

National Cancer Medicines Advisory Group (NCMAG) Programme

## **NCMAG Guiding Principles**

Version | 2.0

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### Details of revision:

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| 1.0                  | 20 March 2024 | Updated to reflect Scottish Medicines Consortium (SMC) policy change to 'SMC Outwith remit criteria' 1 March 2024 - specifically that on-label biosimilars may now be within NCMAG remit | NCMAG Lead Pharmacist |

## 1. Background

### a) Marketing Authorisation

A company must have a marketing authorisation to advertise and sell a medicine. The marketing authorisation defines the medicine's indication. The indication is information which outlines what the medicine can be marketed for: the illness, the ages of the patients that it applies to, how much to give and how to give it. A marketing authorisation (often referred to as a product licence) is obtained from the Medicines and Healthcare products Regulatory Agency (MHRA).

To get a marketing authorisation, the company must prove that the medicine will treat the illness and is safe to use. This is done by trying it first in clinical trials, usually in adults aged 18-65 years. Information from the clinical trials is then given to the MHRA when the drug company applies for a marketing authorisation. Once a medicine has a marketing authorisation it is said to be licensed.

### b) Access to medicines with a Marketing Authorisation (on-label use)

NHSScotland has a well-established and robust process for access to market authorised medicines and indications through the Scottish Medicines Consortium. The Scottish Medicine Consortium (SMC) review submissions from pharmaceutical companies for new medicines as well as new formulations of, and new indications for, established medicines. Each NHS Board in Scotland is expected to make licensed medicines, accepted by SMC, available to clinicians. Not all licensed medicines are routinely available in Scotland. If not accepted for use they are not placed on a local formulary, however there may be clinical circumstances where use is appropriate. In such cases individual requests for use can be made.

### c) Generic & biosimilar medicines (off-patent use)

Newly licensed medicines have a period of market exclusivity to promote a balance between rewarding new drug innovation and potentially greater public access to drugs that result from competition (the patent period). After the patent period has expired generic or biosimilar versions of the medicines can become available. Review of generic and biosimilar medicines are outwith SMC remit. This becomes particularly relevant for medicines where the originator branded version is not recommended for routine use by SMC on grounds of cost effectiveness. There has been no national mechanism for assessing the cost-effectiveness of generic versions of these medicines once available. The Scottish Government strategy 'Beating Cancer: Ambition and Action' (2016) included the aim of assessing opportunities to maximise improvements for access to off-patent drugs.

### d) Use of medicines outside the terms of the Marketing Authorisation (off-label use)

Pharmaceutical companies cannot advertise or make any recommendations about using a medicine outside the terms of its marketing authorisation. Once a medicine is on the market, the company may decide that it is not commercially viable to try extending the original marketing authorisation(s) to other illnesses. For example, the treatment of rarer cancers or after the patent for the medicine has expired ('off-patent').

In addition to clinical research conducted by the pharmaceutical industry, research is also undertaken by clinicians and academic research organisations. This research provides new evidence to support the use of medicines in different cancers, at different stages of disease or in a different dose to the original marketing authorisation(s).

There are clinical situations when the use of a medicine outside the terms of the marketing authorisation may be judged by the prescriber to be in the best interest of the patient on the basis of available evidence. This is referred to as 'off-label' use. Medicines may be prescribed 'off-label' in the following circumstances:

- For an illness not specified within the marketing authorisation
- For administration by a different route
- For administration of a different dose or schedule
- For a different patient population

Examples of situations where medicines may be prescribed 'off-label' in the treatment of cancer are:

- Rituximab is licensed for use in the two most common B cell lymphomas. It is also effective in the less common types such as mantle cell lymphoma and is used 'off label' to treat patients with these conditions.
- Paclitaxel is licensed to be given once every three weeks. Administering a lower dose once a week has been shown to be as effective in some cancers but with fewer side-effects.

