Off licence and off label prescribing in children: litigation fears for physicians

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So-called “off label” and unlicensed prescribing refers to the use of medicines outside of the indications for which they are licensed by national regulatory bodies. Off label prescribing is quite common in children, as most drugs are developed only on the basis of trials with adults. Nevertheless, physicians and hospitals can be wary of using medicines in this way for fear of litigation if adverse events occur. Given this unsatisfactory state of affairs, regulatory bodies are beginning to request robust data from pharmaceutical companies with regard to the use of their products in children. In the meantime, off label prescribing remains acceptable if there is no suitable alternative and physicians are confident that they are using agents in accordance with the body of respected medical opinion.

Unlicensed medicines. Some medicines prescribed for children have never been approved (for example, oral midazolam), or the product is not licensed at all (for example, caffeine). In addition, there are also compounds that are licensed for children, but not for adults (for example, methylphenidate).

The prescription of off label and unlicensed medicines for children applies especially in neonatal medicine and hospital practice, but it is also quite prevalent in the community, where the much larger numbers of children mean that it is a major issue.

THE SITUATION IN THE UK

Doctors are allowed to prescribe off label. In the UK, this is covered by the Medicines Act 1968 and the EC Pharmaceutical Directive 89/341/EEC which outlines requirements of the EEC pharmaceutical legislation relating to medicinal products for human use. However, the recent usage by the MHRA of terms such as “contra-indicated” in its statement about the use of drugs (for example, selective serotonin reuptake inhibitors (SSRIs)) in children seems to intrude into medical practice rather than pharmaceutical marketing regulation. Managing authorities, such as NHS Trusts or individual practices, on the other hand, may issue guidelines discouraging or even prohibiting the use of off label or unlicensed medications. Individual doctors may fear litigation by parents if there are adverse reactions to such medicines. Indeed, adverse reactions are more common than with licensed drugs, partly because dosing schedules for drugs developed with reference to adult populations have often not been assessed for children.

FUTURE TRENDS

The current situation regarding the licensing of medicines for children is a profoundly unsatisfactory state of affairs both for children and their doctors. In the US, the FDA has taken several steps to improve matters, including an initiative which requires pharmaceutical companies to

Abbreviations: EMEA, European Medicines Agency; FDA, Food and Drug Administration; MHRA, Medicines and Healthcare products Regulatory Agency.

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review their data to see if adult derived data on effectiveness or dosing can be extrapolated to children. In a paper reviewing this issue it was pointed out that there are occasions where the reverse may apply—approval for a drug indication in childhood may need to be extended into adulthood. Attention deficit/hyperactivity disorder (ADHD) in childhood may need to be extended into adulthood. 16 16 16 16 16 16

Table 1  European examples of unlicensed and off label prescribing for children

<table>
<thead>
<tr>
<th>Reference</th>
<th>Prescribing site</th>
<th>Unlicensed (ICUs) (%)</th>
<th>Off label (ICUs) (%)</th>
<th>Unlicensed and off label (ICUs) (%)</th>
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<tr>
<td>'t Jong et al 7</td>
<td>ICUs</td>
<td>54.0</td>
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<td>Wards</td>
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<td>Chalumeau et al 9</td>
<td>Outpatients</td>
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<td>McIntyre et al 10</td>
<td>General practice</td>
<td>0.3</td>
<td>10.5</td>
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</tr>
</tbody>
</table>

ICUs, intensive care units.

number of UK paediatricians was obtained as to its content and recommendations.

REFERENCES