APR. 25

INFORMATIVE NOTE

HEALTHCARE, LIFE SCIENCES & PHARMACEUTICALS

Use of medicines under off-label conditions

National Commission of Pharmacy and Therapeutics guidance note 19/March/2025

The National Commission of Pharmacy and Therapeutics (Comissão Nacional de Farmácia e Terapêutica – **"CNFT"**) approved Guidance Note 19/March/2025 on the use of medicines under off-label conditions on 14 March 2025.

Off-label use – the use of a medicine for an unapproved indication or in an unapproved age group, dosage or route of administration – is becoming increasingly important in clinical practice. This importance is justified by the complexity, length of time and financial cost associated with the process of technical and scientific evaluation of a medicine or a new therapeutic indication. The off-label use of medicines thus allows medicines to be used to treat pathologies for which the medicine does not have an approved therapeutic indication.

Off-label prescribing has become increasingly common and there are no specific regulations governing the practice. For this reason, the CNFT has considered it necessary to make a number of proposals, the main aim of which is to help standardise the actions of the Local Pharmacy and Therapeutics Commissions (Comissões de Farmácia e Terapêutica Locais – "**Local CFTs**") when they receive requests for authorisation to use off-label medicines.

The CNFT therefore proposes:

A review of the conditions for the use of off-label medicines

The use of off-label medicines is restricted and depends on meeting all of the following conditions:

- There is no drug (active ingredient) with an approved indication for the patient's clinical situation, or the off-label use itself has a favourable risk-benefit ratio compared to the available alternatives;
- Off-label use is based on scientific evidence that therapeutic outcomes with a favourable risk-benefit ratio for the patient can be expected with the use of drugs in this regimen;
- A guarantee that the patient is properly monitored.

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Classification of applications for off-label use

The CNFT also proposes that local CFTs classify applications for off-label use into three different groups, depending on the specific case and conditions of use:

	Grouping	Consent
Group 1	Use of off-label medicines o Which have **recognised clinical evidence** and fully established off-label use in clinical practice; o Which have been used off-label for **more than 3 years** o Which have published consensus therapeutic guidelines and can be considered as **"established use"**.	The process of obtaining patient consent can be **simplified** by **limiting its written form to medicines** (active substances) **for hospital use, but always with a note in the relevant clinical record.**
Group 2	Medicines that have been in use for **at least three years** for other indications and where experience of use suggests that there is **adequate knowledge of adverse effects, and a cost that has been negotiated and approved by the National Health Service.**	There must be a **prior assessment by the local CFT and Ethics Committee ("EC")** on a case-by-case basis, taking due account of the available scientific evidence and the clinical condition of the patient. Informed consent must be provided in **writing.**
Group 3	Off-label use of **innovative medicines** (active substances) with significant complexity and lack of safety and efficacy data.	**Prior assessment by the CFT and the EC is required on a case-by-case** basis, taking due account of the available scientific evidence and the clinical condition of the patient. As innovative medicines are usually expensive, it is essential that the CFC carries out not only a pharmacotherapeutic assessment but also an **economic assessment** (cost-effectiveness). Informed **consent** must always be given in **writing,** and the final decision, duly informed, must be **validated by the board of directors of the organisation involved.**

Conditions of the medicine supply chain for off-label prescriptions

In addition to the conditions on which the off-label use of medicines depends and the categorisation of each use, the CNFT also indicates the conditions that must be met by the medicine supply chain in order to issue the prescription in question:

- The prescription for use in a hospital or primary health care setting must indicate that it is for off-label use and this information must be recorded in the patient's clinical file;
- When authorised by the CFT, the scientific evidence or clinical consensus must be considered on a case-by-case basis in the specific context of the disease, the objectives to be achieved and the patient;

The pharmacist must have the necessary conditions to adequately inform the patient about the correct use by having access to the patient's clinical information at the time of dispensing.

- Adequate patient monitoring must be ensured, with the clinical success and risk indicators to be recorded and the times for monitoring and informing the Local CFT being defined at the time of authorisation;
- The local decision-making process must be adapted to the degree of urgency, react in a timely manner and provide for exception mechanisms;
- When validating Group 1, the pharmacist must take into account the suitability of the off-label use of the medicine in accordance with locally approved therapeutic protocols. In the absence of a therapeutic protocol, applications must be submitted to the local CFT and EC for prior assessment;
- The pharmacist must have the necessary conditions to adequately inform the patient about the correct use by having access to the patient's clinical information at the time of dispensing;
- The healthcare professional administering the medicine must be aware that it is an off-label use and of the need to monitor for unusual adverse reactions and the appropriate measures to control them. ■

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