MANAGEMENT IN CONFIDENCE

CLINICAL PRIORITIES ADVISORY GROUP
04 March 2020

Agenda Item No	2.1
National Programme	Trauma
Clinical Reference Group	Specialised ENT & Ophthalmology
URN	1919

Title
Serum eye drops for the treatment of severe ocular surface disease

Actions Requested	1. Support the adoption of the policy proposition
	2. Recommend its approval as an IYSD

Proposition
This policy statement proposition provides the criteria for serum eye drops, a commissioned product, for the indication of severe ocular surface disease. The policy statement details the criteria for selection to start and stop treatments. This is already a well-established treatment and the cost of the eye drops has not changed. However, the eye drops were removed from tariff and added to the excluded drug list in 2019/20 which had caused some confusion in funding which this policy proposition resolves.

Clinical Panel recommendation
The Clinical Panel recommended that the policy proposition progress as a routine commissioning policy statement.

The committee is asked to receive the following assurance:	
1.	The Head of Clinical Effectiveness confirms the proposal has completed the appropriate sequence of governance steps and includes an: Evidence Review; Clinical Panel Report.
2.	The Head of Acute Programmes confirms the proposal is supported by an: Impact Assessment; Stakeholder Engagement Report; Consultation Report; Equality Impact and Assessment Report; Clinical Policy Proposition. The relevant National Programme of Care Board has approved these reports.

3.	The Director of Finance (Specialised Commissioning) confirms that the impact assessment has reasonably estimated a) the incremental cost and b) the budget impact of the proposal.
4.	The Clinical Programmes Director (Specialised Commissioning) confirms that the service and operational impacts have been completed.

The following documents are included (others available on request):	
1.	Clinical Policy Statement
2.	Engagement Report
3.	Evidence Summary - 3 evidence papers
4.	Clinical Panel Report
5.	Equality Impact and Assessment Report

No	*Outcome measures*	*Summary from evidence review*
1.	Survival	Not applicable
2.	Progression free survival	Not applicable
3.	Mobility	Not applicable
4.	Self-care	Not applicable
5.	Usual activities	Not applicable
6.	Pain	Not applicable
7.	Anxiety / Depression	Not applicable
8.	Replacement of more toxic treatment	Not applicable
9.	Dependency on care giver / supporting independence	Not applicable
10.	Safety	Noble et al (2004) reported a crossover study of 16 patients (31 eyes, as one patient had only one eye). Patients were randomised to be treated with three months of autologous serum eye drops followed by three months of conventional treatment, or three months of conventional treatment followed by three months of autologous serum eye drops. During this trial, one patient developed cataracts causing significant visual loss treated successfully by cataract extraction. No other adverse events were reported.

11.	Delivery of intervention	Not applicable

No	Outcome measure	Summary from evidence review
1.	Rose Bengal staining	Rose Bengal is a bright red stain that is adsorbed to and absorbed by compromised epithelial cells, mucus and fibrous tissue. Following installation, the eye is observed in white light. In the absence of a complete tear film, and especially in the case of mucin deficiency, rose Bengal is taken up by healthy epithelial cells. Accordingly, this stain is especially useful for investigating dry eye conditions; that is, a dry eye may display extensive staining with rose Bengal, especially if there is a mucin deficiency. Noble et al (2004) reported a crossover study of 16 patients (31 eyes, as one patient had only one eye). See table 1 section 10. No difference was detected between the two groups (treatment with autologous eye drops, and treatment with conventional treatment).
2.	Faces scale	The “faces” scale is a single item, seven category rating scale where the subject is asked to grade their level of comfort (or pain) to match the appearance of one of seven “faces”, which vary in apparent effect. The seven faces are assigned scores of 1 to 7 so the response intervals are assumed to be equidistant on a valid linear scale. Statistical techniques allow the conversion of categorical data into valid linear measurement. This is gaining widespread use in ophthalmology for visual disability and quality of life outcomes assessment. Noble et al (2004); reported a crossover study of 16 patients (31 eyes, as one patient had only one eye). See table 1 section 10. 12 out of 16 patients reported an improvement in comfort with treatment of autologous serum eye drops.
3.	Impression cytology	Impression cytology refers to the application of a cellulose acetate filter to the ocular surface to remove the superficial layers of the ocular surface epithelium. These cells can then be subjected to histological, immunohistological, or molecular analysis.

		Noble et al (2004) reported a crossover study of 16 patients (31 eyes, as one patient had only one eye). See table 1 section 10. Impression cytology analysis in 31 eyes confirmed a statistically significant difference between serum and conventional treatment (p,0.05, Wilcoxon) with impression cytology being better on serum by inspection (n=25, 12 improved, three deteriorated, 10 unchanged). Not all impression samples could be graded (n=1) or taken bilaterally (n=5) and thus no comparison was possible in six eyes.
4.	Schirmer's test	A Schirmer's test determines whether a person's eye produces enough tears to keep their eye moist and healthy. To conduct a Schirmer's test a piece of filter paper is placed inside the lower eyelid of both eyes and the person closes their eyes. After 5 minutes the filter paper is removed. The clinician then assesses how far the tears have moved down the paper. In general, the smaller the amount of moisture on the paper, the fewer tears the person has produced. The test is mainly performed on people experiencing dry eyes. Franchini et al (2019) carried out a systematic review and meta-analysis. They identified 19 randomised controlled trials comparing the use of autologous serum eye drops to controls (artificial tears alone, saline, placebo, bandage contact lenses, umbilical cord serum, hyaluronic acid or no treatment), with a total of 729 patients. Results of the Schirmer test were available from five trials. Pooled data did not show a clear difference on the Schirmer test (mean difference 1.05; 95% confidence intervals range from -0.17 to -2.26) with the use of serum eye drops.
5.	Tear film break up time	Tear film break up time is a clinical test used to assess dry eye disease. Fluorescein is instilled into the patient's tear film, and the patient is asked not to blink while the tear film is observed. The tear film break up time is recorded as the number of seconds that elapse between the last blink and the appearance of the first dry spot in the tear film. A tear film break up time of under ten seconds is considered abnormal. Franchini et al (2019) carried out a systematic review and meta-analysis. See table 2 section 4. Pooled data from six trials (544 eyes) showed a slightly higher increase in tear film break up times in autologous

		serum compared to control (mean difference 2.68; 95% confidence intervals 1.33 to 4.03).
6.	Ocular Surface Disease Index	The Ocular Surface Disease Index is a 12 item questionnaire designed to provide a rapid assessment of the symptoms of ocular irritation consistent with dry eye disease and their impact on vision-related functioning. Franchini et al (2019) carried out a systematic review and meta-analysis. See table 2 section 4. Pooled data from three trials (224 eyes) showed a greater decrease in the Ocular Surface Disease Index in autologous serum drops compared to controls (mean difference -11.17; 95% confidence intervals range from -16.58 to -5.77).

Considerations from review by Rare Disease Advisory Group
Not applicable

Pharmaceutical considerations
The clinical commissioning policy proposition recommends serum eye drops for the treatment of severe ocular surface disease for all age groups. This is a special (i.e. unlicensed) product which is excluded from tariff.

Considerations from review by National Programme of Care
1) The proposal received the full support of the Trauma PoC Board on the 12th February 2020