health
Department:
Health
REPUBLIC OF SOUTH AFRICA

POLICY FOR CLASSIFYING MEDICINES INTO THERAPEUTIC CLASSES FOR PURPOSES OF THERAPEUTIC INTERCHANGE

VERSION 9.0; 6 July 2021

1 Purpose

The purpose of this policy is to provide guidance for the placement of medicines in therapeutic classes to support therapeutic interchange for purposes of procurement, prescribing, and providing alternatives for prescribers in the case of challenges to medicine access and supply.

2 Scope

2.1 This policy is applicable at national, provincial, district and facility levels.

2.2 This policy relates to the placement of medicines into therapeutic classes and the therapeutic interchange of medicines in such classes.

2.3 This policy does **not** relate to generic substitution as provided for in the Medicines and Related Substances Act (Act 101 of 1965) or to therapeutic interchange by a pharmacist or other person dispensing a prescription, which is not provided for in South African legislation *(Refer Section 6: Legislative provisions).*

3 Objective

The objective of this policy is to outline:

3.1 Allocation of medicine into therapeutic classes;

3.2 Responsibilities for implementation of therapeutic interchange;

3.3 Conditions under which therapeutic interchange can take place.

4 Definitions

4.1 **Pharmaceutical and Therapeutics Committee (PTC)** means a multidisciplinary committee, established at provincial, district or institutional levels whose core function is to maintain a medicines formulary system; promote rational medicine use including patient safety and; support procurement and financial management relating to medicine[1].

4.2 **Procurement** refers to the process of acquiring supplies, including those obtained by purchase, donation, and manufacture.

4.3 **Therapeutic class** means a group of medicines which have active ingredients with comparable therapeutic effects. Medicines in a therapeutic class may or may not belong to the same pharmacological class, may differ in chemistry or pharmacokinetic properties, and may possess different mechanisms of action, result in different adverse reactions, and have different toxicity, and drug interaction profiles. In most cases, these

[1]National Department of Health. National Policy for the Establishment and Functioning of Pharmaceutical and Therapeutics Committees in South Africa. 19 January 2015.

medicines have close similarity in efficacy and safety profiles, when administered in equipotent doses for a specific indication[2].

4.4 **Therapeutic interchange** means the prescribing of a medicine in the place of a medicine that was originally prescribed, provided that both medicines are from the same therapeutic class.

4.5 **International non-proprietary name** (INN) means the unique name which is globally recognised and facilitates the identification of pharmaceutical substances or active pharmaceutical ingredients[3].

4.6 **National Essential Medicines List Committee** (NEMLC) refers to the non-statutory, advisory, committee constituted in terms of the National Drug Policy (1996) and appointed by the Minister of Health. The primary objective of the NEMLC is to develop and review a list of essential medicines for use in the public sector using generic names.

4.7 **Expert Review Committee** of NEMLC refers to the standing committees constituted to support the NEMLC in the development of the Standard Treatment Guidelines (STGs) and Essential Medicines List (EML).

5 Background

5.1 The Minister of Health has appointed the National Essential Medicines List Committee (NEMLC) to formulate and revise the Standard Treatment Guidelines (STGs) and Essential Medicines List (EML). External stakeholders are given an opportunity to provide input during the review process.

5.2 Therapeutic classes are mentioned in the “Medicine treatment” section of the national STGs which provides a class of medicines followed by an example such as, HMGCoA reductase inhibitors (statins) e.g. simvastatin. These therapeutic classes have been designated where none of the members of the class offer any significant benefit over the other members of the class for a specific indication.

5.3 Although medicine selection informs contracting, these two processes may not occur in a synchronised fashion. The least expensive medicine in a therapeutic class at the time of the review is currently cited in the STGs and EML.

6 Legislative provisions[4]

6.1 Section 22F of the Medicines and Related Substances Act (Act 101 of 1965) provides for **Generic Substitution** -

[2]Gray T, Bertch K, Galt K, Gonyeau M, Karpiuk E, Oyen L, Sudekum MJ, Vermeulen LC; American College of Clinical Pharmacy. Guidelines for therapeutic interchange-2004. Pharmacotherapy. 2005 Nov; 25(11):1666-80.
[3] World Health Organisation. International Non-proprietary names, 2016. http://www.who.inc/medicines/services/inn/en/
[4]Medicines and Related Substances Act (Act 101 of 1965).

Subject to subsections (2), (3) and (4) of Section 22F, a pharmacist or a person licensed in terms of section 22C (1) (a) shall -

(1) (a) inform all members of the public who visit the pharmacy or any other place where dispensing takes place, as the case may be, with a prescription for dispensing, of the benefits of the substitution for a branded medicine by an interchangeable multi-source medicine, and shall, in the case of a substitution, take reasonable steps to inform the person who prescribed the medicine of such substitution;

(b) dispense an interchangeable multi-source medicine instead of the medicine prescribed by a medical practitioner, dentist, practitioner, nurse or other person registered under the Health Professions Act, 1974, unless expressly forbidden by the patient to do so.

