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ADIS DRUG EVALUATION

Suprachoroidal Space Triamcinolone Acetonide: A Review in Uveitic Macular Edema

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Abstract

Triamcinolone acetonide injectable suspension for suprachoroidal use (Xipere®; SCS triamcinolone acetonide) is a corticosteroid approved in the USA for the treatment of macular edema associated with uveitis. Suprachoroidal injection of SCS triamcinolone acetonide results in preferential distribution into the posterior segment, which may reduce the risk of corticosteroid-related adverse events, such as cataracts and intraocular pressure (IOP) elevation. In a multicenter phase III trial in patients with non-infectious uveitic macular edema, SCS triamcinolone acetonide significantly and rapidly improved visual acuity and reduced signs of macular edema compared with sham treatment. SCS triamcinolone acetonide was generally well tolerated, with the most common adverse event being eye pain on the day of the procedure. The risk of corticosteroid-related IOP elevation appeared to be reduced in unrescued patients in the SCS triamcinolone acetonide group compared with patients in the sham control group who received rescue therapy. SCS triamcinolone acetonide is a novel and useful treatment option for uveitic macular edema.

Plain Language Summary

Uveitic macular edema is a major cause of blindness in the developed world. Intravitreal and periocular application of corticosteroids (e.g., triamcinolone acetonide) may be effective for uveitis and macular edema, but these routes are often associated with cataracts and corticosteroid-related intraocular pressure (IOP) elevation. Recently, a triamcinolone acetonide suspension for injection into the suprachoroidal space (Xipere®; SCS triamcinolone acetonide) has been approved for the treatment of uveitic macular edema. The suprachoroidal route preferentially distributes the drug to the back of the eye, resulting in a reduced risk of corticosteroid-related adverse events. In a pivotal clinical trial, SCS triamcinolone acetonide rapidly improved visual acuity and resolved macular edema in patients with non-infectious uveitis. SCS triamcinolone acetonide was generally well tolerated, with the most common ocular adverse event being eye pain on the day of procedure. In unrescued patients in the SCS triamcinolone acetonide group, there appeared to be a reduced risk of corticosteroid-related IOP elevation versus patients who received rescue therapy in the sham control group. SCS triamcinolone acetonide is a novel and useful treatment option for uveitic macular edema.

Digital Features for this Adis Drug Evaluation can be found at https://doi.org/10.6084/m9.figshare.20128592

SCS triamcinolone acetonide: clinical considerations in uveitic macular edema

First drug to receive approval for injection into the suprachoroidal space, and first approved treatment for uveitic macular edema

Improves visual acuity and reduces macular edema

Generally well tolerated

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1 Introduction

Uveitis is a group of intraocular inflammatory disorders affecting the uveal tract and its surrounding tissues [1]. It is responsible for up to 15% of all instances of complete blindness in the developed world [1]. One of the most common complications of uveitis is macular edema, which causes vision impairment in one-third of all uveitis patients [2]. Macular edema may persist even after inflammation is brought under control; therefore interventions should aim to resolve both inflammation and macular edema [2].

Glucocorticoids have long been used in the treatment of uveitis and macular edema; systemic glucocorticoids are effective but are associated with adverse events, including hypokalemia, diabetes, Cushing's syndrome, osteoporosis, adrenal insufficiency, cardiovascular disease, and immunosuppression [2, 3]. Application of corticosteroids through periocular and intravitreal routes to treat uveitis results in much lower systemic concentrations of the drug and reduces the incidence of adverse events associated with systemic therapy. However, local application of corticosteroids comes with its own set of risks, most commonly elevations in intraocular pressure (IOP) and an increased risk of cataracts [3]. Corticosteroid-related IOP elevation can lead to glaucoma and is thought to be caused by the effects of glucocorticoids on aqueous outflow in the trabecular meshwork [3]. Glucocorticoids can also induce pathological proliferation and survival of, as well as the production of reactive oxygen species in, lens epithelial cells, which promotes the development of cataracts [4].

A novel approach to reducing the risks of locally administered ocular corticosteroids is to inject them into the suprachoroidal space (SCS), which is a potential space located between the choroid and sclera, bound anteriorly by the scleral spur and posteriorly by the optic nerve [5]. The scleral spur hinders the movement of drug into the anterior segment, and a pressure differential within the eye promotes posterior movement of the drug in the SCS [5]. Thus, drug injected into this space is distributed to the posterior segment, while keeping concentrations at the trabecular meshwork and lens, in the anterior segment, low.

