SNOMED CT Medicinal Product Model Specification v3.0

SNOMED International Release Medicinal Product Model	
including reference to the ISO IDMP Suite of Standards	
Date:	**20200531**
Version:	**3.0**
Status:	**Final**

Amendment History

Version	Date	Editor	Comments
0.1	20171130	Julie James	First draft for comment
0.2	20171215	Julie James	Second draft; some comments resolved, concentration strength for CD added; some additional detail added; formatting issues for tables in Appendix A addressed
0.3	20180329	Julie James	Third draft; additional diagrams added; ingredient count added; strength patterns added; basic description of groupers added
0.4	20180430	Julie James	Fourth draft; diagrams updated, additional text added to clarify ingredient count. Feedback comments addressed
1.0	20181012	Julie James	**Final version; comments addressed, all SCT diagrams taken from SCA, CD presentation and concentration strength clarified, additional information for grouper concepts, glossary added**
2.0	20190520	Julie James	Updated version for summer 2019 release; references to release versions removed; typo corrections, minor clarifications added, dose form information updated
3.0	20200531	Julie James	Diagrams updated to use the axiom modelling. Updated section headings for easier navigation. Additional figures giving examples of grouper concepts. Removed Appendix B - reference to HL7 Structured Product Label Ingredient Roles as no longer relevant (IDMP not focusing on SPL for implementation)

Glossary of Terms and Abbreviations

The following table contains the definition of terms and abbreviations used within this document that are specific to this domain and therefore which provide their primary definition.

Term /Abbreviation	Definition
Active ingredient substance	The substance that provides the intended therapeutic effect of the medicinal product, described usually but not always without modifiers such as esters, salts or other non-covalent derivatives
Administrable dose form	The (pharmaceutical) dose form of a medicinal product for administration to a patient, after any necessary transformation (from the manufactured dose form) has been carried out
Basis of strength substance BoSS	The substance against which the strength quantity of a medicinal product is measured
Clinical Drug CD	A representation of a medicinal product based on description of 1) its precise active ingredient substances only and explicitly, 2) the stated basis of strength substance(s) with strength, expressed as presentation strength with unit of presentation or as concentration strength as appropriate, and 3) with its manufactured dose form
Clinical Drug presentation CD presentation	A representation of a medicinal product based on description of 1) its precise active ingredient substances only and explicitly, 2) the stated basis of strength substance(s) with strength, expressed as presentation strength with unit of presentation or as concentration strength as appropriate, and 3) with its manufactured dose form
Clinical Drug concentration CD concentration	A representation of a medicinal product based on description of 1) its precise active ingredient substances only and explicitly, 2) the stated basis of strength substance(s) with strength, expressed as concentration strength and 3) with its manufactured dose form
Combination Grouper	A concept grouping together medicinal products based on both the chemical structure and behaviour (mechanism of action) of their active ingredient substance(s)
Concentration strength	A type of strength description where the amount of the basis of strength substance present per unitary amount (volume, mass) of the single clinical drug being represented
Disposition Grouper	A concept grouping together medicinal products based on the behaviour (mechanism of action) of their active ingredient substance(s)
Dose form (Pharmaceutical dose form)	The physical manifestation or formulation of a medicinal product that contains the active ingredient substance(s) intended to be delivered to a patient; the pharmaceutical dose form may be a manufactured dose form or an administrable dose form

IDMP	**Identification of Medicinal Products** A suite of ISO standards concerned with the unique identification of medicinal products, primarily within the regulatory domain of use The suite includes: ISO 11615:2017 *Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated medicinal product information* ISO 11616:2017 *Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated pharmaceutical product information* ISO 11238:2018 *Health informatics -- Identification of medicinal products -- Data elements and structures for the unique identification and exchange of regulated information on substances* ISO 11239:2012 *Health informatics - Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated information on pharmaceutical dose forms, units of presentation, routes of administration and packaging* ISO 11240: 2012 *Health informatics - Identification of medicinal products -- Data elements and structures for the unique identification and exchange of units of measurement*
Intimate container	The receptacle or vessel used to contain (or bound) liquid medicinal products into countable entities
Manufactured dose form	The (pharmaceutical) dose form of a medicinal product as it is presented by the manufacturer into the supply chain, before any transformation into an administrable dose form
Medicinal Product MP	An abstract representation of a medicinal product based on description of active ingredient substance(s) that it contains (regardless of any modification of those active ingredient substance(s)), but not exclusively limited by those substances, in that other substances may be present
Medicinal Product only MP only	An abstract representation of a medicinal product based on description of only and exclusively the active ingredient substance(s) that it contains but regardless of any modification of those active ingredient substance(s)
Medicinal Product precisely MP precisely	An abstract representation of a medicinal product based on description of only and exclusively the precise active ingredients it contains
Medicinal Product Form MPF	An abstract representation of a medicinal product based on description of active ingredients it contains, but not limited by that description, and on the (generalised) intended site of use for the product
Medicinal Product Form Only MPF only	An abstract representation of a medicinal product based on description of only and exclusively the active ingredient(s) it contains and on the (generalised) intended site of use for the product
Structural Grouper	A concept grouping together medicinal products based on the chemical structure of their active ingredient substance(s)
Precise active ingredient substance	The substance that provides the therapeutic effect of the medicinal product, described using the fullest and most specific description of the substance *as it is used in the product(s) being represented. This may include* various modifiers, such as salts, esters, polymers (e.g. pegylation), and/or solvates
Presentation strength	A type of strength description where the amount of the basis of strength substance present in the unit of presentation of or in the volume (or mass) of the single clinical drug being represented
Therapeutic Role Grouper	A concept grouping together medicinal products based on a broad description of their use in treatment of disease
Unit of presentation	A qualitative concept that describes a countable entity in which the clinical drug is presented, or in which it is bounded

1. **Introduction**

1.1. **Purpose**

The SNOMED CT Medicinal Product hierarchy provides concepts to describe medicinal products at various levels of abstraction with international applicability and support for interoperability in patient care and health data analysis. It provides a foundation from which member nations can extend with additional concepts suitable for their own healthcare culture and practice, or to which existing terminology can be mapped if required.

This document describes the model for the concepts in the SNOMED Medicinal Product hierarchy; when populated, this model will provide:

- concepts in the international release to meet the core use cases
- a foundation for national medicinal product terminologies
    - for member nations with an existing terminology, the model underpinning the concepts will facilitate both direct use or mapping
    - for member nations without an existing terminology, the concepts provide a consistent starting set of concepts and a model to develop from

The document is primarily a specification; ongoing development will be through the documentation and actual implementation of the machine readable concept model for the Medicinal Product hierarchy and population of this model will be directed by the detailed Editorial and Terming Guidance for the hierarchy (see: Drug Concept Model - Editorial Guidelines for Modeling and Terming).

This document also provides a description of how aspects of the SNOMED Medicinal Product hierarchy correspond with the suite of standards in ISO, collectively known as the "Identification of Medicinal Products standards" (IDMP).[1] These IDMP standards provide a conceptual model for the unique identification of a medicinal product globally, and terminology standard concepts to support this (for example, to describe substances and dose forms). The domain of use for the IDMP standards is primarily regulatory, but since regulatory information is the source and underpinning for the description of medication and medicinal product concepts in a clinical medicinal product terminology, both internationally and nationally, it is important that the SNOMED CT Medicinal Product model and supporting concepts are in harmony with those standards. Compatibility with the IDMP model for identification of medicinal products with facilitate information flow between the two domains of use, for example to support pharmacovigilance. However, there is no sense that this harmony entails “full and exact compliance”; there would be little value in exact duplication. The SNOMED CT Medicinal Product hierarchy therefore provides classes of concepts that are additional to those present in the IDMP model, to support the specific SNOMED CT and patient care/health data analysis use cases.

1.2. **Scope**

The scope of specification for the concept model for representation of medicinal products in the international release of SNOMED CT is limited to pharmaceutical and biological products only; products that represent blood products, foods, additives, and complementary medicines (including homoeopathic products) are currently out of scope. The representation of autologous medicinal products (those created from tissue from and administered back to an individual) is also out of scope. Currently, vaccines, although they are biological medicinal products, are also out of scope.

The international medicinal product model and concepts in the international release will be described in their more abstract form; real or actual products (including branded products and those marketed without a brand name) as authorised by medicines regulatory agencies within jurisdictions are not within scope. Describing the packages in which medicinal products are placed into the supply chain are also not within scope.

1.3. **Audience**

This document is written for those responsible for the development and maintenance of Medicinal Product concepts within SNOMED CT, both in terms of the machine readable concept model and the populating of that model. It is also of value to those in member nations who are or who wish to use Medicinal Product concepts from international release, either directly (with extension where appropriate) or by mapping, in any national medicinal product terminology. It is relevant to those responsible for clinical or research systems using medicinal product concepts in both active medication processes (prescribing, dispensing and administration of medicines) or in recording of medication information, and also particularly to those responsible for systems providing decision support for medication safety.

2. **Model for the representation of Medicinal Products in SNOMED CT**

2.1. **Use cases for the SNOMED CT Medicinal Product hierarchy**

The main use cases for the SNOMED CT Medicinal Product hierarchy are as follows:

1. To provide a consistent and usable set of international medications concepts for member nations to use as a foundation for national medicinal product terminology
    a. For those member nations with an existing terminology, the improved model underpinning the concepts will facilitate both direct use or mapping
    b. For those member nations without an existing terminology, the concepts provide a consistent starting set of concepts and a model to develop from, reducing resource (especially set up costs) and risk in development
2. To provide compatibility with the IDMP model, where possible, for identification of medicinal products. Having compatibility between the patterns used to describe medicinal products in the regulatory environment and those used in clinical care will facilitate the information flow between the two domains of use. For all licensed medicinal products, the prime source of information for their description is their regulatory data; compatibility therefore streamlines the flow of information for maintenance of the clinical terminology. Similarly, for example in pharmacovigilance, the flow of information from clinical records into regulatory reporting, both for suspect and concomitant

medications involved in safety events is streamlined. Describing the relationship between the SNOMED CT Medicinal Product hierarchy and the IDMP model also shows how some SNOMED CT medicinal product concepts complement and add value to IDMP-based concepts, particularly for patient care
3. To facilitate international interoperability of medication concepts for (for example) patient summaries and cross-border care; this is supported most efficiently when the medication concepts themselves are from national extensions built upon or mapped to the international core
4. To facilitate development of international medication decision support, such as allergy checking and duplicate therapy checking, thereby reducing costs of maintenance and implementation
5. To support the use of a classifier on both international and national medicinal product concepts, to facilitate maintenance of the hierarchy
6. To support analysis of medication information in healthcare data for various research purposes
7. To provide medication concepts to support sufficiently defining concepts in other hierarchies within SNOMED CT

2.2. Model: General Comments

2.2.1. Open and closed world views: the existential and universal restrictions in the Medicinal Product model

SNOMED CT as an ontology is constructed on the principle of an open world view (the existential restriction) with each concept having a distinct fully specified name. The implication of the open world view for the medicinal product hierarchy is that a concept represents the set of (real world) medicinal products that contains "(at least) some substance X as an active ingredient", but may contain other unspecified active ingredient substances. This 'open world' view is useful for analysis and in some types of decision support. However, the regulation of medicinal products for sale/supply is based on the 'closed world' view (the universal restriction), where **all** active ingredient substances must be explicitly described. This is also the premise for description of medicinal products in the medication process (prescribing, dispensing and administration). Therefore the Medicinal Product hierarchy differs from other concept hierarchies within SNOMED CT in that some classes of concepts within it are modelled using this 'closed world' view which states that a concept represents a medicinal product that contains "only substance X" as an active ingredient"; no other active ingredient substances are present within it. To implement that "closed world view" with the existing tools and systems of SNOMED CT, the "ingredient count" proxy has been developed; some description of this is given below, with further detailed information being available in the machine-readable concept model. For further details on the open and closed world views, please refer to the relevant SNOMED documentation and training materials, e.g. Description Logic: Advanced Features.

2.2.1.1. IDMP Compatibility

IDMP, being a suite of standards developed in and for the regulatory domain, uses a "closed world" view. The active ingredient substance(s) present in a product **must** be listed in full, with no exceptions, so IMDP exists is the "closed world" view and therefore would be compatible with the "universal restriction" only; the existential restriction is not compatible with the concepts in the IDMP suite of standards, which is particularly important to note for the abstract concepts within IDMP in ISO 11616 (PhPIDs, especially L1, L3 and L4).

2.2.2. Stated and inferred views in the medicinal product model

For further details on the meaning of stated and inferred views, please refer to the relevant SNOMED documentation and training materials for example at 2.3.1 Stated and Inferred Concept Definitions and 8 Alternative Views of Concept Definitions

2.3. Medicinal Product model diagrams

The diagrams below shows the overall Medicinal Product model. Note that in each diagram, no role or disposition grouper concepts are shown. Definitions and detailed descriptions are given in the sections below this overall model introduction. This first diagram is a UML (Unified Modeling Language) class model illustrating the five classes of concepts in the model and the relationships between them, in their three groups (MP, MPF and CD) plus an additional optional sixth sub-class to be populated in limited cases and likely in national extensions only (MP Precise Only). Two classes use the existential restriction (MP and MPF) and four use the (proxy for the) universal restriction (MP only, MPF only, CD and MP Precise Only); MP Precise Only is the optional sub-class that represents a product described explicitly and only by its *precise* active ingredient substances i.e. including clinically significant modification such as "dexamethasone *sodium phosphate*". MP classes are shown in shades of blue, MPF classes in shades of yellow and the CD class in green.

