Child prescribing gets health and safety check

Doctors who prescribe medicines for children have never been sure of their precise effect due to limited research and a general reluctance to conduct paediatric clinical trials. But, as Elisabethann Wright and Susan Clements report, European legislation is set to give prescribers new assurances that the medicines they use to treat youngsters are safe

IT HAS been estimated that more than half of medicines prescribed for children in Europe have not been tested or authorised for this use. In newborn babies, the figure rises to 90 per cent, according to the European Commission.

This means a doctor writing a prescription for a child cannot be sure the medicine will be truly effective, what dose is appropriate or exactly what the side-effects may be.

This is because a lack of research and development to adapt medicinal products to the needs of children has left prescribers no alternative but to use products 'off label' — with the associated risks.

The BMA has long been concerned about the use of medicines that are unlicensed for children. When the BMA's 2004 book *Medical Ethics Today* was published it said that, according to the National Audit Office, at that time 90 per cent of hospitalised children were being given medicines unlicensed for them.

The association was also involved in publishing the *British National Formulary for Children* in September 2005, the first national guide to children's medicines.

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New legislation

Now it looks like the lobbying has paid off. New European legislation — the Paediatric Medicines Regulation — came into force in January this year and, from next month, paediatricians will have new assurances that the medicines they are using to treat children are safe.

The regulation aims to balance the ethical issues raised by conducting trials on children with concerns arising from their treatment with products that have not been tested on them, and the effects, both positive and negative, that have not been assessed.

It aims to increase the development of medicines that are intended to treat children, to encourage research into medicines for use in treating children, and improve the quality and quantity of information available in this area.

The new rules mean all pharmaceutical companies seeking to sell their medicines in the EU, whether or not the products are intended to treat children, must comply with stringent requirements or face a possible financial penalty.

The intention is that:

- Data will be generated on the safe and effective use of medicines in all the relevant paediatric age groups
- Medicines will be available to children in appropriate formulations
- Funding will be provided for the study of off-patent medicines
- Studying medicines for use in children will be rewarded by a six-month extension to the patent holder's monopoly on the product
- A new identifying symbol will be introduced to be used on packaging for products that have been authorised for use in children.

In practical terms the rules mean researchers developing new medicines must produce a PIP (paediatric investigation plan) to be approved by the paediatric committee of the European Medicines Agency. This will outline the trials to be conducted in children, taking into account different age groups.

Exemptions and waivers

There will be certain exemptions to this — the requirement to agree a PIP will not extend to generic products, products containing substances acknowledged to have well-established medicinal use as well as herbal and homoeopathic medicines.

Drug companies can also seek waivers or deferrals from the obligation to provide paediatric studies. A waiver may be granted, for example, where evidence is provided that the medicinal product, or class of products, is likely to be ineffective or unsafe in part or all of the paediatric population; where the disease or condition for which the drug is intended occurs only in the adult population; or where a specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

Deferrals of any of the measures included in the PIP must be justified on scientific or technical grounds — for example, where similar tests have not been conducted in adults yet or on grounds related to public health.

Openness

The results of PIP clinical trials will be held on the EU's database of clinical trials in the interests of openness and to avoid repetition of studies.

Companies seeking authorisation to sell their medicinal product must include the results of the PIP or proof of the waiver or deferral. Companies that produce orphan drugs — those that are not commercially viable because of the rarity of the condition they treat — will be rewarded with two years' extra exclusivity.

For older medicines, there will be a paediatric-use marketing authorisation, which gives special protection to firms developing paediatric uses for existing drugs, the patent for which has expired.

The regulation should lead to increased assurance concerning the quality, safety and efficacy of medicinal products prescribed for paediatric use. However, obligations are strict.

It remains to be seen whether the industry will consider the benefits adequate to compensate for the additional studies undertaken and costs involved.

Additional reporting by Lisa Pritchard. Elisabethann Wright and Susan Clements are lawyers at Hogan & Hartson

LEGISLATIVE TIMELINE

July 2007 Paediatric committee of the European Medicines Agency launches

July 2007 The paediatric-use marketing authorisation, which will give protection to firms developing paediatric uses for existing drugs for which the patent has expired, comes into force

October 2007 EU member states should inform the European Commission of the 'effective, proportional and persuasive penalties' they are proposing for non-compliance with the regulation

January 2008 Identifying symbol introduced

July 2008 Applications for marketing authorisations relating to medicines not authorised by the European Commission by January 26, 2007 should include the results of studies conducted in compliance with a paediatric investigation plan

January 2009 Applications for variation or extension concerning a new indication, pharmaceutical form or route of administration of an existing marketing authorisation should include the results of paediatric studies.