Triamcinolone acetonide injectable suspension for suprachoroidal use (Xipere®), henceforth SCS triamcinolone acetonide, is a corticosteroid indicated for the treatment of macular edema associated with uveitis in the USA [6]. SCS triamcinolone acetonide is administered via a proprietary SCS Microinjector®. This procedure uses microneedle technology, which allows the SCS to be accessed more reliably than with a standard hypodermic needle and does not require incision or surgical imaging so can be performed outside of an operating room environment [5]. This article reviews the efficacy and tolerability of SCS triamcinolone acetonide in uveitic macular edema, with a brief overview of its pharmacological properties.

2 Pharmacodynamic Properties of Triamcinolone Acetonide

Triamcinolone acetonide is a synthetic glucocorticoid receptor agonist that binds directly to intracellular glucocorticoid receptors, causing the receptor to translocate to the nucleus and trigger a broad spectrum of anti-inflammatory responses [7]. In animal models, these responses include: production of lipocortins, which suppress the release of pro-inflammatory arachidonic acid from plasma membranes [8]; a reduction in immune cell infiltration [9], likely by suppressing immune cell recruitment and immune cell activation [10]; and a decrease in vascular permeability and vascular proliferation through downregulation of vascular endothelial growth factor (VEGF) [11]. Together, these effects reduce macular edema and improve visual acuity in patients (Sect. 4).

3 Pharmacokinetic Properties of SCS Triamcinolone Acetonide

In an animal study, suprachoroidal injection of triamcinolone acetonide resulted in high drug concentrations in the posterior segment of the eye and low concentrations in the anterior segment [12]. The ocular distribution of 4 mg triamcinolone acetonide (formulated for intravitreal administration; Triesence®) was compared over 91 days when administered suprachoroidally versus intravitreally in New Zealand white rabbits. Compared with the intravitreal route, suprachoroidal administration produced a 12-fold higher drug exposure in the posterior segment of the eye (the retinal pigment epithelium, choroid, and sclera), while the exposure was reduced by ≥ 96% in the anterior segment tissues (lens, iris/ciliary body) and aqueous humor. With suprachoroidal administration, triamcinolone acetonide concentrations remained high in the posterior segment for the first two months, with concentrations becoming similar to that of intravitreal delivery by the end of the 3-month study period.

The major routes of drug clearance from the SCS into the systemic circulation is through the choriocapillaris and diffusion across the sclera [13]. The particle size in the formulation of triamcinolone acetonide plays a key role in its ocular retention [5], with most particles being unable to diffuse across the sclera or be cleared by choriocapillaris. Systemic concentrations of the drug are typically low with suprachoroidal administration; in patients with non-infectious uveitis who were given two doses of SCS triamcinolone acetonide

4 mg, 12 weeks apart, plasma drug concentrations were < 1 ng/mL at weeks 4, 12, and 24 of the 24-week study [14].

Of the minimal amount of triamcinolone acetonide that reaches the blood, 68% is bound to plasma proteins; any unbound triamcinolone acetonide is metabolized into three less-active metabolites: 6β-hydroxytriamcinolone acetonide, 21-carboxytriamcinolone acetonide, and 21-carboxy-6β-hydroxytriamcinolone acetonide [10]. These metabolites are then rapidly eliminated in the urine (40%) and feces (60%) [10].

4 Therapeutic Efficacy of SCS Triamcinolone Acetonide

This section focuses on the efficacy of SCS triamcinolone acetonide in the pivotal phase III PEACHTREE trial [15] and its extension (MAGNOLIA) [16]. SCS triamcinolone acetonide improved visual acuity in a phase I/II trial [17] and reduced central subfield thickness (CST) in a phase II trial (DOGWOOD) [18] in patients with macular edema due to non-infectious uveitis; these data are not discussed further.

