

they are produced, may result in a degree of natural variability in molecules of the same active substance, particularly in different batches of the medicine. This variation is maintained within strict acceptable limits. Examples of biological medicines include insulins and monoclonal antibodies. **EvGr** Biological medicines must be prescribed by brand name and the brand name specified on the prescription should be dispensed in order to avoid inadvertent switching. Automatic substitution of brands at the point of dispensing is not appropriate for biological medicines. **⚠**

Biosimilar medicines

A **biosimilar medicine** is a biological medicine that is highly similar and clinically equivalent (in terms of quality, safety, and efficacy) to an existing biological medicine that has already been authorised in the European Union (known as the reference biological medicine or originator medicine). The active substance of a biosimilar medicine is similar, but not identical, to the originator biological medicine. Once the patent for a biological medicine has expired, a biosimilar medicine may be authorised by the European Medicines Agency (EMA). A biosimilar medicine is not the same as a generic medicine, which contains a simpler molecular structure that is identical to the originator medicine.

Therapeutic equivalence **EvGr** Biosimilar medicines should be considered to be therapeutically equivalent to the originator biological medicine within their authorised indications. **⚠** Biosimilar medicines are usually licensed for all the indications of the originator biological medicine, but this depends on the evidence submitted to the EMA for authorisation and must be scientifically justified on the basis of demonstrated or extrapolated equivalence.

Prescribing and dispensing The choice of whether to prescribe a biosimilar medicine or the originator biological medicine rests with the clinician in consultation with the patient. **EvGr** Biological medicines (including biosimilar medicines) must be prescribed by brand name and the brand name specified on the prescription should be dispensed in order to avoid inadvertent switching. Automatic substitution of brands at the point of dispensing is not appropriate for biological medicines. **⚠**

Safety monitoring Biosimilar medicines are subject to a black triangle status (▼) at the time of initial authorisation. **EvGr** It is important to report suspected adverse reactions using the Yellow Card Scheme (see Adverse reactions to drugs p. 14). For all biological medicines, adverse reaction reports should clearly state the brand name and the batch number of the suspected medicine. **⚠**

UK Medicines Information centres have developed a validated tool to determine potential safety issues associated with all new medicines. These 'in-use product safety assessment reports' will be published for new biosimilar medicines as they become available, see www.sps.nhs.uk/home/medicines/.

National funding/access decisions The Department of Health has confirmed that, in England, NICE can decide to apply the same remit, and the resulting technology appraisal guidance, to relevant biosimilar medicines which appear on the market subsequent to their originator biological medicine. In other circumstances, where a review of the evidence for a particular biosimilar medicine is necessary, NICE will consider producing an evidence summary (see *Evidence summary: new medicines*, www.nice.org.uk/about/what-we-do/our-programmes/nice-advice/evidence-summaries-new-medicines).

National information In England, see www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/biosimilars-statement.pdf.

In Northern Ireland, see niformulary.hscni.net/ManagedEntry/bios/Pages/default.aspx.

In Scotland, see www.scottishmedicines.org.uk/About_SMC/Policy_statements/Biosimilar_Medicines.

In Wales, see www.wales.nhs.uk/sites3/Documents/814/BIOSIMILARS-ABUHBpositionStatement%5BNov2015%5D.pdf.

Availability The following drugs are available as a biosimilar medicine:

- Adalimumab p. 665
- Enoxaparin sodium p. 96
- Epoetin alfa p. 586
- Epoetin zeta p. 588
- Etanercept p. 667
- Filgrastim p. 599
- Infliximab p. 35
- Insulin glargine p. 476
- Insulin lispro p. 473
- Rituximab p. 550
- Somatropin p. 492

Complementary and alternative medicine

An increasing amount of information on complementary and alternative medicine is becoming available. Where appropriate, the child and the child's carers should be asked about the use of their medicines, including dietary supplements and topical products. The scope of *BNF for Children* is restricted to the discussion of conventional medicines but reference is made to complementary treatments if they affect conventional therapy (e.g. interactions with St John's wort). Further information on herbal medicines is available at www.mhra.gov.uk.

BNF for Children and marketing authorisation

Where appropriate the *doses, indications, cautions, contra-indications, and side-effects* in *BNF for Children* reflect those in the manufacturers' Summaries of Product Characteristics (SPCs) which, in turn, reflect those in the corresponding marketing authorisations (formerly known as Product Licences). *BNF for Children* does not generally include proprietary medicines that are not supported by a valid Summary of Product Characteristics or when the marketing authorisation holder has not been able to supply essential information. When a preparation is available from more than one manufacturer, *BNF for Children* reflects advice that is the most clinically relevant regardless of any variation in the marketing authorisation. Unlicensed products can be obtained from 'special-order' manufacturers or specialist importing companies.

As far as possible, medicines should be prescribed within the terms of the marketing authorisation. However, many children require medicines not specifically licensed for paediatric use. Although medicines cannot be promoted outside the limits of the licence, the Human Medicines Regulations 2012 do not prohibit the use of unlicensed medicines.

BNF for Children includes advice involving the use of unlicensed medicines or of licensed medicines for unlicensed uses ('off-label' use). Such advice reflects careful consideration of the options available to manage a given condition and the weight of evidence and experience of the unlicensed intervention. Where the advice falls outside a drug's marketing authorisation, *BNF for Children* shows the licensing status in the drug monograph. However, limitations of the marketing authorisation should not preclude unlicensed use where clinically appropriate.

Prescribing unlicensed medicines Prescribing unlicensed medicines or medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescriber's professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines, and also inform the