(2) If a pharmacist is forbidden as contemplated in subsection (1) (b), that fact shall be noted by the pharmacist on the prescription.

(3) When an interchangeable multi-source medicine is dispensed by a pharmacist he or she shall note the brand name or where no such brand name exists, the name of the manufacturer of that interchangeable multi-source medicine in the prescription book.

(4) A pharmacist shall not sell an interchangeable multi-source medicine-

(a) if the person prescribing the medicine has written in his or her own hand on the prescription the words 'no substitution' next to the item prescribed;

(b) if the retail price of the interchangeable multi-source medicine is higher than that of the prescribed medicine; or

6.2 *'interchangeable multi-source medicine'* is defined in the Medicines Act as *'medicines that contain the same active substances which are identical in strength or concentration, dosage form and route of administration and meet the same or comparable standards, which comply with the requirements for therapeutic equivalence as prescribed';*

6.3 Regulation 2 of the General Regulations published in terms of the Medicines Act describes the requirements for *therapeutic equivalence*, namely -

(1) *A medicine is considered therapeutically equivalent to another medicine if both medicines are -*

(a) pharmaceutically equivalent, in that they contain the same amount of active substances in the same dosage form, meet the same or comparable standards and are intended to be administered by the same route; or

(b) pharmaceutical alternatives, i.e., contain the same active moiety but differ either in chemical form of that moiety or in the dosage form or strength; and

(2) after administration of the same molar dose, their effects with respect to both efficacy and safety are essentially the same.

(2) Therapeutic equivalence is determined from comparative bioavailability, pharmacodynamic, clinical or in vitro studies which meet the requirements and accepted criteria for bioequivalence as determined by the Authority'.

6.4 It must be noted that South African law does not allow for a product in the same therapeutic class, but different from the product prescribed, to be dispensed by a pharmacist or pharmacist's assistant. Such interchange requires a new prescription,

which may be informed by the designation of a therapeutic class in the Standard Treatment Guidelines.

7 Designation and use of therapeutic classes

7.1 The NEMLC will designate therapeutic classes for a condition, where appropriate.

7.2 The NEMLC will identify a list of medicines by INN, dosage form and dose that fall into each therapeutic class.

7.3 The Affordable Medicines Directorate will maintain the list of medicine that fall into each therapeutic class.

7.4 Such therapeutic classes may be used during the contracting process to achieve the most economically advantageous contract, offer the market the largest volume, and increase the number of competitors, thereby offering the opportunity for cost efficiencies by stimulating robust competition. It must be noted that when a medicine is placed in more than one therapeutic class, and dose titration or dose adjustment is likely to occur, this must be taken into consideration during the contracting process to enable continuity of clinical care.

7.5 The designation of medicines into therapeutic classes may also assist with remedial actions to mitigate challenges to security of supply, by providing suggested alternatives which have already been approved by NEMLC, for therapeutic interchange by prescribers.

8 Procedure for the establishment of therapeutic classes

8.1 In order to establish therapeutic classes, the appropriate Expert Review Committee of NEMLC will:

- 8.1.1 Identify a medical condition for a population of interest;
- 8.1.2 Identify all possible therapies used to treat the condition in the population of interest;
- 8.1.3 Identify the parameters for comparison of the medicines (see section 8.2 below);
- 8.1.4 Conduct a rigorous evidence based review to evaluate the outcome of interest, using the parameters for comparison, for the therapies being compared.

8.2 The parameters for comparison of therapies may include but are not limited to:

- 8.2.1 Pharmacology of the medicine;
- 8.2.2 Adverse drug reaction profiles;
- 8.2.3 Mechanism of action;
- 8.2.4 Drug interactions;
- 8.2.5 Pharmacokinetics data;
- 8.2.6 Dosage form, route and ease of administration and use;

8.2.7 Potential risks, such as contraindications, warnings, and precautions (including high risk patient populations e.g. elderly patients, pregnancy, liver and kidney disease and co-morbidities);
8.2.8 Requirements for clinical monitoring and patient management;
8.2.9 Availability of product, including but not limited to registration of the product in terms of the Medicines and Related Substances Act (Act 101 of 1965); and
8.2.10 Any additional monitoring and management requirements relating to management of the supply chain, prescribing and dispensing.

8.3 If the evidence based review shows the medicines have a comparable therapeutic effect, and that the therapies are similar with regard to the parameters on which they were compared, the expert review committee will make a recommendation to NEMLC for the designation of these agents into a therapeutic class, providing an appropriate dose and administration recommendation for each therapeutic alternative.