4.1 PEACHTREE Trial

PEACHTREE was a randomized, double-masked, sham-controlled, multinational, 24-week phase III trial [15]. Eligible patients (age ≥ 18 years) had macular edema secondary to non-infectious uveitis, which was defined as the presence of intraretinal or subretinal fluid and a retinal CST of ≥ 300 µm. Uveitis could be of any cause and in any anatomical location (i.e., anterior, intermediate, posterior, or pan-uveitis). Patients were required to have a Best Corrected Visual Acuity (BCVA) of ≥ 5 Early Treatment Diabetic Retinopathy Study (ETDRS) letters (Snellen equivalent, 20/800) and ≤ 70 letters read (Snellen equivalent, 20/40) in the study eye. Use of systemic corticosteroid (≤ 20 mg of oral prednisolone per day or equivalent), stable (≥ 2 weeks) doses of immunomodulatory therapies, or both, were permitted in the study. Exclusion criteria included any active ocular disease or infection in the study eye other than uveitis, and IOP > 22 mmHg or uncontrolled glaucoma. Patients with an IOP ≤ 22 mmHg in the study eye and receiving no more than two IOP-lowering medications were permitted in the study.

Patients received a single unilateral injection of SCS triamcinolone acetonide 4 mg or sham procedure at day 0 and week 12 [15]. Patients whose macular edema or uveitis progressed (a decrease of ≥ 10 ETDRS letters from baseline, an increase of ≥ 100 µm CST from baseline, a worsening of inflammation by ≥ 1.5 steps or increase from grade 3+ to 4+, or if the investigator judged uveitic complications had not improved and required treatment) during the study were permitted to receive rescue therapy from week 4 onwards [19]. The primary endpoint was the proportion of patients with an increase of ≥ 15 ETDRS letters in BCVA from baseline at 24 weeks in the intent-to-treat population [15]. An increase of ≥ 15 ETDRS letters (or three lines of vision) corresponds to a halving of the visual angle and, therefore, represents a clinically meaningful improvement.

Demographics and baseline disease characteristics were generally well balanced between the treatment groups. For the overall population, mean age was 50.2 years, mean BCVA in the study eye was 54.2 ETDRS letters read and the mean CST in the study eye was 498.7 µm. In active and sham groups, respectively, mean time since uveitis diagnosis was 177.4 weeks and 107.1 weeks, 49% and 65.6% of patients were phakic [15], and 29% and 23% of patients were receiving systemic corticosteroids [20].

SCS triamcinolone acetonide provided clinically meaningful improvement in the vision of patients with uveitic macular edema [15]. Significantly more patients in the SCS triamcinolone acetonide group than in the sham group achieved a ≥ 15 ETDRS-letter improvement from baseline at 24 weeks (primary endpoint; Table 1). The improvement in BCVA was apparent from as early as week 4 of the study (Table 1); this improvement was durable and remained statistically significant compared with the sham group throughout the study [15]. At the beginning of the study, 90 patients in the SCS triamcinolone acetonide group and 59 in the sham group had BCVA scores of < 70 ETDRS letters (legal visual acuity requirement for driving in most states of the USA). Of these patients, significantly more from the SCS triamcinolone acetonide than sham group had BCVA score ≥ 70 ETDRS letters at 24 weeks (Table 1).

SCS triamcinolone acetonide also improved macular edema [15]. Patients in the SCS triamcinolone acetonide group had a significantly greater reduction in CST than those in the sham group at 24 weeks; the between-group difference was significant as early as week 4 and remained significant throughout the study (Table 1). Accordingly, a significantly greater proportion of SCS triamcinolone acetonide than sham recipients had resolution of macular edema (i.e., CST reduced to < 300 µm) (Table 1).

SCS triamcinolone acetonide improved other signs of inflammation associated with uveitis [15]. Of the patients who experienced signs of inflammation (anterior chamber cells, anterior chamber flare, and vitreous haze) at baseline, two thirds of those in the SCS triamcinolone acetonide group experienced a resolution of inflammation at 24 weeks.

Treatment with SCS triamcinolone acetonide kept symptoms of uveitis from progressing and reduced the need for rescue therapies [15]. In the SCS triamcinolone acetonide and sham groups, respectively, 13.5% and 72.0% of patients required rescue therapy, with a median time to rescue of 89 days and 36 days in those receiving rescue ($p < 0.001$ for the difference in the respective distribution for time to rescue

Table 1 Efficacy of SCS triamcinolone acetonide in patients with non-infectious uveitic macular edema [15]

