments

Version	Date	Safety Concerns	Comment
		<p><u>Potential Risks</u></p> <p>Prolonged use: clouding of the lens in the eye (cataract)</p> <p>Delayed wound healing</p> <p>Changes in the thickness of the front of the eye (cornea)</p> <p>Risk of inhibition of fetal adrenal cortex, intrauterine growth delay associated with the use during pregnancy</p> <p>Risk of adrenal suppression, increase of pressure inside the eye or clouding of the lens in the eye associated with use in children</p> <p>Risk of increase of pressure inside the eye or clouding of the lens in the eye associated with the use in elderly</p> <p>Risk of inhibition of the function of the adrenal cortex in breastfed infant</p> <p><u>Missing information</u></p>	
1.5	21 March 2017	<p><u>Identified Risks</u></p> <p><u>Viral eye infection (herpes)</u></p> <p><u>Ocular infections (bacterial or fungal)</u></p> <p><u>Prolonged use or overdose: increase of pressure inside the eye (ocular hypertension, glaucoma)</u></p> <p><u>Cloudy patches of the cornea (corneal calcifications)</u></p> <p><u>Potential Risks</u></p> <p><u>Prolonged use: clouding of the lens in the eye (cataract)</u></p> <p><u>Delayed wound healing</u></p> <p><u>Changes in the thickness of the front of the eye (cornea)</u></p> <p><u>Risk of inhibition of fetal adrenal cortex, intrauterine growth delay associated with the use during pregnancy</u></p> <p><u>Risk of adrenal suppression, increase of pressure inside the eye or clouding of the lens in the eye associated with use in children</u></p> <p><u>Risk of increase of pressure inside the eye or clouding of the lens in the eye associated with the use in elderly</u></p> <p><u>Risk of inhibition of the function of the adrenal cortex in breastfed infant</u></p>	Consolidated version following D210 approval

Version	Date	Safety Concerns	Comment
		<u>Missing information</u>	