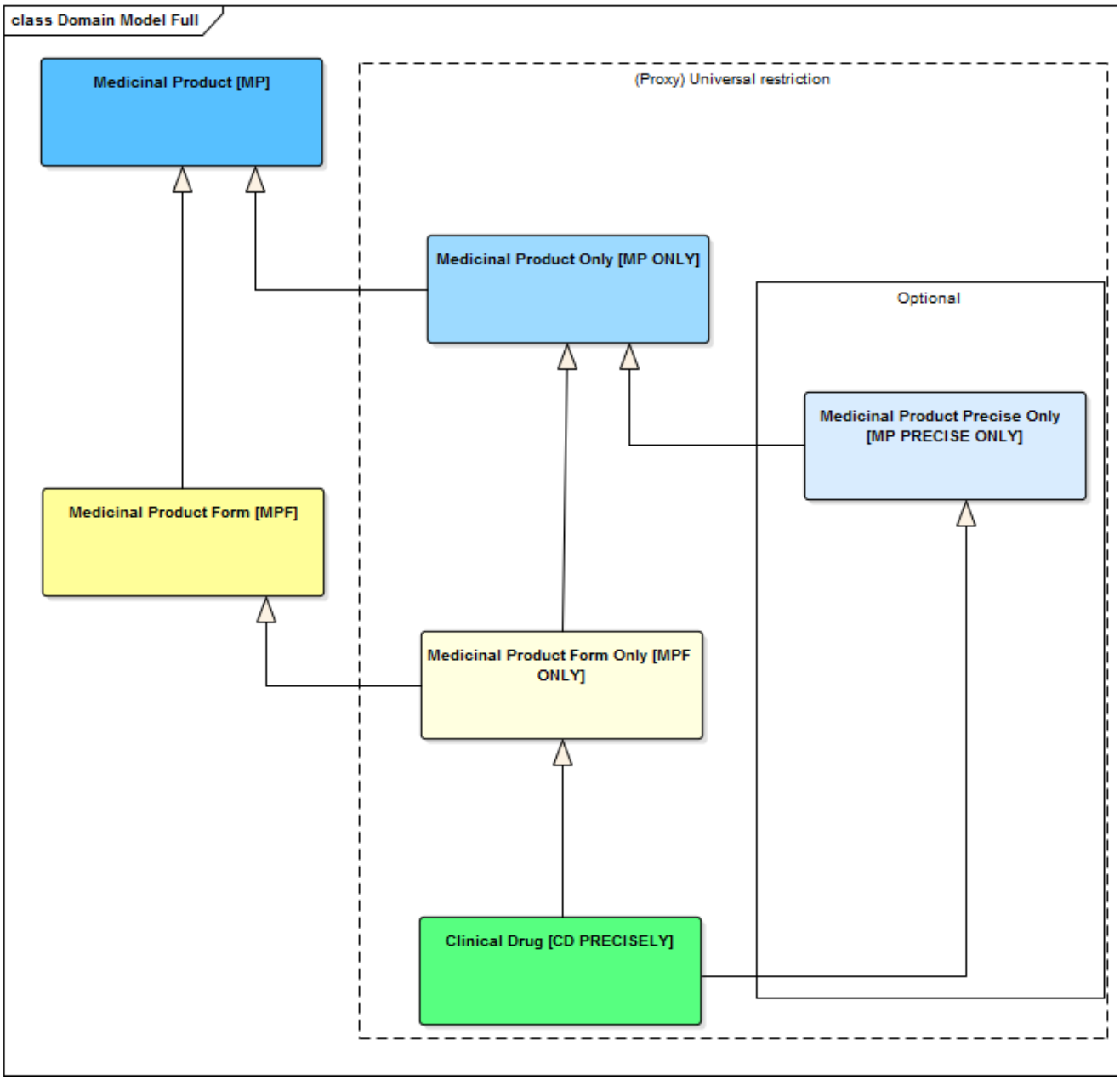


Figure 1: Medicinal Product concept model - International

The second diagram, below, is in SNOMED notation (inferred view), and shows only the five classes that will be populated in the international release, at least for the foreseeable future.
The Medicinal Product model is parented by the 763158003 |Medicinal product (product)| concept, an abstract concept representing an item that has been formulated and manufactured for administration to humans (or animals) for treatment or prevention of disease, for diagnosis of illness or to restore, correct or modify physiological function and which contains an active ingredient substance or combination of substances. This parent concept acts both to scope the domain and, in the future, will separate medicinal products from other products in a larger Products hierarchy, which may include medical devices and certain other products such as foods and cosmetics.

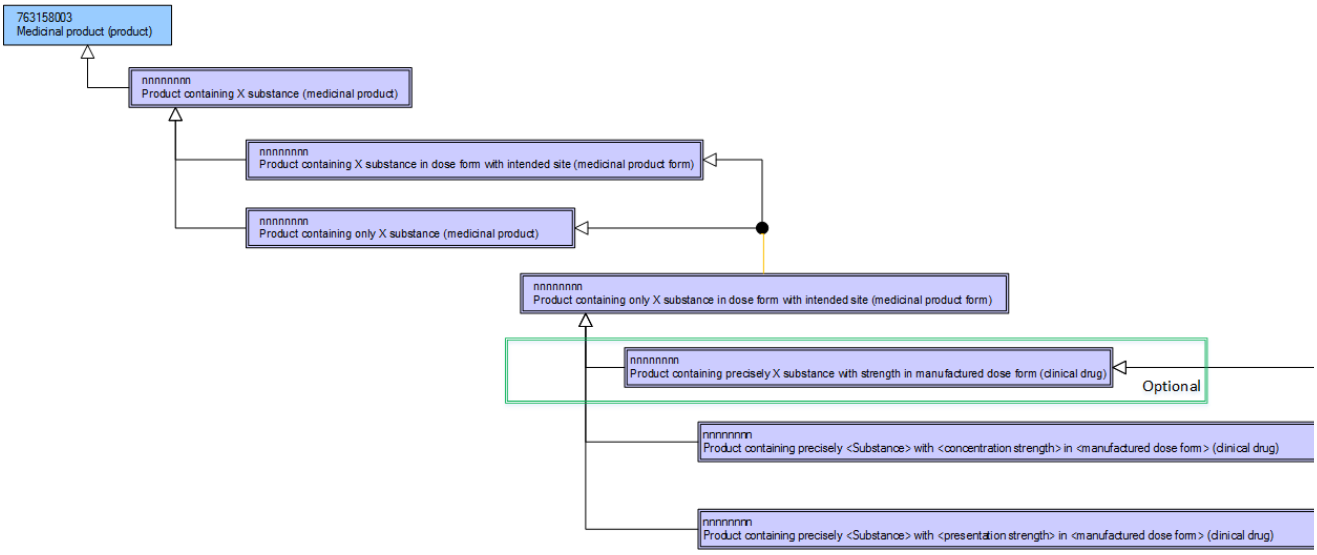


Figure 2: Medicinal Product concept model - International - SNOMED notation

The third model diagram below includes multi-ingredient medicinal products, and therefore has increased complexity. It again shows the three groups (MP, MPF and CD) with MP classes shown in shades of blue, MPF classes in shades of yellow and the CD class in green; each with two single active ingredient representations (X and Y) and one multi-ingredient representation (X + Y) and then the relationships between these. It shows how the single ingredient "containing" classes (the open world classes) subsume the appropriate multi-ingredient class, whereas the single ingredient "containing only" classes (the closed world classes) do not subsume the multi-ingredient class. The optional MP Precise Only class is present but is not shown with any multi-ingredient products, to limit complexity. MP Precise Only multi-ingredient products are discussed below in the Ingredient Count section.

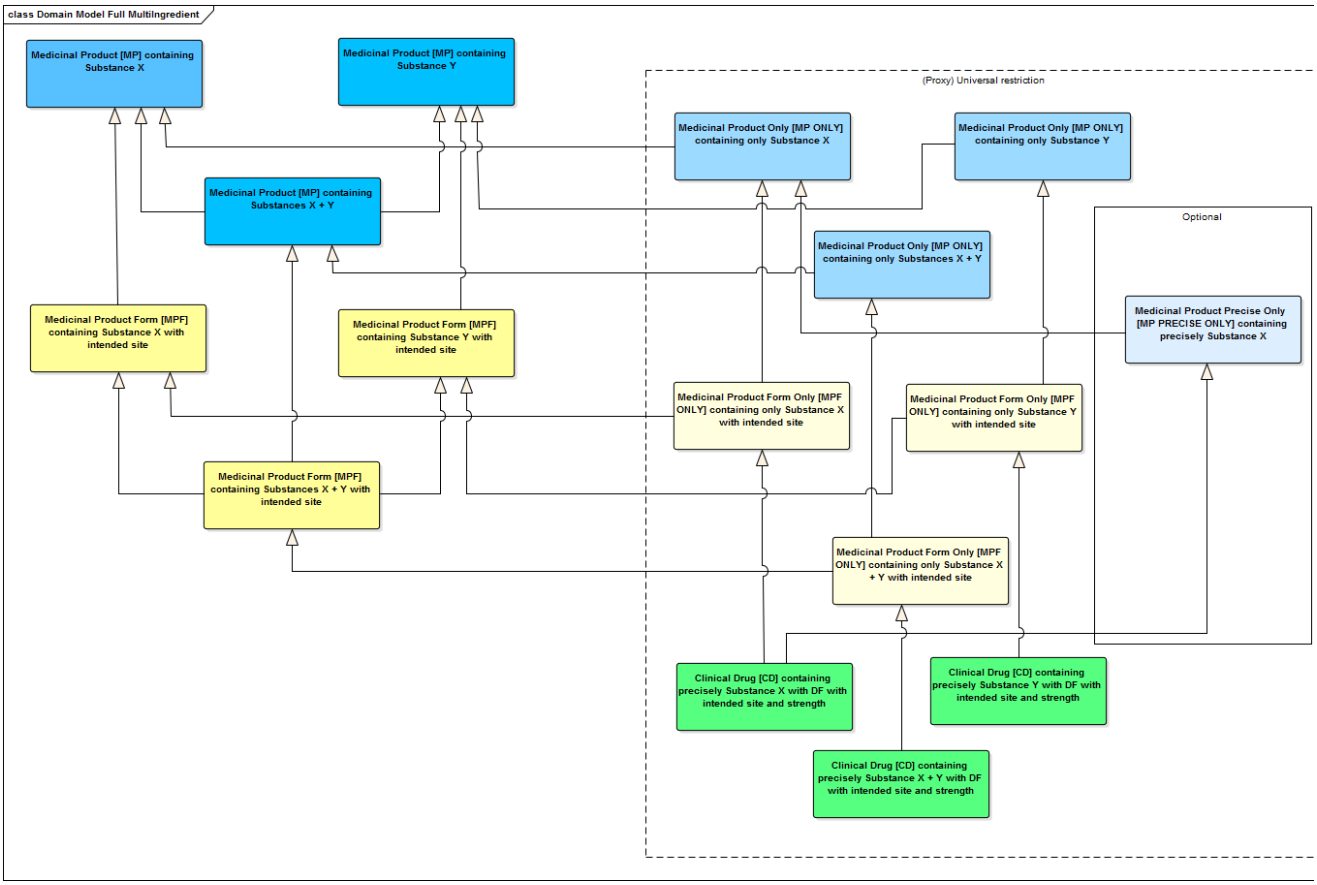


Figure 3: Medicinal Product concept model - International - showing multi-ingredient concepts

In the sections below, each group of classes and its members are defined and described in detail, with their attributes. Detailed definition and discussion of the attributes themselves follows on in a separate section.

2.3.1. Model population

The population of the international release is currently limited to description of those products for which there was already available content within SNOMED CT and for which verification has been obtained by reference to concepts in a small number of national medicinal product terminologies. There is nothing in the specification that deals with availability of medicinal products for use; neither the presence of a concept nor an absence of a concept gives any sense of its availability in the supply chain globally. Indeed, even when a medicinal product ceases to be available anywhere in the global supply chain, its representation will remain as a valid concept for use in historic records and Medication History and Medication Profiles. The rules and principles for ongoing maintenance of concepts within this model are part of the Editorial Guidelines for Modeling and Terming (see above).

In maintaining a medicinal product terminology, concepts are authored to describe those things that exist and can be used in clinical care and/or clinical research. This means that it is the more granular concepts that are usually recognised first, then the less concrete concepts are abstracted from these. In many medicinal product terminologies, this results in their being lowest level child concepts for every parent concept within the model classes. Due to the historic nature of some of the content in the SNOMED CT international release Medicinal Product hierarchy, there will be higher level parent concepts (i.e. MP and MPF concepts) that do not have clinical drug concepts associated with them. These MP and MPF concepts may have had clinical drug type concepts associated with them in the past, but the veracity and provenance of the detailed information to support these CD concepts could not be confirmed, so they have been inactivated whereas the more abstract MP and MPF concepts remain in the international release to support historic data use cases such as analysis and Medication Profiles.

New medicinal products, both from newly authorised therapeutic substances and in new formulations of existing therapeutic substances, are constantly appearing globally. The principles and process for the ongoing maintenance of and addition of new content to the Medicinal Product hierarchy are being developed.

2.3.1.1. IDMP Compatibility

The definition of the 763158003 |Medicinal product (product)| concept as providing the scope of the hierarchy is in agreement with the *scope* of the concept of a medicinal product in IDMP. This is a positive position generally and particularly for any future mapping exercise that might be undertaken, since there should be few concepts that cannot be mapped at some level of granularity. However, in IDMP, and specifically in ISO 11615, the Medicinal Product class represents an authorised medicinal product that consists of one or more Manufactured Items as authorised and available; in this sense it is much more concrete concept than the SNOMED parent concept. This difference is not of great significance other than to understand that the same term ("medicinal product") has a different and more specific meaning in IDMP than in the SNOMED CT Medicinal Product model. Also, the IDMP ISO 11615 model explicitly describes "combination medicinal products" (also known as 'kit' products, 'component' products, 'multi-component packaged products' etc.) where the package placed into the supply chain contains more than one type of component element (clinical drug) within it; since these are correctly packaged products, and packaged products are out of scope of the Medicinal Product hierarchy for the international release, these combination products are not represented in this SNOMED model.