Parameter	Suprachoroidal injections at day 0 and week 12	
	Triamcinolone acetonide 4 mg ($n=96$)[a]	Sham-treated ($n=64$)[a]
Best corrected visual acuity		
Patients with a ≥ 15 ETDRS letters increase from baseline at week 24 (%)[b]	46.9**	15.6
Mean improvement at week 4 (ETDRS letters)	9.6**	1.3
Patients achieving ≥ 70 ETDRS letters at week 24 (%)	54**	20
Macular edema		
Mean decrease in CST at week 24 (μm)	152.6**	17.9
Mean decrease in CST at week 4 (μm)	148.5**	4.2
Patients with a CST < 300 μm at week 24 (%)[c,d]	55*	14

CST central subfield thickness, *ETDRS* Early Treatment Diabetic Retinopathy Study, *SCS* suprachoroidal space

*p value not stated, **$p < 0.001$ vs sham treated

[a]Intention-to-treat population

[b]Primary endpoint

[c]Macular edema was considered resolved when CST was < 300 μm

[d]Data from Clearside Biomedical Clinical Study Report [30]

therapy). The first rescue in these patients involved topical corticosteroids (39%), intravitreal corticosteroids (30%), systemic corticosteroids (13%), periocular steroids (11%), and non-steroidal anti-inflammatory drugs (7%) [19]. Most of these patients eventually required additional rescue therapy with intravitreal or periocular corticosteroids.

Post hoc analyses of PEACHTREE data found that treatment with SCS triamcinolone acetonide was effective, irrespective of whether patients were receiving systemic glucocorticoids [20], the anatomical location of uveitis (anterior, intermediate, posterior, or pan) [21], or duration of the disease [22]. In patients not receiving systemic corticosteroids, a significantly ($p < 0.001$) larger proportion of patients in the SCS triamcinolone acetonide versus sham group achieved a ≥ 15-ETDRS letter improvement in BCVA from baseline (48.5 vs 16.3%) and resolution in their macular edema (64.2 vs 12.8%) at 24 weeks, indicating that SCS triamcinolone acetonide has efficacy as a standalone agent [20]. In the SCS triamcinolone acetonide group, similar improvements in BCVA were observed in patients receiving and not receiving systemic corticosteroids, with 42.9% and 48.5% of patients experiencing a ≥ 15-ETDRS letters improvement at week 24 in these groups [20]. Another post hoc analysis compared efficacy outcomes between 83 unrescued patients in the SCS triamcinolone acetonide group and 46 rescued patients in the sham group, in which rescue treatment involved intravitreal or periocular corticosteroid injections in 80.4% of patients [19]. The difference in the proportion of patients achieving ≥ 15 ETDRS letters in BCVA at 24 weeks between these two groups (51.9 vs 37.0%) did not reach statistical significance, although the reduction in CST was significantly ($p = 0.040$) greater in the unrescued active treatment versus rescued sham group (174.0 vs 148.5 μm).

4.2 MAGNOLIA Extension Study

Patients from selected centers completing PEACHTREE without requiring rescue therapy were enrolled in MAGNOLIA for an additional 24 weeks' follow-up ($n = 28$ in the SCS triamcinolone acetonide and 5 in the sham group) with no further treatment [16]. The primary endpoint of MAGNOLIA was time to rescue therapy from the date of first study treatment administration in PEACHTREE. During MAGNOLIA, 11 (39%) patients in the SCS triamcinolone acetonide group and three (60%) in the sham group required rescue therapy; 14 (50%) of patients in the SCS triamcinolone acetonide group did not require rescue therapy for up to 9 months after the second dose [16].

Over the entire 48-week period of PEACHTREE and MAGNOLIA, the median time to rescue therapy relative to the last dose was 257 days in the SCS triamcinolone acetonide group and 55.5 days in the sham group, with Kaplan-Meier survival curves predicting a significant ($p < 0.001$) between-group difference [16]. In SCS triamcinolone acetonide recipients who did not require rescue therapy, the mean increase in BCVA was 16.8 ETDRS letters at the end of PEACHTREE (week 24) and 12.1 letters at the end of MAGNOLIA (week 48). The corresponding mean reduction in CST was 178.1 and 174.5 μm.

5 Tolerability of SCS Triamcinolone Acetonide

SCS triamcinolone acetonide was generally well tolerated in patients with non-infectious uveitis with associated macular edema in clinical trials [14–18]. As the only large comparative study, PEACHTREE (Sect. 4.1) will be the focus of this section. PEACHTREE safety findings were confirmed in a companion, open-label, phase 3 safety trial (AZALEA) [14].

