NHS
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Commissioning Support Unit

Prescribing tip: Interim Information. Please access the most up to date guidance

Boron excipients in Chloramphenicol Eye Drops: New safety warning in children < 2 years

Boron, which is the characteristic element of boric acid, is a widely occurring element. Boric acid is used as an antimicrobial preservative, as a buffering agent to control the pH and as a tonicity-adjusting agent. (1) Boric acid or its salts can be found in medicines including some ophthalmic preparations. **Chloramphenicol eye drops (standard and single use) is an example of an ophthalmic medicine which contains boric acid as an excipient.** Chloramphenicol eye ointment does not contain boric acid.

Fertility studies with boron compounds in rats and mice identified a risk of reduced fertility. As a result the **European Medicines Agency** (EMA) has recommended upper limits on the daily exposure to boron-containing excipients, expressed as equivalent doses of elemental boron. The EMA has instructed that preparations which contain boric acid (and borates) above a certain threshold need to include a warning and appropriate information in their package leaflet. (1) (2)

Amount of boron per age group which may impair fertility if exceeded: (1)

- Children under 2 years – safety limit: 1mg boron/day
- Children under 12 years – safety limit: 3mg boron/day
- Children under 18 years – safety limit 7mg boron/day (*this amount may also cause harm to the unborn child*)
- Adults from 18 years – safety limit: 10mg boron/day (*this amount may also cause harm to the unborn child*)

Many UK manufacturers (though not all have done so yet) of chloramphenicol eye drops have added the following contraindication to their product: *This medicinal product must not be given to a child less than 2 years old as it contains boron and may impair fertility in the future* (3)

The Royal College of Ophthalmologists (RCOphth) have issued a **Safety Alert** in which they highlight important points for consideration, followed by this summary:

- Whilst a theoretical risk to future fertility from boron-containing excipients in chloramphenicol eye drops should not be dismissed lightly, a decision to stop using chloramphenicol eye drops in children also carries risks as there are certain circumstances when there is no suitable alternative preparation. **More details are available in this safety alert**
- More data on the concentration of borates in individual formulations are required however the available data at this time suggests that the recommended maximum daily dose of boron is unlikely to be exceeded with conventional eye drop regimes, even for children under the age of two.
- At the present time, the RCOphth believes that the benefits of chloramphenicol eye drops in paediatric ophthalmic practice for appropriate indications and with courses of appropriate duration outweigh the possible risks posed by boron ingestion.(4)

This advice may change as more information becomes available. The RCOphth seeks to works with the MHRA & the DHSC to ensure the advice given by all national bodies and suppliers is proportionate and supports clinical requirements.

References

1. CHMP. Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' (SANTE-2017-11668) [pdf]. European Medicines Agency; 22nd November 2019.
2. CHMP. Questions and answers on boric acid and borates used as excipients in medicinal products for human use. 9th October 2017 [pdf].
3. Electronic Medicines Compendium. https://www.medicines.org.uk/emc/
4. The Royal College of Ophthalmologists. Safety Alert: Boron additives in Chloramphenicol drops; should ophthalmologists be concerned? 22nd April 2021.

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