2.4. Grouper concepts

Medicinal products and their representations in a terminology can be put into groups in many ways, both in terms of abstraction and aggregation of product descriptions. In the SNOMED CT Medicinal Product model, the following grouping concepts will be used:

- groupings based on the pharmaceutical characteristics of manufactured medicinal products, and the primary subject of this model and documentation:
    - Medicinal product - grouping based on active ingredient substance(s)
    - Medicinal product form - grouping based on active ingredient substance(s) combined with a grouping of the site of administration of manufactured dose form (parenteral dose forms, oral dose forms etc.)
        - These concepts are also grouped using the site of administration of manufactured dose form as a grouping concept
    - Clinical drug - a grouping based on active ingredient substance(s), with their strength, combined with manufactured dose form
- groupings based on the chemical or behavioural characteristics that the products exhibit:
    - Disposition - grouping based on mechanism of action of the active ingredient substance(s) in the product
    - Structure - grouping based on structural patterns of the active ingredient substance(s) in the product
    - Structure and Disposition - combination of the above

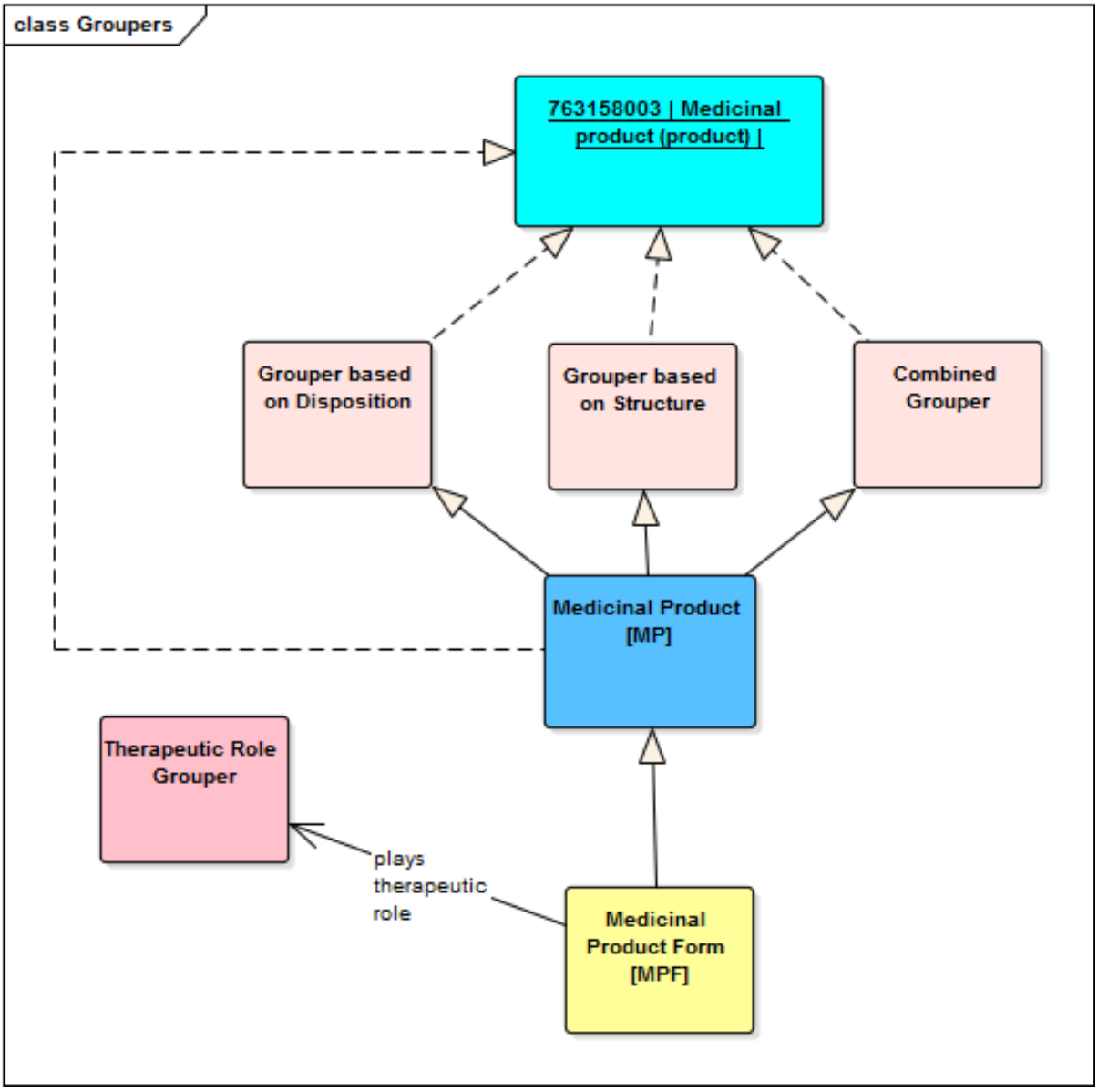


Figure 4: Medicinal Product grouping concepts

2.4.1. Groups of Products based on Disposition

Disposition is a behaviour that something can exhibit (or participate in) given the appropriate context in which to do this. For example, a person may be "disposed" (or pre-disposed) to fidget in their seat when in a stressful situation such as an interview. For medicinal products, disposition behaviour can be thought of as "mechanism of action" of its active ingredient substance(s): the behaviour that the active ingredient substance(s) in the product exhibit when used clinically. Disposition (mechanism of action) is distinguishable from therapeutic role, which is context dependent: for example the mechanism of action of timolol is as a beta-adrenoceptor antagonist; this action can be used therapeutically to reduce hypertension when administered in a product given orally or to treat glaucoma when administered in a product intended to be given ophthalmically. Medicinal products can be collected together into groups based on the disposition of their active ingredient substance(s).

Disposition is a characteristic of the active ingredient substance(s) present in the Medicinal Product, therefore disposition grouping concepts are assigned (inferred) by the classifier to Medicinal Products and include all their child concepts.

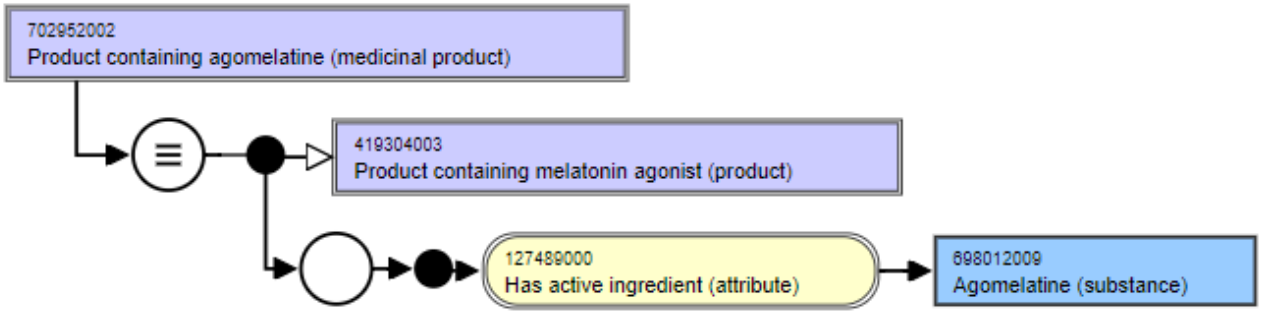


Figure 5: Medicinal Product showing membership of a disposition grouping (melatonin agonist)

2.4.2. Groups of Products based on (Chemical) Structure

All substances have spatial arrangement of the atoms and molecules and bonds that they are constituted from and which therefore govern the final shape that the substance takes; this arrangement is their "structure". Substance structures often follow patterns so that similar structures are grouped together and are often particular name patterns. Medicinal products can be collected together into groups based on the structural pattern (s) of their active ingredient substance(s).

Structure-based grouping is a characteristic of the active ingredient substance(s) present in the Medicinal Product, therefore structure-based grouping concepts are assigned (inferred) by the classifier to Medicinal Products and include all their child concepts.

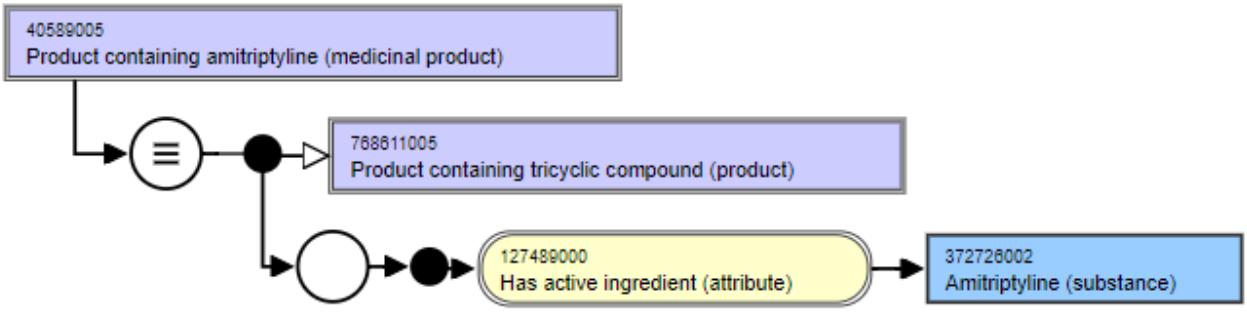


Figure 6: Medicinal Product showing membership of a structural grouping (tricyclic compound)

2.4.3. Groups of Products based on Structure and Disposition

For some medicinal products, their clinical usefulness is related to the combination of both their structure and their disposition; it is the structure that produces the disposition; for example clemastine, a substance whose anti-histamine behaviour is based upon its structure being ethanolamine derived.

Since structure-based grouping and disposition are characteristics of the active ingredient substance(s) present in the Medicinal Product, combined 'structure and disposition grouping' concepts are assigned (inferred) by the classifier to Medicinal Products and include all their child concepts.

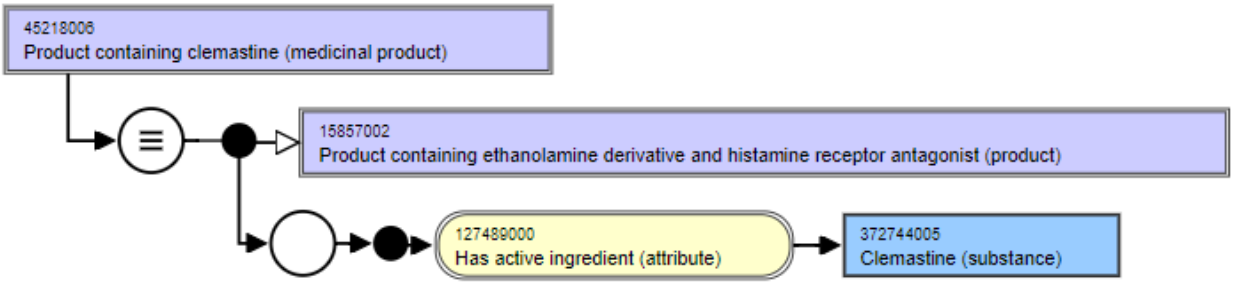


Figure 7: Medicinal Product showing membership of a structure-and-disposition grouping (ethanolamine derivative and histamine receptor antagonist)

2.4.4. Groups of Products based on Therapeutic Role

Medicinal products can be collected together into groups based on the therapeutic role that they are designed to fulfil. Roles are very context dependent and may change over time and with changing circumstances (including the culture and practice of healthcare). Roles are therefore not definitional for medicinal products. Therapeutic role is a broader concept than 'indication for use' of a medicine. Indication may describe information such as the disease(s) that the product may be used in, the intended effect (prophylaxis, cure, symptom relief etc.), the role within an overall treatment regimen (first line, adjunctive etc.) and specific populations for use (e.g. in adults, in children) whereas therapeutic role describes the general condition that the product may be used to treat (e.g. Product acting as antidementia agent) or describes the general treatment effect of the product (e.g. Product acting as haemostatic). Since therapeutic role is often closely associated with product formulation (targeting the therapeutic substance to the correct site of action), therapeutic roles may be assigned to Medicinal Product Form concepts and occasionally to Clinical Drug concepts; if all the products share a therapeutic role, it can be assigned at the higher MP level.