In PEACHTREE, the incidence of treatment-related ocular adverse events was 30.2% in the SCS triamcinolone acetonide group compared with 12.5% in the sham group [15]. The incidence of treatment-emergent adverse events leading to study discontinuation, however, was similar in both arms of the trial (5.2 vs 7.8%). Three serious adverse events were reported, all in SCS triamcinolone acetonide recipients, but none of these were deemed related to treatment.

The most common ocular adverse events with SCS triamcinolone acetonide were eye pain on the day of the procedure, corticosteroid-related IOP elevation (includes all events that did not occur on the day of the procedure), IOP elevation on the day of the procedure, cataract, and eye pain on any day post procedure (Fig. 1) [15].

The incidence of corticosteroid-related IOP elevation, cystoid macular edema, and uveitis were numerically higher in the sham- than in the SCS triamcinolone acetonide group (Fig. 1) [15]. The most common non-ocular adverse event with SCS triamcinolone acetonide was headache (incidence 5%) [6]. Tolerability and safety findings from PEACHTREE are supported by those from AZALEA [14].

In the US prescribing information, IOP elevation and eye pain events in PEACHTREE were categorized as non-acute (defined as not occurring on the day of the injection procedure, or occurring on the day of the injection procedure and not resolving on the same day) and acute (defined as occurring on the day of the injection procedure and resolving on the same day) [6]. While the incidence of non-acute IOP elevations was similar between the SCS triamcinolone acetonide and sham groups (14 vs 14%), SCS triamcinolone acetonide treatment was associated with a numerically higher incidence of acute IOP elevation (6 vs 0%), non-acute eye pain (12 vs 0%), and acute eye pain (3 vs 0%).

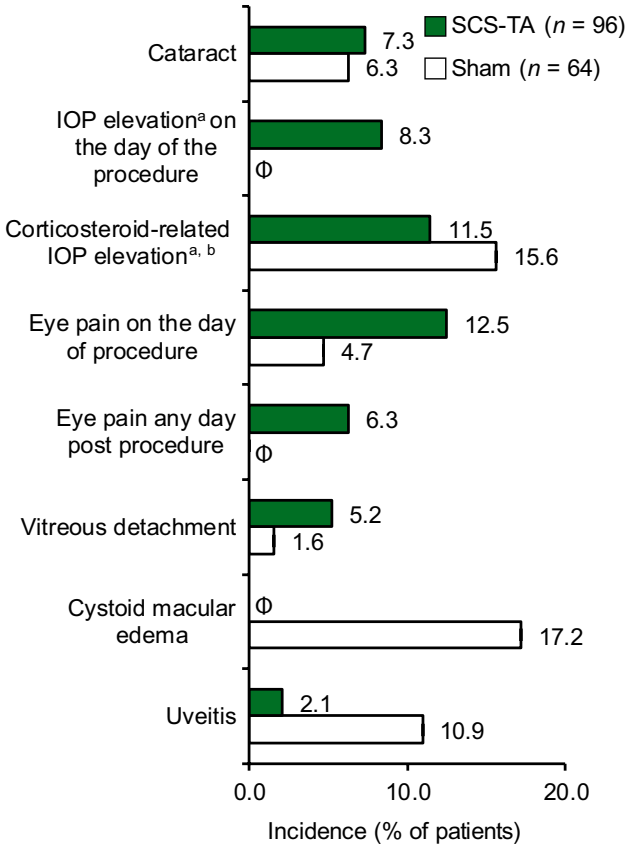

Fig. 1 Most common (incidence ≥5% in either treatment group) ocular adverse events in the 24-week PEACHTREE trial [15]. *IOP* intraocular pressure, *SCS-TA* triamcinolone acetonide formulated for injection into the suprachoroidal space. [a]IOP elevation includes: IOP increase, ocular hypertension and glaucoma; was defined as a >10 mmHg increase from baseline measurements or a total of ≥30 mmHg. [b]All corticosteroid-related IOP elevation in the sham group occurred following corticosteroid use from rescue therapy. Φ indicates an incidence of 0%.

