



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

PDCO evaluation of ophthalmology Paediatric Investigation Plans

- Thorsten Olski, Dr.med. MSc, Paediatric Team, EMA

Expert Meeting Ophthalmology, October 29th 2011





Main considerations

- Low prevalence and difficult recruitment
- Appropriate endpoints and practical feasibility of measurements
- No extrapolation of safety
- Extrapolation of efficacy?
- How to avoid unnecessary trials?
- What is the paediatric need?



Anterior segment: conditions

- Treatment of pain and inflammation
- Prevention of corneal graft rejection
- Atopic keratoconjunctivitis, vernal keratoconjunctivitis, ...
- Limbal stem cell deficiency



Reduction of pain and inflammation - questions arisen

- 3 products discussed. 2 NSAIDs and 1 NSAIDs fixed dosed combination for **postcataract surgery**
- Full waivers requested stating "lower efficacy compared to steroids and the potential risk of bleeding"
- Full waivers agreed by PDCO based on no "significant therapeutic benefit over existing treatment options"



Therapeutic need



Reduction of pain and inflammation - questions arisen

Therapeutic need



- Applicants cite the use of general anaesthesia for cataract surgery in children against studies on local anaesthetics
- Paediatric need for local anaesthetics, antiinflammatory products in this condition? NSAIDs?
- paediatric need in related conditions?



Atopic keratoconjunctivitis and vernal keratoconjunctivitis issues

- Differential diagnosis of both conditions?
- Geographic variation in their absolute and relative prevalence?
 - Inclusion / exclusion criteria
 - Waiver for atopic dermatitis requested by applicants

- How feasible are trials in the age group below 8 years?
 - Age cut off for waiver



Atopic keratoconjunctivitis and vernal keratoconjunctivitis issues

- Active-controlled trials necessary in vernal keratoconjunctivitis or placebo-control acceptable?
 - Optimal study duration/seasonal occurrence?
 - Efficacy endpoint at 4 months?
 - Visual acuity as a valuable additional secondary endpoint?
-
- Composite efficacy score (Oxford scale) of mts 1-4 suggested
 - 2nd EPs photophobia, tearing, itching (all by VAS)
 - 8 month safety follow-up



Atopic keratoconjunctivitis and vernal keratoconjunctivitis issues

- Disease severity/clinical circumstance that would justify the use of ciclosporin?
- Paediatric need



Prevention of corneal graft rejection issues arisen in PIP applications

- “Treatment of neovascularisation prior and/or after a corneal grafting in prevention of corneal graft rejection”. Neovascularisation has been suggested as a surrogate for prevention of corneal graft rejection. Acceptable?
- To which extent do you consider extrapolation from adult trials possible and would you therefore consider clinical studies be conducted in prepubertal children necessary? Based on the prevalence of keratoplasty, the fraction of paediatric patients, and the fraction of high risk patients, how far do you consider paediatric clinical trials feasible?



Prevention of corneal graft rejection issues arisen in PIP applications

- Preferred efficacy endpoint?
- Paediatric need in addition to corticosteroids for more potent immunosuppressant agents in the treatment of paediatric patients, e.g. ciclosporin, in particular in high-risk patients?
- Based on the prevalence of keratoplasty, the fraction of paediatric patients, and the fraction of high risk patients, how far do you consider paediatric clinical trials feasible?



Limbal stem cell deficiency

Autologous stem cell transplants discussed.

- Do you see a need to verify the feasibility and tolerability of the procedure/treatment on children?
- Given the low prevalence to which extent would you consider clinical investigations in children feasible?

Limited number of patients acknowledged by PDCO.



Bacterial conjunctivitis

- Do you see a paediatric need for further ophthalmic fluoroquinolones given the already available products and their treatment positioning?
- Moxifloxacin as a comparator?
- With data in neonates and from 1 – 18 years, possible extrapolation to children 1-12 months?