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Pharmalgen for the treatment of bee and wasp venom allergy

Consultation on technical content of assessment report for
NICE technology appraisal

Response from Royal College of Paediatrics and Child Health

With thanks to:

- [redacted], Consultant Paediatrician
- [redacted], Academic NAIID
- [redacted], Medicines Committee
- [redacted], Medicines Committee
- [redacted], NW Paediatric Allergy Network
- [redacted], NW Paediatric Allergy Network.

Section number Indicate **section number** -or- **"general"** if your comment relates to the whole report	**Comments** If possible, please provide evidence (citations) to support your statements
General	Should the report look at the evidence re timing of sting related anaphylaxis and the risk from further stings? It is our understanding that if the interval from the anaphylaxis to start of therapy is delayed the risk falls dramatically e.g. After 1 year the risk of future severe reactions returns to baseline.
General	Children have a better outlook than adults in terms of risks of future anaphylaxis and should not be treated with immunotherapy unless there are unusual circumstances, such as keeping bees and being regularly exposed.
General	Would a reference to the actual levels of specific IgE indicating allergy be helpful? Lots of clinics use IgE as opposed to skin testing.
3.4	The major consideration not addressed in this excellent review is that the current comparator treatment option of Adrenalin and attempts at avoidance is not always effective. The most recent data from Dr. R. Pumphrey presented at the 2011 EAACI show that anaphylactic deaths occur despite the use of adrenalin.
General	None of the studies included children and therefore the overall conclusions are only relevant to adults. The need for venom immunotherapy in children is very much less than adults because the natural history of reactions in children is for upwards of 85% to have a lesser reaction on subsequent exposure. There will never be sufficient data from controlled trials of venom immunoRx in children unless there was a very extensive national and international collaboration.
3.5	Contra-indications include chronic heart disease. However, the comparator adrenalin is also contra-

	indicated in such cases. Thus a careful balance of risk/benefit is required. If immunotherapy reduces the risk of needing to use adrenalin this may be the preferred option.
General	The assessment group have carried out a thorough exercise and we would support their conclusions.
General	The methodology by which the literature review has been conducted is very thorough and the authors have highlighted papers where the age range includes children. Overall, the outcomes and conclusions apply to adult practice although on Page 54, the last table applies to children and concludes from the Meta analysis that VIT should be recommended for children with moderate to severe reactions, but not for children with skin reactions alone. In order to further support this conclusion, the points made in 2.6, page 12, regarding further research would be to set up systems to collect data when VIT is administered to children, why, how, types of reactions and recurrent symptoms and signs of reactions, cost etc.
2.4 Page 10	We note that the trials are of poor quality, although the overall age range includes children and no studies were conducted in the UK.
2.5 Page 11	We note 'that the current use of PhVIT in clinical practice in the NHS appears to be based on limited and poor clinical effectiveness research'.
2.6 Page 12	We agree with the points made with respect to further work specifically collecting data for the paediatric age group separately to the adult age group so that meaningful conclusions can be drawn from this to influence our clinical practice. We note for example that reference 6 (bottom of page 13) reports anaphylaxis more commonly in males and in people under 20 years. For any prospective data collection, how many children are under 16, and of age range 16 – 19? This information influences transitional service planning.
3.2.1 Page 14	Mueller grading system Table 1 There is discrepancy as the grades of 'general' and 'severe' have respiratory overlap and the description of 'general' is 'gastrointestinal' when there are respiratory signs described in this category. This is not a system we use in UK paediatric practice.
3.2.2 Page 14	The authors have quoted where possible, prevalence rates in children of local and systemic reactions.

3.4 Page 16	In UK practice, the use of the epipen for children 30kg and over in a dose of 0.3 mg and in a dose of 0.15mg in children under 30kg is common practice. There also need to be teaching programmes for professionals in schools, after school clubs etc. in the use of the epipen for children (this could be cross referenced to the RCPCH Anaphylaxis Care pathway).
3.4.2 Page 17	Assessing the effectiveness of VIT The recommendations as per AAAAI guidelines are in the main geared to adult practice, hence the need to prospectively collect more data for children and young people. Intradermal testing in children is difficult and again experience of this in the UK needs to be quantified, including the risks experienced.
Page 38 Table 7	Conclusions of intervention and patient characteristics show analyses of studies with an age range of 19 – 56.
Page 50 Table 13	The authors have quoted a number of papers with regard to non comparative PhVIT studies which have included an age range for children.
Page 54	We note the conclusion of the meta-analysis regarding children recommending VIT they have a moderate or severe reaction but not for a local reaction, and making a risk/benefit analysis. In the context of this meta-analysis, and as the authors have concluded, there is a need to collect prospective data on the clinical symptoms and signs including QOL, the interventions and outcomes (clinical and economic), risk/benefit analysis in a consistent way.
Page 64	We note the 2006 study by Brown et al (ref 93) and its reported limitations in this review. The paper concludes that VIT should not be offered to children as it is cured by prevention of re -stinging over time.

If you have any queries about this response, please contact [redacted] on clinical.standards@rcpch.ac.uk.