5.1 Adverse Events of Special Interest

Use of corticosteroids in the eye may increase the risk of cataract development, IOP elevation, and secondary ocular infections. The incidence of cataract development was comparable between the SCS triamcinolone acetonide and sham groups in PEACHTREE (Fig. 1). Over the 24 weeks of the MAGNOLIA extension study, 7 (25%) patients in the SCS triamcinolone acetonide group and 1 (20%) patient in the sham group developed new or had worsening cataracts [16]. There was an association between receiving rescue therapy, which mostly involved the use of intravitreal or periocular corticosteroids (Sect. 4.1), and an increased risk of cataract development (post hoc analysis of PEACHTREE) [19]. Among patients in the SCS triamcinolone acetonide group, the incidence of cataract development was 23.1% (3 of 13) and 4.8% (4 of 83) with and without rescue therapy. Among patients in the sham group, only patients who received rescue therapy developed cataracts, with an incidence of 8.7% (4 of 46).

IOP elevations on the day of procedure occurred only in SCS triamcinolone acetonide recipients (Fig. 1) [15]. Patients should be monitored for elevation of IOP immediately after administration of SCS triamcinolone acetonide [6]. On the other hand, unrescued patients receiving SCS triamcinolone acetonide had a numerically lower incidence of corticosteroid-related IOP elevation relative to patients who received rescue treatment in the sham group [19]. In the sham group, none of 18 unrescued patients and 10 of 46 (21.7%) rescued patients experienced corticosteroid-related IOP elevation [19]; all 10 cases occurred in the 37 (27%) patients who received intravitreal or periocular corticosteroid injection as additional therapy [15]. In the SCS triamcinolone acetonide group, 9 of 83 (10.8%) unrescued patients and 2 of 13 (15.4%) rescued patients experienced corticosteroid-related IOP elevation [19]. Consistent with this finding, 7.2% of unrescued SCS triamcinolone acetonide recipients and 13% of rescued sham recipients required IOP-lowering medications [19]. Of note, over the course of MAGNOLIA, there was just one new case of IOP elevation in the SCS triamcinolone acetonide group [16].

While eye pain, both on the day and any day after the procedure, was common with SCS triamcinolone acetonide (Fig. 1) [15], there were no serious adverse events (e.g., endophthalmitis or choroidal hemorrhage) attributed to the injection procedure in any of the studies involving SCS triamcinolone acetonide for the treatment of uveitic macular edema [14–18]. However, patients should be advised to report any symptoms (such as eye pain, redness of eye, photophobia, blurring of vision) suggestive of these conditions without delay [6]. Patients should also be monitored for hypothalamic-pituitary-adrenal axis suppression, Cushing's syndrome, and hyperglycemia, as with the prolonged use of any corticosteroid [6].

6 Dosage and Administration of SCS Triamcinolone Acetonide

SCS triamcinolone acetonide is approved for the treatment of macular edema associated with uveitis in the USA [6]. The recommended dose is 4 mg (0.1 mL of a 40 mg/mL suspension) administered using the proprietary SCS Microinjector®. The injection should be administered under aseptic conditions, with adequate anesthesia, after application of a broad-spectrum microbicide to the periocular skin, eyelid, and ocular surface. Two microneedles, 900 µm and 1100 µm in length, are provided with the microinjector to accommodate interpatient ocular anatomical differences. If the SCS could not be reached with the 900 µm microneedle, then the 1100 µm microneedle can be used. The microneedle is inserted into the sclera 4.0–4.5 mm posterior to the limbus, with the microneedle held perpendicular to the surface. A loss of resistance indicates the microneedle has been inserted into the correct anatomical location. The drug is injected slowly over 5–10 s, and the microneedle is kept in place for a further 3–5 s after the drug has been dispensed. A sterile cotton swab is applied to the injection site as the needle is withdrawn; light pressure is applied for a few seconds with the swab after removal of the microneedle. For patient safety reasons, SCS triamcinolone acetonide should only be administered using the proprietary SCS Microinjector®.

SCS triamcinolone acetonide is contraindicated in patients with ocular or periocular infections, including viral diseases of the cornea and conjunctiva (herpes simplex keratitis, vaccinia, varicella), mycobacterial infections, and fungal diseases. Local prescribing information should be consulted for detailed information regarding preparation and administration of SCS triamcinolone acetonide, contraindications, use in special patient populations, and warnings and precautions.