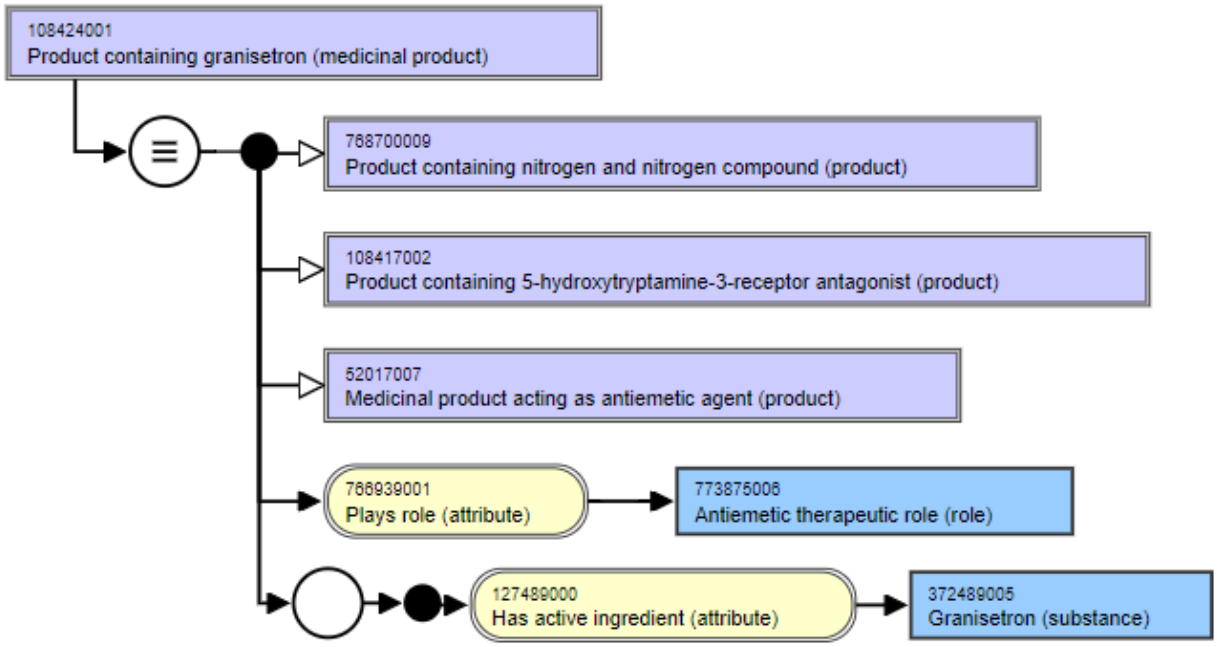


Figure 8: Anti-emetic agent therapeutic role, assigned at Medicinal Product

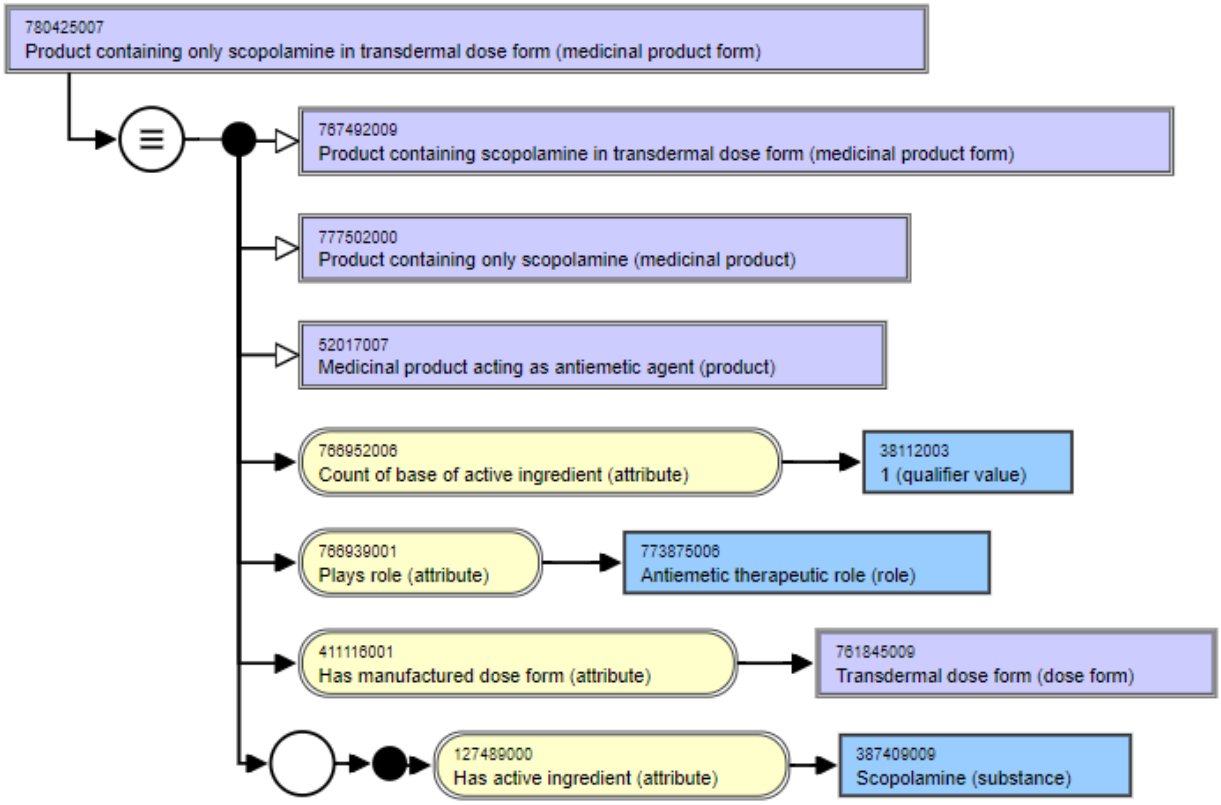


Figure 9: Anti-emetic agent therapeutic role, assigned at Medicinal Product Form (only)

In each of the sections below, the various model classes and their attributes are defined, described in detail and diagrams provided. In addition, their relationship to IDMP is described and a note as to their population status within the upcoming releases of SNOMED CT is provided.

3. **Medicinal Product (MP)**

An abstract representation of a medicinal product without reference to its dose form or its strength. This group of concepts has three types, of which is the parent is the "MP containing", with the "MP only" and the optional "MP precisely" being child concepts of that parent.

3.1. Medicinal Product (MP containing) (open world view)

3.1.1. Definition of MP (containing)

An abstract representation of a medicinal product based on description of active ingredient substance(s) that it contains (regardless of any modification of those active ingredient substance(s)), but not exclusively limited by those substances, in that other substances may be present.

For example, "Product containing amoxicillin" represents products that **must contain some amoxicillin** (with any type of modification, be it amoxicillin sodium or amoxicillin trihydrate, or no modification, as in amoxicillin (base)), but *may also* contain other active ingredients, such as clavulanic acid.

In stating “an abstract representation of a medicinal product” the concept definition implies that at least one medicinal product exists or has existed globally that has that set of active ingredient substance(s); this precludes the possibility of generating MPs representing theoretical, or indeed all possible, combinations of sets of active ingredient substances.

3.1.2. Example diagrams for MP (containing)

Stated template view:

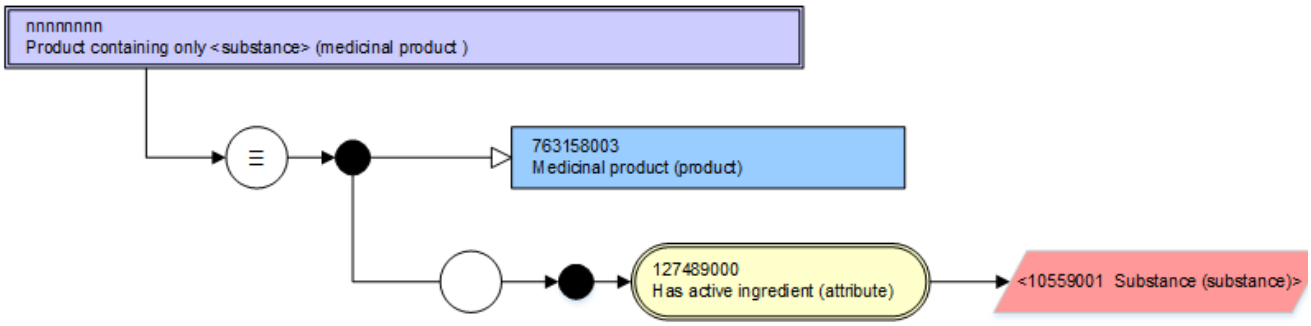


Figure 10: Medicinal Product (containing) stated template view

Example: single active ingredient product: stated view followed by the inferred view that shows the grouper concepts associated with the product:

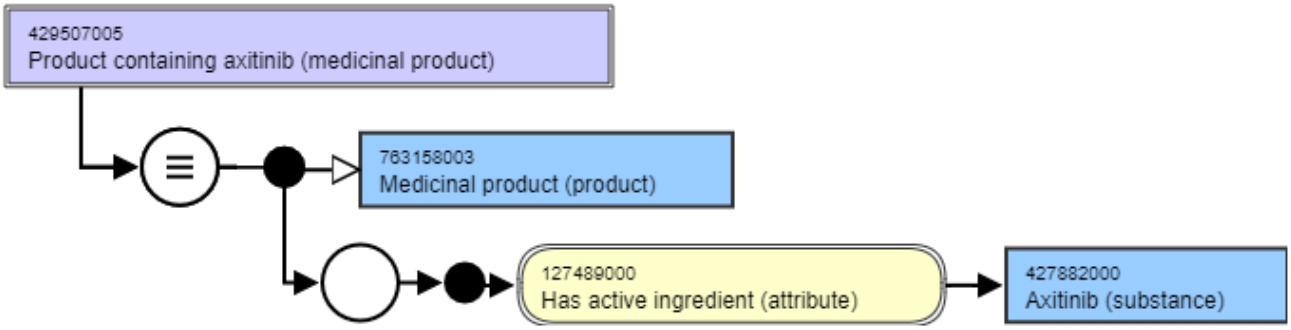


Figure 11: Medicinal Product (containing) example stated view

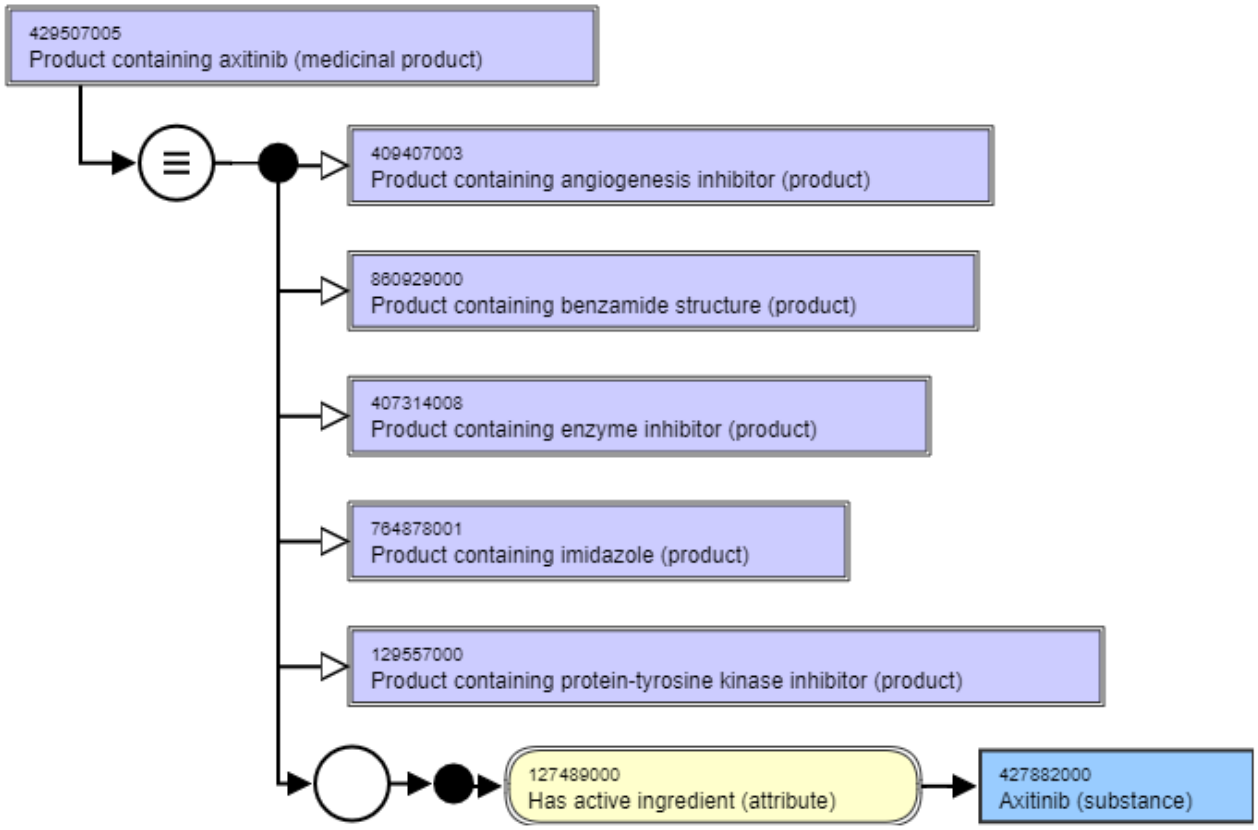


Figure 12: Medicinal Product (containing) example inferred view

Example: multiple active ingredient product: stated view followed by the inferred view that shows the grouper concepts associated with the product:

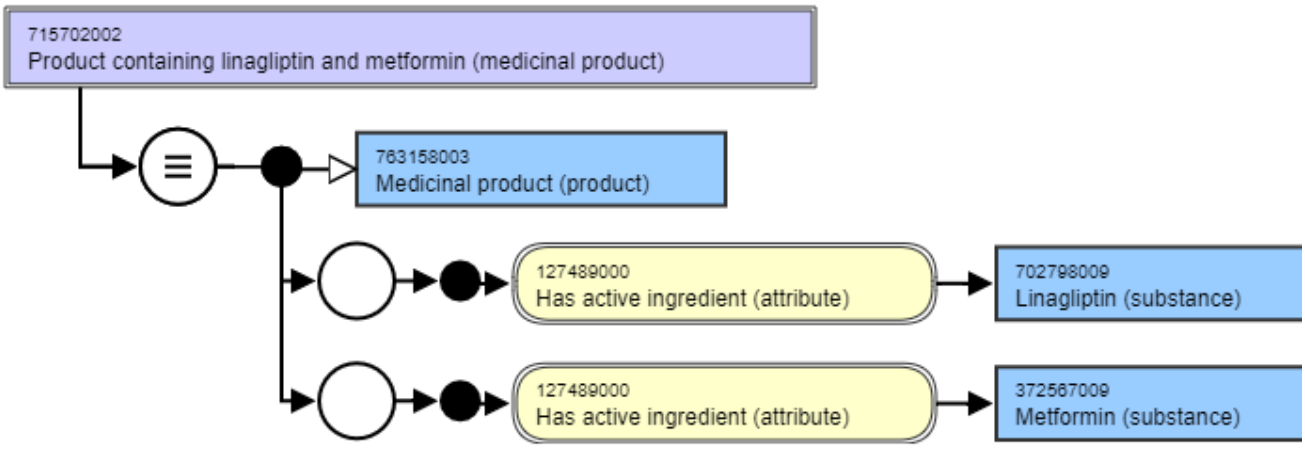


Figure 13: Medicinal Product (containing) example stated view - multi-ingredient concept

