Therapeutic Moiety

Therapeutic Moiety (TM)

Definition and Description

The TM is the functional and clinically significant part of the active ingredient substance(s) present in a medicinal product, and as such, the TM class is an abstract representation of a medicinal product without reference to strength and dose form, focusing only on active ingredient substance(s).

As an abstraction of the NTP class, the TM acts as a grouping concept and the TM itself is often the basis of strength substance for the group of related NTPs. For multi-ingredient products, the TM describes all of the individual active moieties, as an NTP can be associated with only one TM. For example, an NTP containing ipratropium and salbutamol will be associated with the "ipratropium and salbutamol" TM, and will not be associated with the individual TM for "ipratropium" or the TM for "salbutamol". Not all NTPs have to be associated with a TM, although currently all medicinal product NTPs do (the device NTPs do not). NTPs for combination products associate to a multi-ingredient TM describing the active ingredient substance(s) present in all their components.

Therapeutic Moiety Naming Pattern

The Formal Name and the French Description of the TM shall describe the functional part of the active ingredient substance(s) present in a medicinal product (i.e., usually without salt or modifier description – but see below) using the INN, USAN or occasionally CSD name, as reflected in the related NTP concepts, and respecting the Canadian Clinical Drug Data Set guidance for naming substances with a specific letter in the name (e.g., penicillin G).

For example:

- INN
  - sumatriptan
  - amoxicillin
  - amlodipine
  - salbutamol
- USAN
  - nitroglycerin
  - acetaminophen

When a single active moiety has more than one TM, because of clinically significant modifications, then the TM Formal Name and the French Description of the TM shall include the modification, and when necessary indicate the base moiety as TM so as to avoid any ambiguity.
For example:

- dexamethasone (base)
- dexamethasone phosphate

The dexamethasone (base) TM groups only those NTPs that have dexamethasone base as their basis of strength substance, whereas the dexamethasone phosphate TM groups those NTPs that have this substance as their basis of strength substance. If the “(base)” designation were not present, a TM described just as “dexamethasone ”could be interpreted to represent all dexamethasone NTPs regardless of their basis of strength substance (a sort of grandparent concept), making it ambiguous to use.

Therapeutic Moiety Challenges

Therapeutic Moiety for “Elemental Medicines”

Because the TM is “the functional part of the active ingredient substance(s) present in a medicinal product”, it can be difficult to describe TMs for elemental substances, for example potassium and iron; the TM could be “potassium chloride” or just “potassium”; it could be “ferrous sulfate” and “ferric chloride” or just iron.

In almost all cases, the salt/modifier has a significant effect on the clinical use of elemental substances (e.g. it usually dictates the dose quantity that must be prescribed) and therefore prescribers are familiar with and wish to describe both the element and its salt/modifier which is also usually the basis of strength substance). Therefore the “functional part of the active ingredient substance(s) present in a medicinal product” for these medicinal products is “the element with its salt/modifier”, so the therapeutic moiety should reflect this. This pattern is also seen in other national medicinal product terminologies that have a concept class similar to the TM.

Examples:

- potassium chloride
- ferrous sulfate
- ferrous gluconate
- aluminum hydroxide
- sodium phosphate

Therapeutic Moiety for Medicines with significant salts/modifiers

For some medicines, more than one salt/modifier is used as the precise ingredient substance in various manufactured products AND the salt/modifier has clinical significance, usually affecting the description of the strength. Examples include phenytoin, and many of the corticosteroids such as dexamethasone, liposomal products and pegylated products. Some examples are discussed below to illustrate how the authoring of TM concepts requires editorial judgement both to determine clinical significance and the safe description of TM concepts.

Diclofenac:

Diclofenac is available with a variety of NTPs with different precise ingredient substances:

- diclofenac sodium 25 mg gastro-resistant tablet
- diclofenac sodium 50 mg gastro-resistant tablet
- diclofenac sodium 75 mg prolonged-release oral tablet
- diclofenac sodium 100 mg prolonged-release oral tablet
- diclofenac sodium 50 mg suppository
- diclofenac sodium 100 mg suppository
- diclofenac sodium 0.1% ophthalmic drops, solution
- diclofenac sodium 1.5% cutaneous solution
- diclofenac diethylamine 2.32% cutaneous gel
- diclofenac potassium 50 mg oral tablet
- diclofenac potassium 50 mg powder for oral solution

As there are three different basis of strength substances, there could possibly be three TMs as sibling concepts based on including the salt/modifier), as shown here:

- diclofenac sodium
- diclofenac potassium
- diclofenac diethylamine

However, in this case, non-pharmacist users are rarely familiar with these different modifiers and their effects, particularly for the modifier(s) used in some of the topical products, and the differences between the salts for the oral form are not considered to be so clinically significant in Canadian healthcare culture and practice that they must be described in a prescription. Pharmacists have the ability to choose the appropriate salt (for example for a prescription written as “diclofenac [TM] 50 mg oral”) based on their discretion and the patient’s requirements.

The most useful Therapeutic Moiety concept would therefore be a single concept based on the moiety itself:

- diclofenac

Phenytoin:

Phenytoin products are available with different precise ingredient substances:

- phenytoin sodium (e.g., Dilantin 30 mg oral capsules)
- phenytoin base (e.g., Dilantin 30 mg per 5 mL oral suspension)

Not only is the basis of strength substance different, 100 mg of phenytoin sodium is equivalent to 92 mg phenytoin (base) and dosage of phenytoin products may be safety critical

There should therefore be two TMs (as sibling concepts):

- Phenytoin (base)
- Phenytoin sodium

In this case, users must be cognisant of the clinically significant differences between the different precise ingredient substances and how they relate to the strength of the medicinal product, and therefore the dose quantity that a patient would receive. Consequently, most users would usually prescribe an NTP (or even an MP) although in hospital practice, especially when a patient is being newly stabilised, a TM might be used in the prescription.

Doxorubicin:

Doxorubicin products are available in both a conventional form and encapsulated in liposomes.

- doxorubicin hydrochloride 10 mg per 5 mL solution for injection vial
- doxorubicin hydrochloride (doxorubicin hydrochloride pegylated liposomal) 20 mg per 10 mL suspension for injection vial

Currently within medicinal product terminology, there is no specific practice for describing liposomal products using, for example, a separate attribute. Despite being acknowledged as less than ideal, the pattern most often adopted is to include the liposomal content as a modification of the active ingredient substance.

The dose quantity used for liposomal products is usually significantly different from the conventional formulation and the side effect profile is also usually different, so it is important to differentiate these at all levels of the terminology. There should therefore be two TMs (as sibling concepts):

- doxorubicin (pegylated liposomal)
- doxorubicin (conventional)