8.4 Supporting evidence should be preferably derived from meta-analyses, systematic reviews or randomised clinical trials published in peer-reviewed literature.

8.5 In order to ensure transparency in decision making, stakeholders will be given an opportunity, by NEMLC, to comment through a call for comment process.

9 Responsibilities of Stakeholders

9.1 It will be the responsibility of the NEMLC to:
9.1.1 Outline in the Standard Treatment Guidelines (STGs) and Essential Medicines List (EML) medicines that fall into a therapeutic class for a particular condition by INN, formulation, route of administration, and dose.

9.2 It will be the responsibility of the Bid Specification Committee to:
9.2.1 Consider the practicality of implementing the NEMLC-approved medicines that fall into a therapeutic class for procurement purposes.
9.2.2 Where NEMLC recommendations are not accepted, to document and share the rationale with the NEMLC within 14 calendar days via the Essential Drugs Programme – this may include:
- Issues related to security of supply
- Practical implications
- Accuracy of the process of quantification

9.3 It will be the responsibility of the Affordable Medicines Directorate to:
9.3.1 Outline processes for the phase in of new products and medicines within a therapeutic class; and phase out of previously recommended medicine. This approach is paramount for quality patient care, patient safety, to minimise disruption of services and prevent any wasteful expenditure in the supply chain.
9.3.2 Disseminate therapeutic class and therapeutic interchange information via circulars and electronic means to all relevant stakeholders pertaining to the use of medicines in a therapeutic class. Information provided will include, but not be limited to,

9.3.2.1 which items on a tender may be awarded per therapeutic class, and cases where the same medicine should be awarded across classes to facilitate dose titration and/or adjustment;
9.3.2.2 advice on the importance of monitoring patients when switching from one member of a therapeutic class to another;
9.3.2.3 monitoring of consumption patterns resulting from switching between therapies; and
9.3.2.4 other indications for specific agents in the therapeutic class.

9.3.3 Provide guidance for procurement of an alternative from a therapeutic class during periods where there are challenges to medicines supply.

9.4 It will be the responsibility of provincial, district and institutional PTCs to:

9.4.1 Timeously facilitate communication of policies around designation of medicines as therapeutic classes from the Department of Health to relevant stakeholders;

9.4.2 Implement and oversee processes to facilitate the switch from one member of the therapeutic class to another, and minimise confusion or risks for patients.

9.4.3 Put processes in place for the monitoring and reporting of adverse events and medication errors and ensure that these processes are followed.

9.5 It will be the responsibility of the prescriber to:

9.5.1 Give careful consideration to how therapeutic interchange will affect the therapy of individual patients including transitioning between agents in a therapeutic class (phasing in/ phasing out).

9.5.2 Ensure that when the therapy of a patient is changed from one medicine to another medicine (which is not generic substitution performed in terms of the Section 22 F of the Medicines and Related Substances Act 101 of 1965) **a new prescription is prepared in line with the legislative requirements** of Regulation 33 of the General Regulations published in terms of the Medicines Act.

9.5.3 Inform patients with regard to any therapeutic interchange made with regard to dosing, administration and reporting of possible adverse events

9.6 It will be the responsibility of the person dispensing a prescription to:

9.6.1 Evaluate prescriptions carefully prior to the dispensing thereof;

9.6.2 In cases where medication errors are detected, take appropriate action;

9.6.3 Ensure that all prescribers and persons dispensing prescriptions are trained on the use of therapeutic classes;

9.6.4 Keep prescribers informed of relevant information regarding the medicine available within the therapeutic class at the time of dispensing; as well as planned changes.

9.6.5 Empower patients to manage their transition from one medicine to another.

10 Monitoring

10.1 Any safety, efficacy and quality related concerns experienced with the use of any medicine must be documented and reported for the purposes of establishing trends and initiating further investigation. This is to establish if these are isolated incidents or batch, manufacturer, or medicine specific. Health care professionals

and PTCs, prescribers, persons dispensing medicine and patients must report any adverse effects in accordance with normal requirements for reporting of adverse drug reaction requirements.

10.2 The Affordable Medicines Directorate will from time to time evaluate the effects of the application of this policy.

Version	Date	Amendment(s)
Initial	17 April 2017	
Version 8.0	3 December 2020	• Legislative provisions: amended for correctness • Designation and use of therapeutic classes: consideration of dose titration or dose adjustment • Responsibilities of Stakeholders – Affordable Medicines Directorate: switching and monitoring
Version 9.0	6 July 2021	• Responsibilities of the Bid Specification Committee added by the Bid Specification Committee • Proposed timeline for communication between Bid Specification Committee and NEMLC added