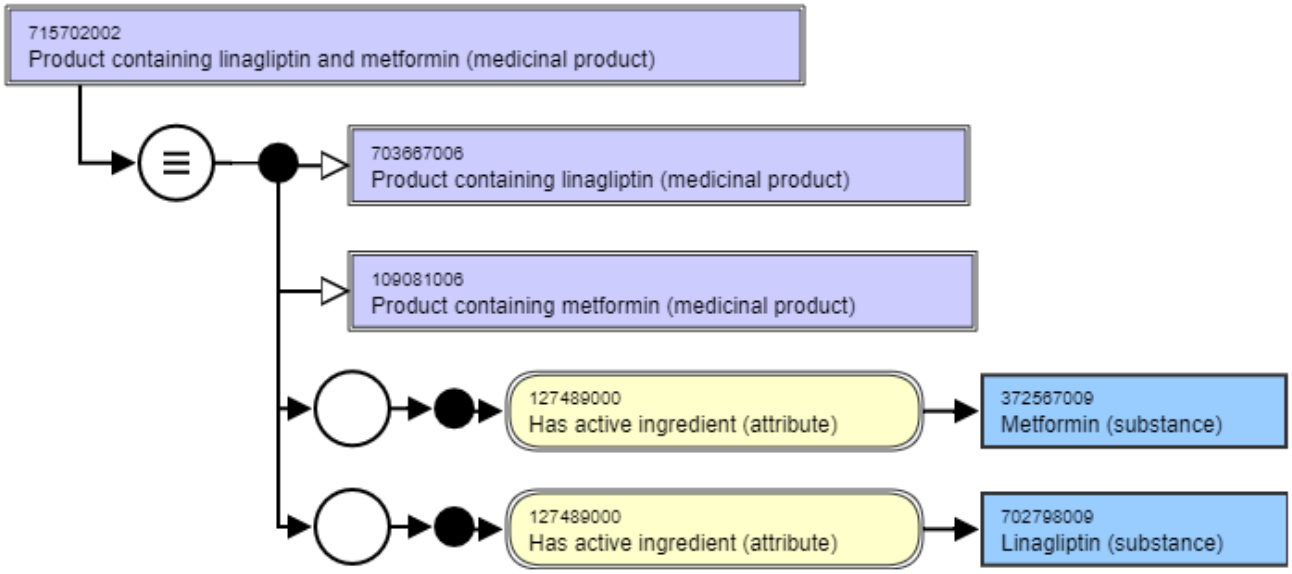


Figure 14: Medicinal Product (containing) example inferred view - multi-ingredient concept

3.1.3. Attributes of MP (containing)

The "containing Medicinal Product" (MP containing) concept is defined by a single attribute:

Semantic tag	(medicinal product)
Definition status	900000000000073002|Sufficiently defined concept definition status (core metadata concept) • Exceptions: none identified
Attribute: **Has active ingredient**	• Range: 105590001|Substance (substance) - descendants only, excluding concepts representing structural groupers, dispositions, or combined substances • Cardinality: 1..* - there is no technical limit on the number of Has active ingredient attributes that may be added to a concept; a practical limit may be imposed at a later date For content in the International Release, this attribute value should represent the base ingredient, not a modification, unless explicitly identified as an exception. This attribute describes the set of active ingredient substances that the concept minimally contains. A set set of active ingredient substances may well have only one member.

3.1.4. Use case(s) supported by MP (containing)

The main use case for describing products containing some active ingredient substance(s), is for analysis; as an aggregation concept for use in research. Details of further use cases will be added as they become available.

3.1.5. Availability of MP (containing) concepts in the international release

This class forms part of the medicinal product content provided in the international release.

3.1.6. IDMP Compatibility for MP (containing)

A concept at this level with the open world view does not correspond to any concept currently in the IDMP suite of standards, although it could act as a parent concept for PhP1 concepts, if use case(s) were identified to require this.

3.2. Medicinal Product (MP only) (closed world view)

3.2.1. Definition of MP (only)

An abstract representation of a medicinal product based on description of only and exclusively the active ingredient substance(s) that it contains but regardless of any modification of those active ingredient substance(s). This is effectively the "set of active moiety(ies)" of the medicinal product.

For example, "Product containing amoxicillin only" represents products that **must contain only amoxicillin** ((with any type of modification, be it amoxicillin sodium or amoxicillin trihydrate, or no modification, as in amoxicillin (base)); they **must not** contain *any* other active ingredients, such as clavulanic acid.

3.2.2. Example diagrams for MP (only)

Stated template view:

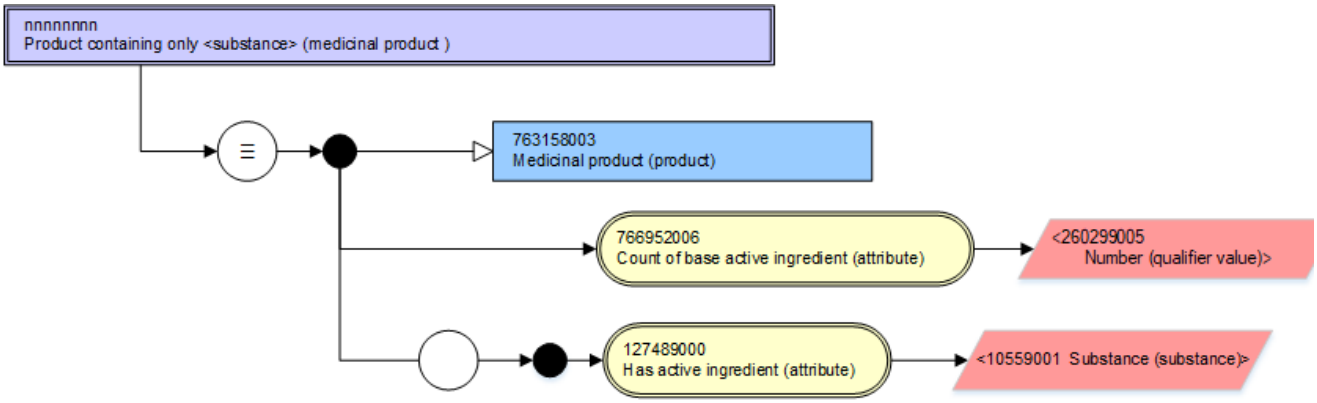


Figure 15: Medicinal Product (only) stated template view

Example: single active ingredient product: stated view followed by the inferred view that shows the grouper concepts associated with the product:

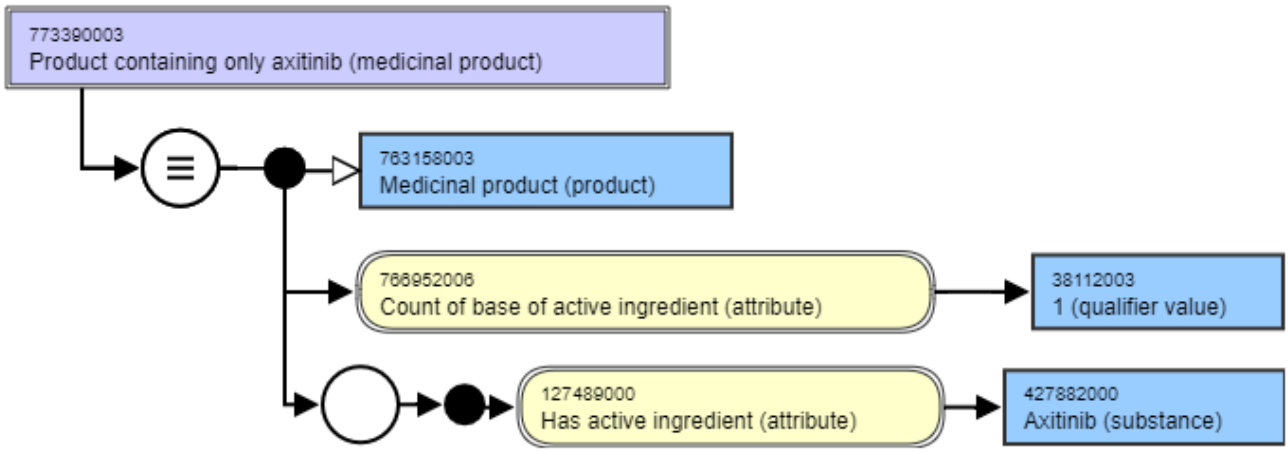


Figure 16: Medicinal Product (only) example stated view

Example inferred view:

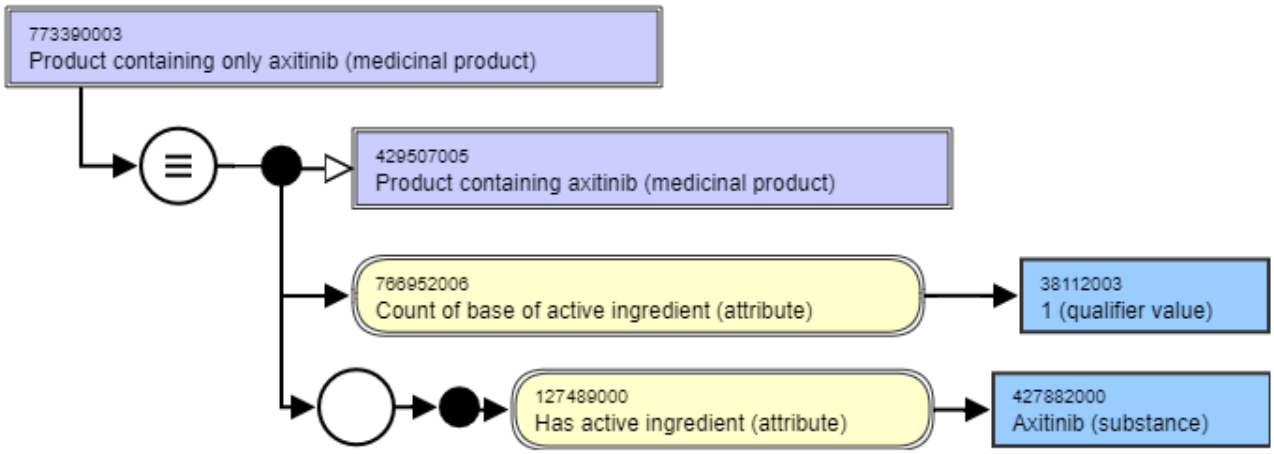


Figure 17: Medicinal Product (only) example inferred view

Example: multiple active ingredient product: stated view followed by the inferred view that shows the MP (containing) parent concept associated with the product:

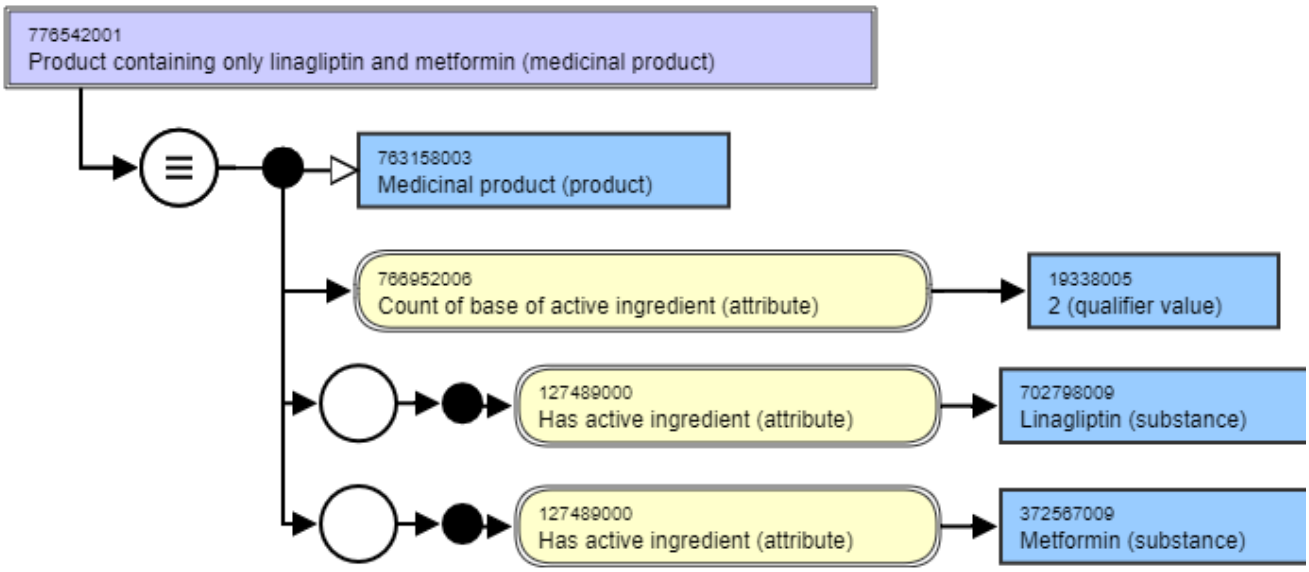


Figure 18: Medicinal Product (only) example stated view - multi-ingredient concept