7 Current Status of SCS Triamcinolone Acetonide in the Management of Uveitic Macular Edema

Due to its complex etiology and interpatient variability, management of uveitic macular edema may involve multiple drug classes targeting different pathological features of the disease, and the regimen of choice depends on the needs of the patient, often with a focus on patient safety [23]. Corticosteroids, administered through various routes, remain the mainstay of treatment for most cases of acute uveitis [23]. The current ophthalmic corticosteroids approved in the USA include fluocinolone acetonide intravitreal implants (Iluvien® [24], Yutiq® [25], Retisert® [26]), dexamethasone intravitreal implant (Ozurdex® [27]), and triamcinolone acetonide intravitreal injection (Triesence® [28]). These formulations are indicated for the treatment of uveitis (Triesence® [28]), posterior segment non-infectious uveitis (Yutiq® [25], Ozurdex® [27], Retisert® [26]), and diabetic or retinal vein occlusion macular edema (Ozurdex® [27], Iluvien® [24]). SCS triamcinolone acetonide is the first (and currently the only) agent specifically approved for uveitic macular edema. It is also the first suprachoroidally delivered formulation to receive regulatory approval.

Currently available clinical evidence supports the use of SCS triamcinolone acetonide in the management of uveitic macular edema (Sect. 4). In the pivotal PEACHTREE

trial, SCS triamcinolone acetonide provided clinically meaningful improvements in visual acuity and resolved macular edema in approximately one-half of patients with non-infectious uveitic macular edema. Improvements were seen in patients irrespective of concurrent systemic corticosteroid usage, anatomical location of uveitis, or duration of disease in patients (Sect. 4). While PEACHTREE was not designed to compare SCS triamcinolone acetonide with rescue therapy, a post hoc analysis showed that efficacy was similar between these two groups with a trend towards a lower impact on IOP for SCS triamcinolone acetonide [19]. Results from the MAGNOLIA extension study indicate that the clinical improvements seen in the PEACHTREE trial were stable for another 24 weeks in approximately half of patients (Sect. 4.2).

The rationale for injecting triamcinolone acetonide into the SCS was to improve its tolerability and safety profile, particularly in regards to intraocular corticosteroid-related adverse events. In PEACHTREE, SCS triamcinolone acetonide was generally well tolerated, with the most common ocular adverse event being eye pain on the day of procedure (Sect. 5). The treatment is associated with a low incidence of corticosteroid-related IOP elevation [15] and an apparent low risk of cataract development (Sect. 5.1). This is attributed to the unique ocular distribution and compartmentalization of the active drug following suprachoroidal injection (Sect. 3). However, a longer follow-up period may be required to fully elucidate the risk of cataracts with SCS triamcinolone acetonide. In a study evaluating the safety of intravitreal triamcinolone acetonide in patients with age-related macular degeneration, the incidence of cataract progression by two or more stages was 8.9% over the first 12 months but increased to 24.2% over 24 months [29].

Microinjector syringe-plunger glide force is an important variable that contributes toward successful suprachoroidal injection [12]. In rabbits, SCS triamcinolone acetonide required lower and less variable glide force than triamcinolone acetonide injectable suspension for intravitreal injection. The lower glide force provides a clear tactile perception of the SCS, which is important for safely administering the drug (Sect. 6) [12].

In summary, SCS triamcinolone acetonide is efficacious and is generally well tolerated, with a low incidence of corticosteroid-related IOP elevation, in patients with uveitic macular edema. Being the first drug approved for injection into the SCS and currently the only treatment approved for uveitic macular edema, it represents a novel and useful treatment option for this condition.

Data Selection SCS triamcinolone acetonide: 134 records identified

Duplicates removed	23
Excluded during initial screening (e.g. press releases; news reports; not relevant drug/indication; preclinical study; reviews; case reports; not randomized trial)	77
Excluded during writing (e.g. review; not relevant drug/indication; small patient number; exploratory analysis)	4
Cited efficacy/tolerability articles	10
Cited articles not efficacy/tolerability	20

Search Strategy: EMBASE, MEDLINE and PubMed from 1946 to present. Clinical trial registries/databases and websites were also searched for relevant data. Key words were triamcinolone acetonide suprachoroidal injectable suspension AND macular edema non-infectious uveitis, suprachoroidal injection triamcinolone acetonide AND macular edema non-infectious uveitis, suprachoroidal CLS-TA AND macular edema secondary to noninfectious uveitis. Records were limited to those in English language. Searches last updated 3-Aug-2022

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40265-022-01763-7.

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Declarations

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Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability Not applicable.

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