In summary, 'off-label' prescribing of medicines becomes necessary if the clinical need cannot be met by medicines with a marketing authorisation. It is estimated that approximately 40% of prescribing of cancer medicines is off-label.

The SGHD National Cancer Plan (2021) includes a commitment that the National Cancer Medicines Advisory Group, working alongside the Scottish Medicines Consortium and existing local systems for access to cancer medicines, will review and evaluate new options for treatment, including maximising the use of off-label cancer medicines and use of new rapid decision-making processes.

#### **e) Off-label use where an on-label alternative is available**

The General Medical Council advise that the prescribing of off-label medicines may be necessary where there is no suitably licensed medicine that will meet the patient's need, or where a suitably licensed medicine that would meet the patient's need is not available. In 2020, the following legal case, with potentially far-reaching implications, supported NHS use of an off-label medicine over licensed medicines for the same indication, on grounds of significant cost saving. Clinical data showed that off-label use of bevacizumab in the treatment of wet age related macular degeneration was as effective and safe as two other medicines, aflibercept and ranibizumab, both licensed for this indication (on-label use). The cost of treating patients with the on-label medicines was significantly greater than with off-label bevacizumab. A group of 12 Clinical Commissioning Groups in the North East of England adopted a policy to promote the use of off-label bevacizumab for the treatment of wet age-related macular degeneration, with the benefit of significant cost savings.

The lawfulness of that policy was challenged by the manufacturers of the on-label medicines. That challenge was rejected by both the High Court and the Court of Appeal. In what was described as a 'landmark case', the Supreme Court refused an application by a manufacturer of one of the on-label medicines to appeal against the decision of the Court of Appeal.

## 2) Role of NCMAG

Individual NHS Boards and cancer networks already have governance processes to facilitate routine access to 'off-label' and 'off-patent' medicine use. Such use should be supported by appropriate evidence and experience. There is an opportunity for a more efficient, systematic 'once for Scotland' approach to facilitate rapid and effective implementation of off-label and off-patent use of cancer medicines into routine practice and help minimise unwarranted variation.

NCMAG provides a robust process for considering proposals and issuing advice to inform NHS Boards and Area Drug and Therapeutic Committees in determining medicines for local use or local formulary inclusion and to work alongside existing local systems for access to new medicine uses.

### **The scope of the framework excludes:**

- a) medicines without any marketing authorisation (unlicensed medicines) in the UK
- b) situations where a marketing authorisation is likely to be sought for the proposed medicine in the off-label use within 24 months
- c) In situations where a regulatory decision on marketing authorisation is pending for a comparator product for the same off-label use as a proposal received, the suitability for NCMAG review will be considered on a case by case basis
- d) established off-label uses which have already become standard of care nationally
- e) paediatric indications
- f) treatments that do not impact on disease behaviour, for example analgesics for cancer pain
- g) medicines and uses within SMC remit.

## 3) Guiding principles

- a) The following guiding principles will be applied by the National Cancer Medicines Advisory Group to fulfil its remit and meet the overall aim to improve consistency, equity and process efficiency. The framework for consideration of 'off-label' or 'off-patent' use of a particular medicine is used to address areas of unmet need and/or improve patient outcomes (efficacy and/or safety).
- b) The framework is not a barrier to local access for individual patients where there is a clinical need.
- c) The work programme will be driven by clinical need with proposals submitted by clinicians.
- d) The primary purpose is clinical need and clinical interest however health economic evaluation may be undertaken where appropriate.
- e) The prioritisation of proposals for national advice will follow agreed criteria based on clinical need and evidence of variation in practice.
- f) The operational framework for national advice is consistent, evidence-based and meets specific criteria and standards.
- g) The framework underpins clinical care and supports shared decision-making discussions between the patient and clinician.
- h) The framework improves equity of access, supports a 'Once for Scotland' approach, minimises unwarranted variation and facilitates rapid and effective implementation of appropriate use of cancer medicines into routine practice.