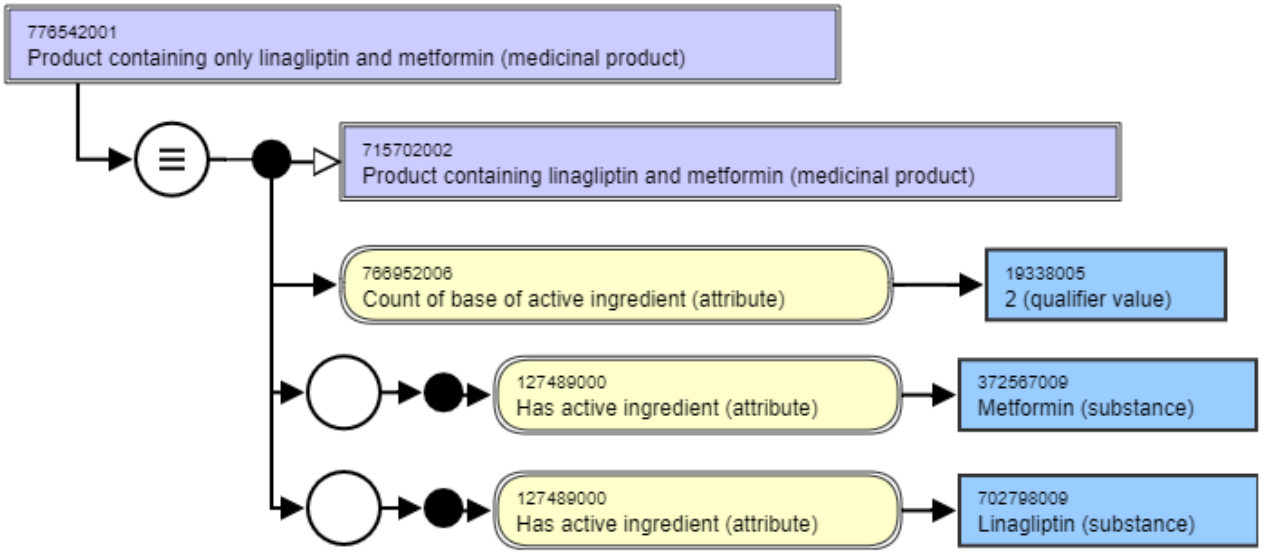


Figure 19: Medicinal Product (only) example inferred view - multi-ingredient concept

3.2.3. Attributes of MP (only)

The " Medicinal Product containing only" (MP only) concept is defined by two attributes describing the active ingredient(s) and the ingredient count:

Semantic tag	(medicinal product)
Definition status	900000000000073002|Sufficiently defined concept definition status (core metadata concept) • Exceptions: none identified
Attribute: **Has active ingredient**	• Range: 105590001|Substance (substance) - descendants only, excluding concepts representing structural groupers, dispositions, or combined substances • Cardinality: 1..* - there is no technical limit on the number of Has active ingredient attributes that may be added to a concept; a practical limit may be imposed at a later date This attribute describes the set of active ingredient substances that the concept minimally contains. A set set of active ingredient substances may well have only one member
Attribute: **Count of base of active ingredient**	• Range: 260299005|Number (qualifier value)| - descendants only • Cardinality: 1..1 This attribute provides the number of base active ingredient substances present in the medicinal product

3.2.4. Use case(s) supported by MP (only)

There are several use cases that the MP (only) concept can support:

- In national extensions; where it is useful for various clinical purposes, such as prescribing scenarios (so called "abstract" or "non-product-based" prescribing) and in medication history and in Medication Profiles
- Internationally and nationally in decision support and in protocols and treatment guidelines
- Internationally and nationally for interoperability of patient medication information such as in patient summaries
- Internationally and nationally for recording adverse events and/or sensitivities to medication, particularly for multi-ingredient preparations where there will be no appropriate single substance concept and it is not possible to say which particular active ingredient is responsible for the issue
- In pharmacovigilance, especially for description of concomitant medications where less information may be available (see also below in IDMP Compatibility)
- In analysis and research
- As a supporting attribute for other concepts elsewhere in SNOMED CT

3.2.5. Availability of MP (only) concepts in the international release

This class forms part of the medicinal product content provided in the international release.

3.2.6. IDMP Compatibility

The MP (only) concept is directly compatible with the ISO 11616 concept of a level 1 Pharmaceutical Product (PhPID_SUB_L1), where the "active substance set" comprises the definition of this concept. Note that, in IDMP, for products using adjuvants it is probable that the adjuvant would be included as part of the "active substance set" and its role explicitly identified. For example aluminium hydroxide is used as an adjuvant in several vaccine products (e.g. hepatitis A, hepatitis B) in addition to the antigen itself to enhance the immune response; it is not an active ingredient per se and it is not an inactive ingredient, it is explicitly an "adjuvant". However, this type of detail of the implementation of the abstract model of ISO 11616 remains unclear, and in its first implementation, vaccines are out of scope for the Medicinal Product hierarchy model in SNOMED CT.

3.3. ** Medicinal Product (MP precisely) (closed world view) - optional concept class - not populated in the International Release **

3.3.1. Definition of MP (precisely)

An abstract representation of a medicinal product based on description of only and exclusively the precise active ingredients it contains.

For example, "Product containing amoxicillin sodium precisely" represents products that **must contain precisely amoxicillin sodium** not amoxicillin trihydrate nor a substance that is any further modification of amoxicillin sodium, should one exist; and they **must not** contain *any* other active ingredients, such as clavulanic acid.

A Medicinal Product (MP precisely) concept may be created in national extensions when use case(s) require this (see below) and for those national extensions where products exist such that the Active Ingredient Count attribute for the MP precisely has a different value from the Active Ingredient Count of the parent Medicinal Product (MP only) concept. It is described here for completeness and to acknowledge that this is a key issue for many national terminologies. For further details and examples, see the Ingredient Count attribute section below.

3.3.2. Example diagrams for MP (precisely)

Example: product with a "multiple modified" active ingredient substance (dexamethasone phosphate is the modified concept that has a further modification to give dexamethasone sodium phosphate): stated view, showing both the count of the base active ingredient and the count of base and modification pair are present, as the substance has a multiple modification (dexamethasone phosphate is the modified concept that has a further modification to give dexamethasone sodium phosphate) **and** there are multi-ingredient concepts that contain this multiple modified substance and at least one other modified ingredient substance that shares the same base substance (dexamethasone) (see next examples). The multi-ingredient concept is "dexamethasone sodium phosphate and dexamethasone acetate". As described in the MRCM rules, the additional ingredient count attributes have to be applied iteratively. The following inferred view shows the correct dexamethasone moiety MP (only) parent concept.

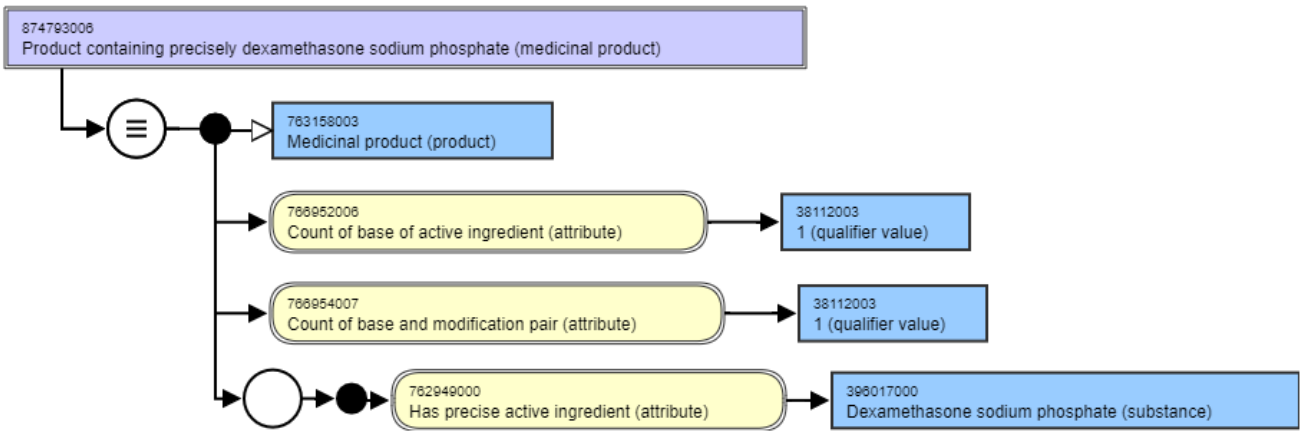


Figure 20: Single Ingredient Medicinal Product (precisely) example stated view

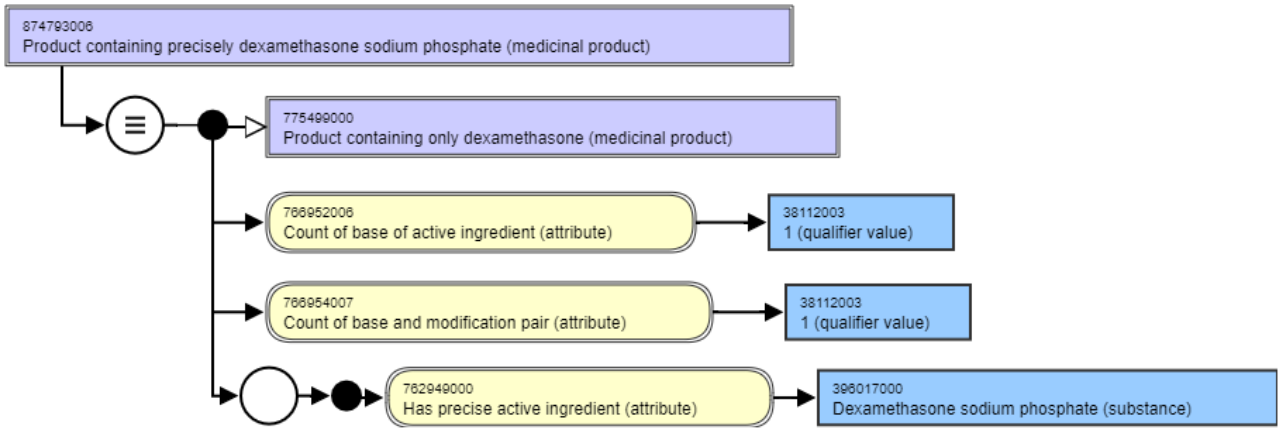


Figure 21: Single Ingredient Medicinal Product (precisely) example inferred view

Example: multi-ingredient concept, where both precise active ingredient substances share the same base moiety substance, showing requirement for two ingredient count attributes; note that because these attributes must be applied iteratively, the MP precisely concepts exist for each single ingredient product

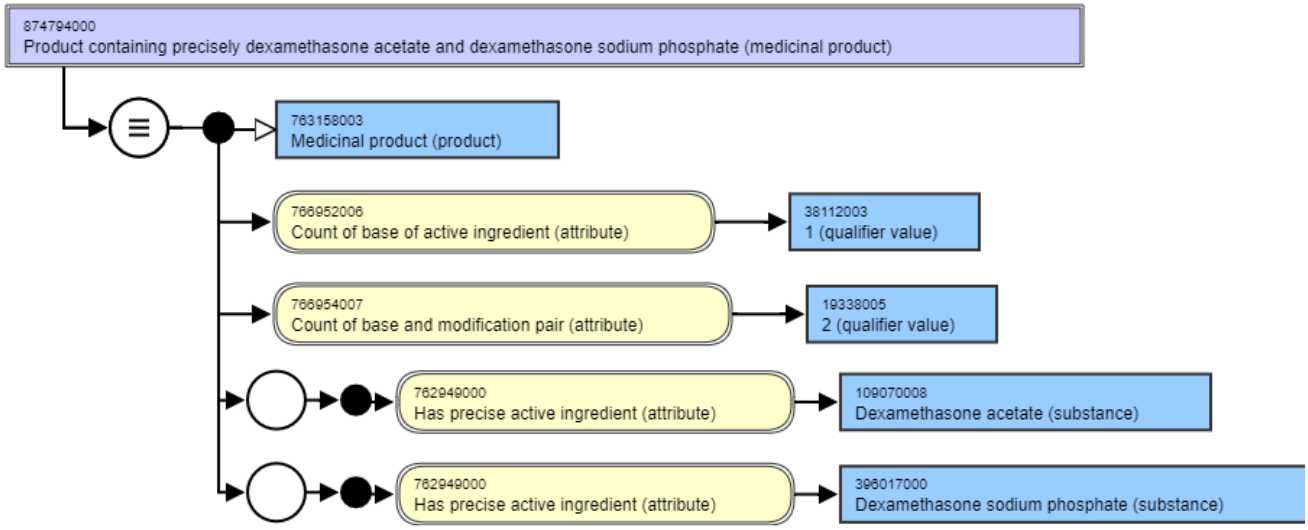


Figure 22: Medicinal Product (precisely) example stated view - multi-ingredient concept

