US FDA Regulatory Considerations for Myopia Control Contact Lenses

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Overview

- FDA classification and regulation of contact lenses for myopia control
- Recap of the US FDA Workshop “Controlling the Progression of Myopia”
- When will contact lenses be FDA approved for myopia control?
- Off label use of myopia control contact lenses
FDA Classification of Contact Lenses

- Class I – Low Risk → no premarket notification
- Class II – Moderate Risk → 510(k)
  - Daily Wear Contact Lenses
- Class III – Significant Risk → PMA
  - Extended Wear Contact Lenses
  - Overnight Corneal Reshaping Lenses
  - Contact Lenses Indicated for Myopia Control (including Daily Wear)
Why are myopia control contact lenses regulated as class III devices?

- IFU for Pediatric Sub-Population

<table>
<thead>
<tr>
<th>Pediatric Subgroup</th>
<th>Approximate Age Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn (neonate)</td>
<td>from birth to 1 month of age</td>
</tr>
<tr>
<td>Infant</td>
<td>greater than 1 month to 2 years of age</td>
</tr>
<tr>
<td>Child</td>
<td>greater than 2 to 12 years of age</td>
</tr>
<tr>
<td>Adolescent</td>
<td>greater than 12 through 21 years of age</td>
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</tbody>
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New safety questions raised:
- Increased risk for adverse events (AEs)?
- Are induced axial length changes stable?
FDA Approval Process for Specialized Indication

Currently Marketed/FDA Approved Material

Clinical Evaluation

Premarket Application (PMA)

FDA Approval
Controlling the Progression of Myopia: Contact Lenses and Future Medical Devices

- **Workshop objectives**
  - Background on myopia and current research
  - Expert consensus on clinical study design for the evaluation of contact lenses indicated for myopia control
  - Development of FDA guidance document
Controlling the Progression of Myopia: Panel 1: Selection of Trial Participants

- Refractive error range?
  - -1.00 to -4.00 D

- How to determine refraction?
  - Cycloplegic autorefraction (tropicamide)

- Is spherical equivalent or spherical component the best measure of myopia progression?
  - Spherical equivalent as long as astigmatism <1.00D

- Maximum astigmatism allowed to enroll?
  - 1.50D

- Maximum anisometropia allowed to enroll?
  - 1.50D
Controlling the Progression of Myopia: Panel 1: Selection of Trial Participants

- Age range of enrolled participants?
  - ~7 to 12 years old
- Should progression affect eligibility?
  - No
- Other enrollment factors to consider?
  - No prior atropine
  - No prior bifocal contact lens wear
  - Ethnicity should reflect US population
Controlling the Progression of Myopia: Panel 2: Study Design & Clinical Outcomes

- Control group?
  - Single vision soft contact lens (test: soft multifocal)
- Primary effectiveness endpoint?
  - Both axial elongation and refractive error change
- Clinically meaningful differences for effectiveness endpoint?
  - No consensus
    - Mean difference in axial length increase equivalent to a refractive change of \( \geq 0.75 \text{D} \)
    - Reduction of progression by average of 50%
    - Maybe smaller effect, such as 30% reduction, may be clinically significant if patient is informed
Controlling the Progression of Myopia: Panel 2: Study Design & Clinical Outcomes

- Minimum study duration?
  - 2 to 3 years (if effectiveness endpoints are met)
- Stability of refractive outcome/”rebound effect”?
  - Evaluated over 6 months to 1 year
- What rate of microbial keratitis is acceptable for contact lens wear in the pediatric population?
  - No greater than the current rates for adult contact lens wearers (definition from Schein et al.)
  - 0.2% incidence
Controlling the Progression of Myopia: Panel 3: Patient-Centric Factors & Outcomes

• What patient-reported outcomes (PRO) should be collected in the clinical trial?
  ▫ Centered towards symptoms

• How should PRO be collected?
  ▫ Focus groups both parents (observable) and patients (vision)

• Could patient preference studies be informative for the benefit-risk determination of myopia control medical devices?
  ▫ Yes, as ancillary study
Controlling the Progression of Myopia: Panel 3: Patient-Centric Factors & Outcomes

• What methods could be used to improve enrollment and retention of patients in these clinical trials?
  ▫ Evaluate drop outs in past studies
  ▫ Offer free comprehensive eye care and products

• How could we better engage the parents, children, and potential advocacy groups to ensure these clinical trials yield results that are informative?
  ▫ Social media
  ▫ Focus groups with parents
  ▫ Better understand resistance to studies
  ▫ Engage pediatricians or others in community
When will an overnight orthokeratology modality or multifocal soft lens design be FDA approved for myopia control?
Example: Study Design

**Initial Study**
- Duration: 4 years total → 3 years with treatment; 1 year regression
- Age: ~ 7 – 12 years old
- Total Patient-Years: 1200 (0.4% incidence of MK)
- Test Arm: 225 subjects
- Control Arm: 175 subjects

**Post-Approval Study**
- Duration: 4 years of follow up
- Age: ~ 7 – 12 years old
- Total Patient-Years: 2000 (0.2% incidence of MK)
- Total Patients: 500 subjects
Challenges Associated with Clinical Trials for Myopia Controlling Lenses

- **Recruitment**
  - Randomization
  - Increased Drop-Out Rate with Children
  - Study Length

- **Endpoints**
  - 1 or 2 Adverse Events (AEs) → Failure
  - Effectiveness Endpoints set too high?
When will an overnight orthokeratology modality or multifocal soft lens design be FDA approved for myopia control?

→ Initial FDA Approval process may take 5 to 7 years
Bottom Line

- Eye care professionals are going to have to continue fitting lenses for Myopia Control OFF LABEL
- Ch. 9 Sec. 396 Federal Food, Drug, and Cosmetic Act “Practice of Medicine”
Off-Label Use of Medical Devices: Ch. 9 Sec. 396 FD&C “Practice of Medicine”

- Practitioner-patient relationship allows for off-label use of medical devices
  - “health care practitioner may prescribe or administer any legally marketed device to a patient within a legitimate health care practitioner-patient relationship.”
- Devices cannot be marketed for off-label use
  - “shall not change any existing prohibition on the promotion of unapproved uses of legally marketed devices”
Off-Label Use of Medical Devices:

- Practitioner should:
  - Be well informed about the product
  - Use firm scientific rationale and sound medical evidence
  - Maintain records on use and effects