Cost-effectiveness of Ikervis® in severe dry eye disease in the UK


Contact: twendt@iconhealth.com, brendy.mortier@gmail.com

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Background:

• Dry eye disease (DED) (keratoconjunctivitis sicca) is a multifactorial disease of the tear and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased sensitivity of the tear film and inflammation of the ocular surface (1-3).

• Currently available treatment options include artificial tear products, lubricants, topical steroids and cyclosporin A (CsA). Artificial tears (AT) aim to alleviate mild to moderate symptoms by replacing or restoring moisture on the ocular surface, providing only short-term relief, and requiring frequent dosing throughout the day. The preservative in many artificial tear products often causes eye irritation.

• Ikervis® is a sterile, polycarbonate-based lubricant ophthalmic emulsion that contains the active ingredient CsA Ph. Eur. at a concentration of 1 mg/ml, 0.1% w/v. CsA has an anti-inflammatory effect on the cornea and the conjunctiva thereby reducing inflammation in the eye (4). The emulsion formulation is specifically designed to prolong the residence time of each eye drop on the epithelial layer of the eye.

• Ikervis® has been shown to be effective in the composite efficacy endpoint (corneal fluorescein staining improvement of at least 3 grade on the modified Oxford Scale and improvement in at least 30% of the Ocular Surface Disease Index which was the model) in a total of 175 eyes in patients with symptoms of keratoconjunctivitis sicca (5).

Methods:

• The Markov model framework to assess the cost-effectiveness of Ikervis® plus AT minus AT with AT alone, while accounting for the AT in adult patients with DED and severe keratitis whose disease had not been adequately responded for by AT alone. A time horizon of 3 months and monthly cycles were used. All costs and benefits were discounted at 3.5% per annum.

• The model captures three frontline therapy states; AT, Ikervis + AT and AT alone.

• Dosage:

  - AT alone: 1-2 drops 4 times/day.
  - Ikervis + AT: 1 drop BID, AT 4 times/day.

• Sensitivity analysis

  - A number of economic scenarios (table 3) including use of a less stringent response criteria (CFS ≥ 3, OSDI ≥ 30%), literature sourced utility values and a 3 month initial treatment period rather than the 6 month initial treatment period used for the base-case analysis were conducted to assess the structural integrity of the model. Use of the CFS≥3, OSDI ≥ 30% response criteria increased the ICER to £35,091 per QALY gained. Literature sourced utility values marginally increased the ICER to £34,765 per QALY gained, and a 3 month initial trial period reduced the ICER to £18,789 per QALY gained.

Base case results:

• The base case analysis shows that, compared to AT alone, Ikervis + AT results in an incremental lifetime cost to the UK National Health Service (NHS) of £1,074 per patient (£10.87 versus £11.98) but offers an additional £2,687 QALYs (0.744 versus 0.597). From Table 3 it can be seen that the incremental cost-effectiveness ratio (ICER) is £19,156 per QALY gained.

• The cost-effectiveness plane arising from the probabilistic analysis is presented in Figure 3 and the associated cost-effectiveness acceptability curve in Figure 4.

• Probabilistic sensitivity analysis confirms that Ikervis + AT produced a benefit to patients, generating a utility gain compared to AT in all 1000 simulations.

• At a cost-effectiveness threshold of £30,000 per QALY gained, Ikervis is cost-effective in approximately 46% of simulations. This increases to 71% at £30,000 per QALY gained. The probabilistic ICER of Ikervis is £14,853 per QALY gained.

• Figure 5 presents graphically the ICER of Ikervis with a range of alternative response utilities. Ikervis becomes cost-effective at a threshold of £30,000 per QALY gained at utilities equal to or above 0.7 (i.e., an incremental gain for responders of 0.3), a smaller value than the observed in both SANSKA and the published literature (7, 8).

• Univariate deterministic sensitivity analysis (Figure 6) highlighted that uncertainty surrounding the absolute utility value for treatment responders has the greatest impact on the ICER.

Conclusion:

• In summary, there is robust evidence from two clinical trials (SANSKA and SICCANOVE (5, 6)) of the efficacy of Ikervis® in patients with severe discomfort and severe keratitis compared to AT without ciclosporine.

• These results demonstrate the improvement in the composite CFS-OSDI endpoint (an OSDI improvement from baseline of 20% and a CFS improvement from baseline at least 2 grade) with Ikervis, indicating a clinically relevant therapeutic benefit in comparison to AT without ciclosporine.

• The base-case ICER of £16,456 per QALY gained is consistent with the evidence of the cost-effectiveness of Ikervis® compared with AT at the lowest cost-effectiveness threshold, of £30,000 per QALY gained.

References

(4) SANSKA: a multicenter, randomized, double-masked, 2 parallel arm, vehicle-control study conducted to assess the efficacy and safety of a new, steroid-free, pharmaceutical solution in the treatment of eye irritation in patients with severe keratoconjunctivitis sicca (KCS). SANSKA (Santen, Sweden; United Kingdom). Br J Ophthalmol. 2011;95(6):779-784
(6) SICCANOVE: a multicenter, randomized, double-masked, 2 parallel arm, vehicle-control study conducted to assess the efficacy and safety of a new, steroid-free, pharmaceutical solution in the treatment of eye irritation in patients with severe keratoconjunctivitis sicca (KCS). SICCANOVE (Santen, Sweden; United Kingdom). Br J Ophthalmol. 2011;95(6):779-784