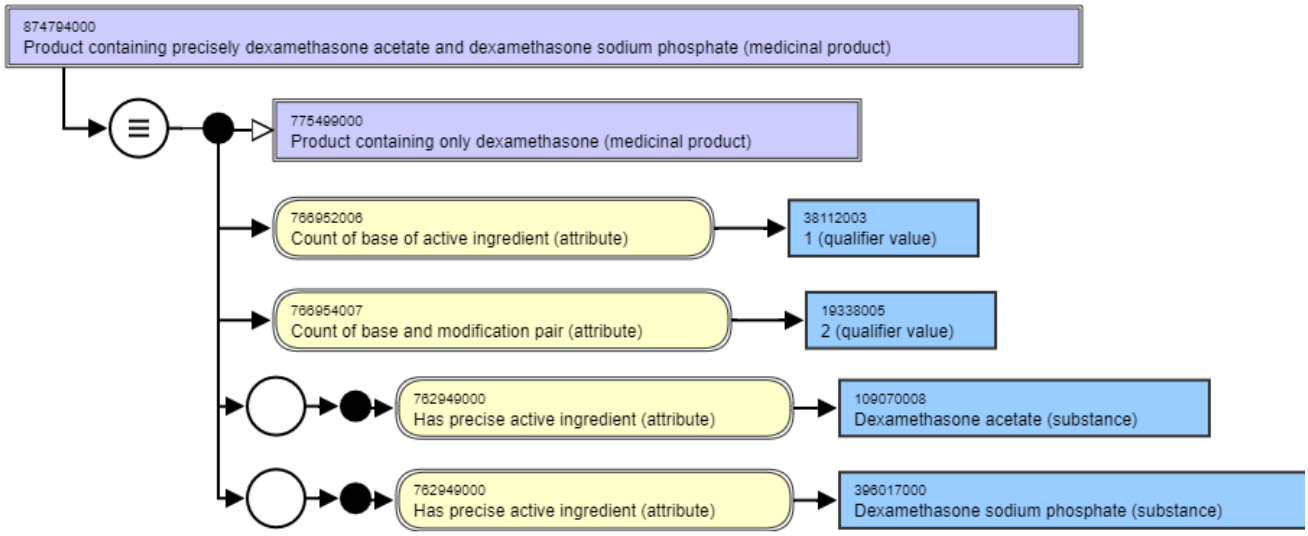


Figure 23: Medicinal Product (precisely) example inferred view - multi-ingredient concept

The count of base and modification pair ensures that this multi-ingredient product does not incorrectly subsume under either of the single ingredient products, since they have a base and modification pair count of one and this has a base and modification pair count of two. It can subsume under the parent "Product containing only dexamethasone" as shown in the diagram above, as "Product containing only Dexamethasone" has a Count of base of active ingredient of 1, and that one is dexamethasone (substance), which is the same as for the "Product containing only Dexamethasone acetate and Dexamethasone sodium phosphate".

The requirement for all the three ingredient count attributes depends significantly on how the substance hierarchy is modelled. For example, with calcium products (calcium lactate and calcium lactate gluconate) if both are considered modifications of "calcium (substance)" then for multi-ingredient products containing both, the three ingredient counts would be required to obtain correct classification for MP only and MP precisely concepts.

For further details, see the Ingredient Count section below.

3.3.3. Attributes of MP (precisely)

The " Medicinal Product containing precisely" (MP precisely) concept is defined by two groups of attributes; to describe the **precise** active ingredient(s) and the ingredient count(s). The ingredient count attributes are applied incrementally, as the requirement arises for MP precisely concepts; this is a pragmatic and incremental approach to maintenance of the hierarchy. Although it is desirable for attributes to be applied globally, this would introduce a significant maintenance burden for what is required in only a minority, although a significant minority, of cases. They are applied when the requirement to describe products that contain two or more active ingredients that are modifications of the same base and are applied from the top down (i.e. from the MP precisely class, down to the clinical drug class, including the MPF precisely if required) within the particular sub-hierarchy base ingredient concept.

In national extensions using the MP precisely concept where there is no MP precisely concept in the international and CD concepts do not have multiple ingredient counts so that classification results are not as expected, it may be necessary to override the international definition of some concepts in the sub-hierarchy in the national extension (e.g. if a CD containing one of the precise ingredient substances has only one count attribute in the international, but requires two or three count attributes in the national in order to get correct classification into an MP precisely concept).

Semantic tag	(medicinal product)
Definition status	900000000000073002|Sufficiently defined concept definition status (core metadata concept) • Exceptions: none identified

Attribute: **Has precise active ingredient**	• Range: < 105590001|Substance (substance)| • Cardinality: 1..* This is the set of precise active ingredient substances that the medicinal product contains. A set of precise active ingredient substances may have only one member
Attribute: **Count of base of active ingredient**	• Range: 260299005|Number (qualifier value)| - descendants only • Cardinality: 1..1 This attribute provides the number of base active ingredient substances present in the medicinal product
Attribute: **Count of base and modification pair**	• Range: 260299005|Number (qualifier value)| - descendants only • Cardinality: 0..1 This attribute provides the number of base active ingredient substances present in the medicinal product This attribute should only be present and valued for multi-ingredient product concepts where two or more active ingredients are share the same base active ingredient (i.e. parent ingredient substance) and for single ingredient product concepts where the active substance is an ingredient in multi-ingredient products. As discussed above, and as described in the MRCM rules, the additional ingredient count attributes have to be applied iteratively
Attribute: **Count of active ingredient**	• Range: 260299005|Number (qualifier value)| - descendants only • Cardinality: 0..1 This attribute provides the number of active ingredients present in the medicinal product This attribute should only be present and valued for multi-ingredient concepts where two or more active ingredients are share the same base active ingredient (i.e. parent ingredient substance) and where one is a further modification of the other (for example, a multi-ingredient product containing both dexamethasone phosphate and dexamethasone sodium phosphate, where the dexamethasone phosphate is a modification of dexamethasone (base) and dexamethasone sodium phosphate is a further modification of the dexamethasone phosphate), and for single ingredient product concepts where the active substance is an ingredient in multi-ingredient products. As discussed above, and as described in the MRCM rules, the additional ingredient count attributes have to be applied iteratively.

3.3.4. Use case(s) supported by MP (precisely)

The use case for the MP (precisely) concept is primarily to provide a more exact and explicit medicinal product concept for use in those scenarios where different modifications of the base active ingredient have clinical significance. There are several groups of products where this is the case, for example the corticosteroids, various of the anti-epileptic medications (e.g. phenytoin and valproic acid), and insulins. The the MP (precisely) class can be deployed in national extensions for those use cases that need it, such as prescribing scenarios (so called "abstract" or "non-product-based" prescribing where no product and no dose form are specified by the prescriber) and in medication history and in medication profiles, and in decision support, in protocols and treatment guidelines. However, all the use cases described for MP (only) could use MP (precisely) as necessary when more exact and explicit representation is required.

3.3.5. Availability of MP (precisely) concepts in the international release

This class will not form part of the medicinal product content provided in the international release. National extensions may require this subclass for certain use cases for particular types of products, as described above.

3.3.6. IDMP Compatibility for MP (precisely)

The MP (precisely) concept may also be directly compatible with the ISO 11616 concept of a level 1 Pharmaceutical Product (PhPID_SUB_L1), where the "active substance set" since it is not clear to what level of granularity ingredient substance description the ingredient substance set will be set at, or indeed whether, as in SNOMED-CT there will be the facility to have alternate levels of substance granularity when it is clinically relevant to do so.

4. Medicinal Product Form (MPF)

An abstract representation of a medicinal product described by its active ingredient substances and a grouping dose form concept (based on the intended site of administration for the dose form group) but without reference to its strength. The grouping dose form concepts are immediate the children of the 736542009 | Pharmaceutical dose form (dose form) | concept and are described in detail in the Editorial Guidance section Grouper Based on Intended Site.

These grouper concepts gather together all the formulations (solid, semi-solid, liquid or gaseous manufactured dose forms) that have the same intended site of administration. The intended site of administration of a dose form concept is a description of the general body site (i.e. not exactly anatomically explicit - no laterality etc.) where the dose form will be administered, For example, products formulated with a dose form of eye drops are required to meet various pharmacopoeial standards of sterility, particulate contamination and pH as they are intended to be administered to an "ocular" site. For further information see section 5.3.2.7 of ISO 11239:2012 *Health informatics - Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated information on pharmaceutical dose forms, units of presentation, routes of administration and packaging*.

4.1. Medicinal Product Form (MPF containing) (open world view)

4.1.1. Definition of MPF (containing)

An abstract representation of a medicinal product based on description of active ingredients it contains, but not limited by that description, and on the (generalised) intended site of use for the product.

For example, "Product containing amoxicillin in oral dosage form" represents products that must contain some amoxicillin (be it amoxicillin sodium or amoxicillin trihydrate or amoxicillin base), but *may also* contain other active ingredients, such as clavulanic acid, in manufactured dose forms such as oral suspension, oral capsule (any type), oral tablet (any type).

4.1.2. Example diagrams for MPF (containing)

Stated template view:

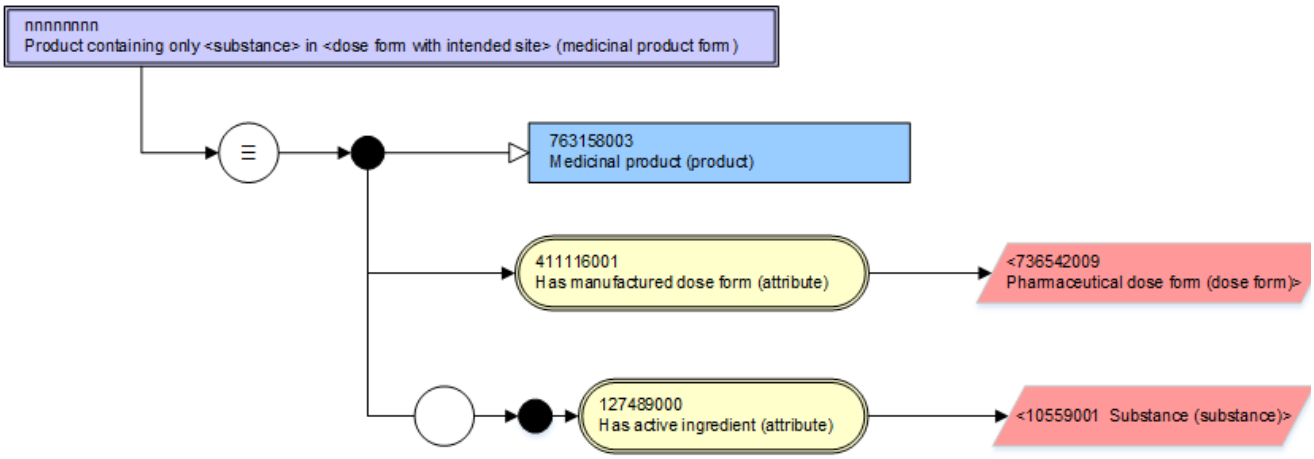


Figure 24: Medicinal Product Form (containing) stated template view

Example: single active ingredient product, oral dose form: stated view followed by the inferred view that shows the parent concepts associated with the product:

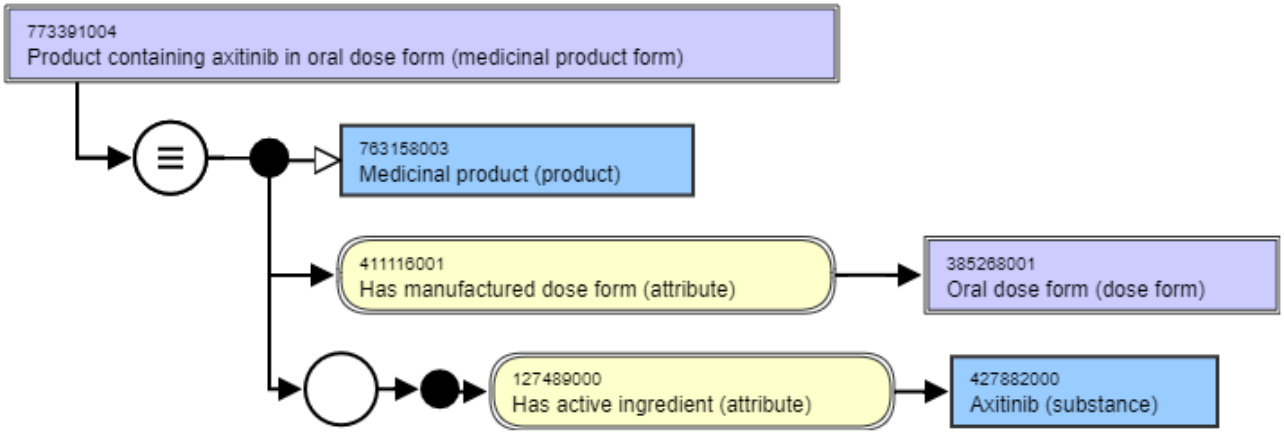


Figure 25: Medicinal Product Form (containing) example stated view

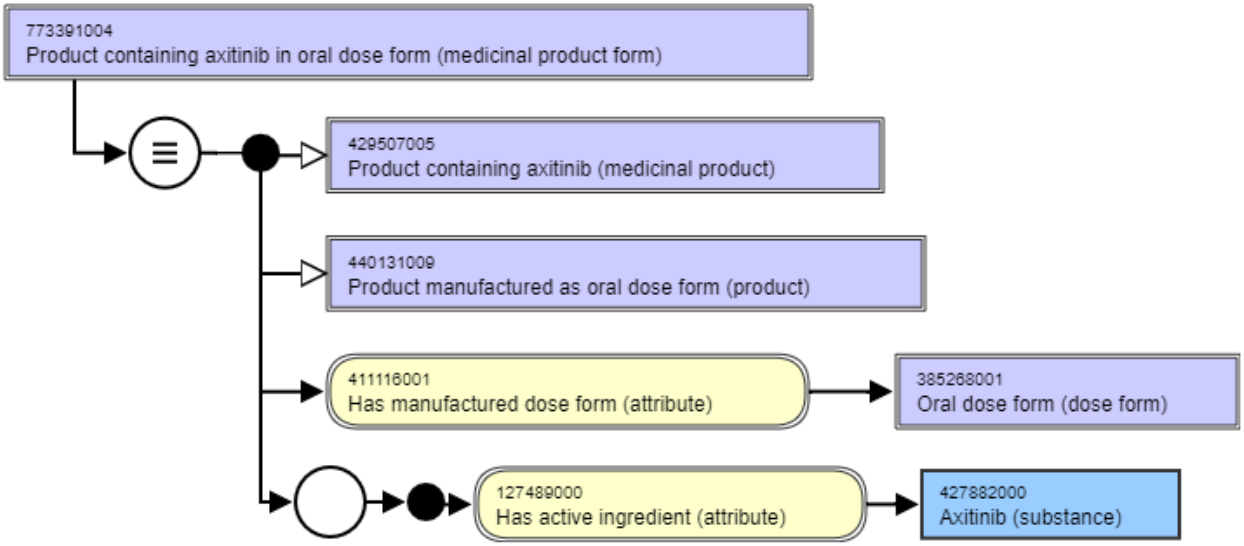


Figure 26: Medicinal Product Form (containing) example inferred view

4.1.3. Attributes of MPF (containing)

The Medicinal Product Form (MPF containing) concept is defined by attributes to describe the active ingredients(s) and to describe the dosage form:

Semantic tag	(medicinal product form)
Definition status	900000000000073002|Sufficiently defined concept definition status (core metadata concept) • Exceptions: none identified

Attribute: **Has active ingredient**	• Range: 105590001|Substance (substance) - descendants only, excluding concepts representing structural groupers, dispositions, or combined substances • Cardinality: 1..* - there is no technical limit on the number of Has active ingredient attributes that may be added to a concept; a practical limit may be imposed at a later date For content in the International Release, this attribute value should represent the base ingredient, not a modification, unless explicitly identified as an exception. This attribute describes the set of active ingredient substances that the concept minimally contains. A set set of active ingredient substances may well have only one member
Attribute: **Has manufactured dose form**	• Range: 736542009|Pharmaceutical dose form (dose form) - descendants that are groupers representing intended site only (e.g. 385268001 |Oral dose form (dose form)|, 385287007 |Parenteral dose form (dose form)|) • Cardinality: 1..1 This attribute describes a grouping dose form concept for the medicinal product, where the grouping is the intended site for administration of the dose form of the product

4.1.4. Use case(s) supported by MPF (containing)

The main use case for the MPF (containing) is for analysis; as an aggregation concept for use in research. It may be that this concept may be used to support the modelling of other concepts in the future.

4.1.5. Availability of MPF (containing) concepts in the international release

This class forms part of the medicinal product content provided in the international release.

4.1.6. IDMP Compatibility

A concept at this level with the open world view does not correspond to any concept currently in the IDMP suite of standards.

4.2. Medicinal Product Form (MPF only) (closed world view)

4.2.1. Definition of MPF (only)

An abstract representation of a medicinal product based on description of only and exclusively the active ingredient(s) it contains and on the (generalised) intended site of use for the product.
For example, "Product containing only amoxicillin in oral dosage form" represents products that must contain only amoxicillin (be it amoxicillin sodium or amoxicillin trihydrate), with no other active ingredients in manufactured dose forms such as oral suspension, oral capsule (any type), oral tablet (any type).

4.2.2. Example diagrams for MPF (only)

Stated template view:

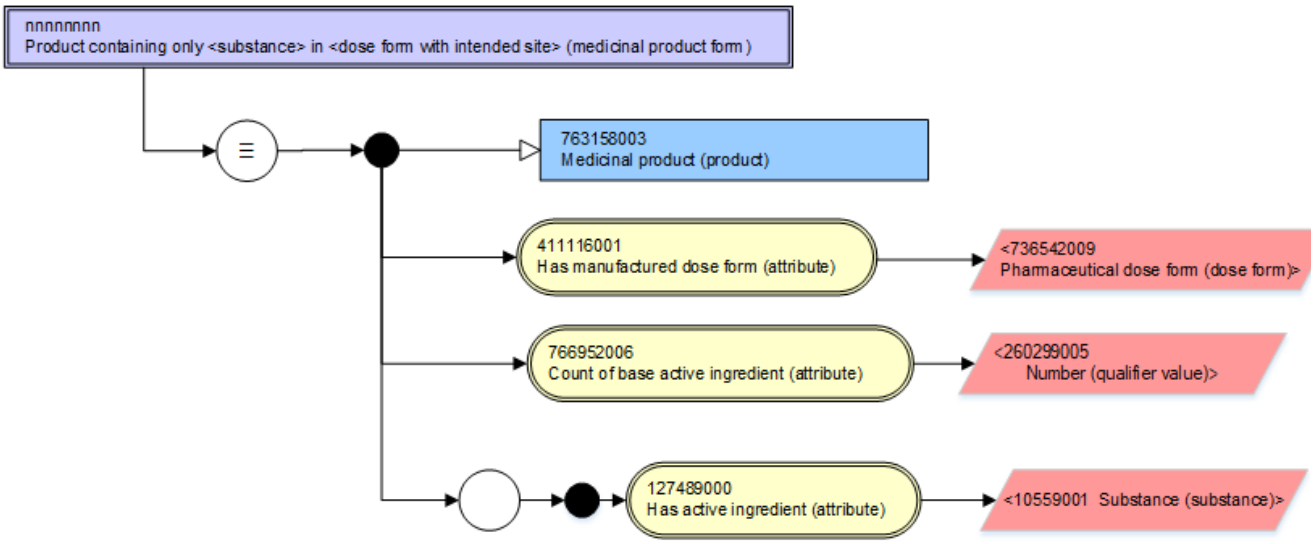


Figure 27: Medicinal Product Form (only) stated template view

Example: single active ingredient product, oral dose form: stated view followed by the inferred view that shows the parent concepts associated with the product:

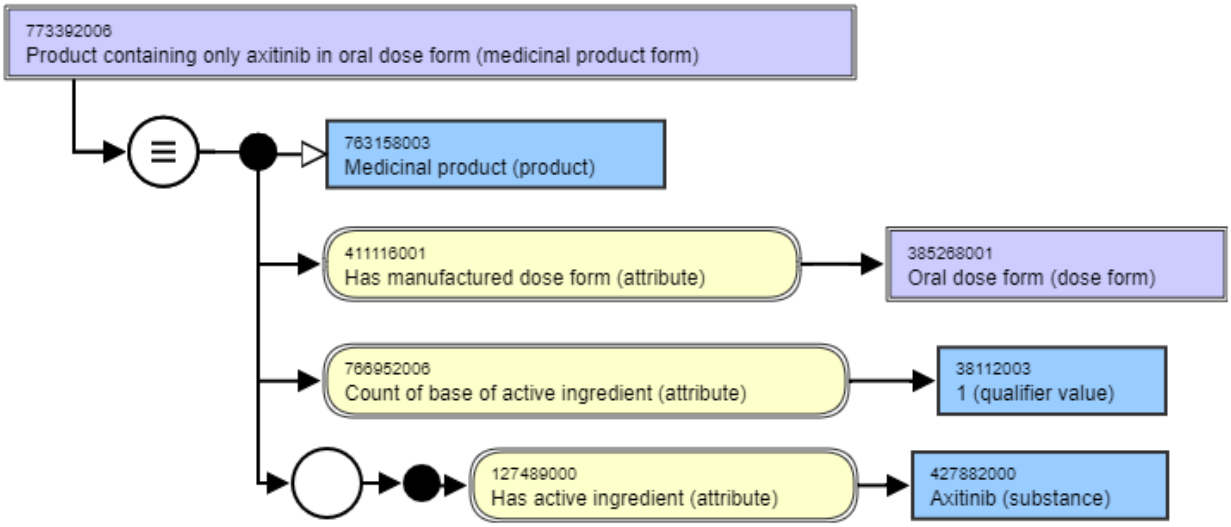


Figure 28: Medicinal Product Form (only) example stated view

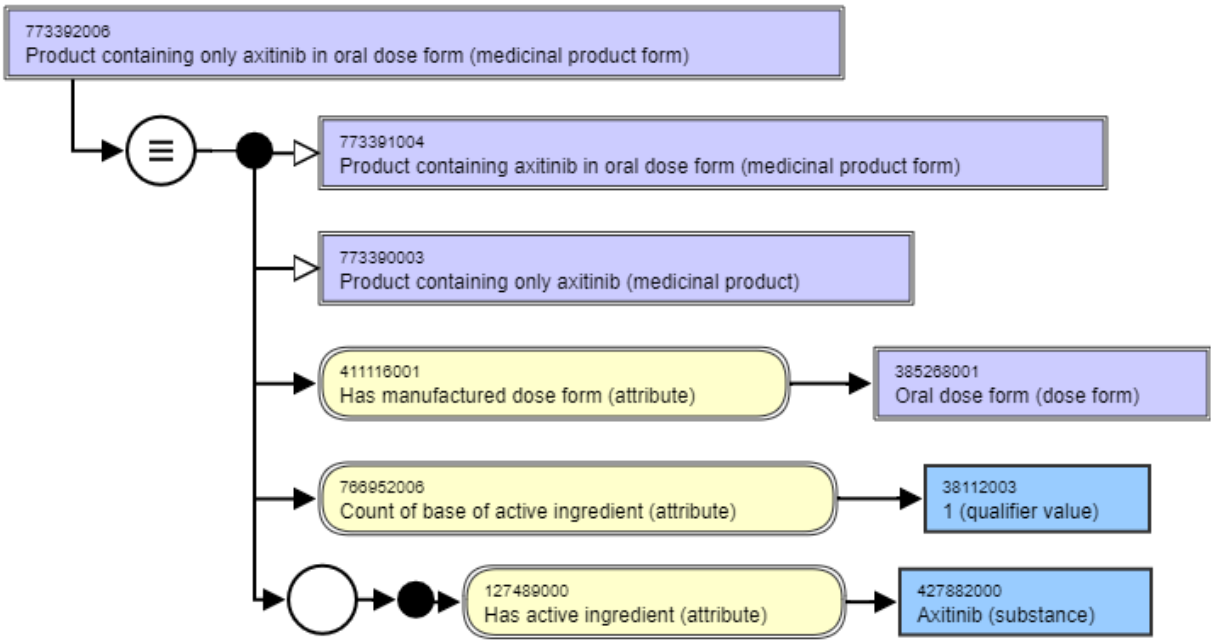


Figure 29: Medicinal Product Form (only) example inferred view

4.2.3. Attributes of MPF (only)

The "containing only Medicinal Product" (MP some) concept is defined by attributes to describe the active ingredient(s), the ingredient count and the dosage form:

Semantic tag	(medicinal product form)
Definition status	900000000000073002|Sufficiently defined concept definition status (core metadata concept) • Exceptions: none identified
Attribute: **Has active ingredient**	• Range: 105590001|Substance (substance) - descendants only, excluding concepts representing structural groupers, dispositions, or combined substances • Cardinality: 1..* - there is no technical limit on the number of Has active ingredient attributes that may be added to a concept; a practical limit may be imposed at a later date This attribute describes the set of active ingredient substances that the concept minimally contains. A set set of active ingredient substances may well have only one member
Attribute: **Count of base of active ingredient**	• Range: 260299005|Number (qualifier value)| - descendants only • Cardinality: 1..1 This attribute provides the number of base active ingredient substances present in the medicinal product
Attribute: **Has manufactured dose form**	• Range: 736542009|Pharmaceutical dose form (dose form) - descendants that are groupers representing intended site only (e.g. 385268001 |Oral dose form (dose form)|, 385287007 |Parenteral dose form (dose form)|) • Cardinality: 1..1 This attribute describes a grouping dose form concept for the medicinal product, where the grouping is the intended site for administration of the dose form of the product

4.2.4. Use cases supported by MPF (only)

There are several use cases that the MPF (only) concept can support:

- Internationally and nationally in decision support (especially drug interaction checking) and in protocols and treatment guidelines
- Internationally and nationally for interoperability of patient medication information such as in patient summaries and medication profiles, where patient information may only be available in using an abstract description (e.g. "patient reports they were taking oral captopril for 5 years")
- Internationally for the provision of cross border care, where a particular formulation of a medicinal product from one jurisdiction may not be present in a second jurisdiction; the MPD (only) class can support finding alternatives
- In pharmacovigilance, especially for description of concomitant medications where less information may be available (see also below in IDMP Compatibility)
- In analysis and research
- As a supporting attribute for other concepts elsewhere in SNOMED CT

4.2.5. Availability of MPF (only) concepts in the international release

This class forms part of the medicinal product content provided in the international release.

4.2.6. IDMP Compatibility

A concept at this level, despite using the universal restriction, does not directly correspond to any concept currently in the IDMP suite of standards. The Level 3 Pharmaceutical Product concept (PhPID_SUB_C3) uses an exact granular *administrable dose form concept* for a product which will have an intended site of administration (bearing in mind that the exact implementation of ISO 11616 is not yet known). The MPF uses a more abstract dose form grouping concept where the grouping is on the basis of the intended site of administration for *manufactured* dose form. However, there should be little difference in the intended site of administration between a manufactured dose form and its administrable form for those dose forms that do not require transformation. For some groups of products, the MPF (only) concept has the potential to bring additional value to users beyond PhPID C3 because it is a larger grouping concept.
For example: the dose form intended site concept 385276004 | Ocular dose form (dose form) | covers 14 more granular pharmaceutical dose forms, of which two would undergo transformation to different administrable dose forms, but still with the ocular intended site. This means that the single MPF grouping concept will be relevant to a considerably larger group of actual products than the 12 potential PhPID C3 concepts for the same active ingredient substance(s) that might exist in IDMP.

4.3. **Medicinal Product Form (MPF precisely) (closed world view)**

This concept class, which is not shown in any of the overall diagrams in the introductory section, would be a representation of a medicinal product based on description of only and exclusively the precise active ingredient(s) it contains and on the (generalised) intended site of use for the product. For example, "Product containing precisely amoxicillin trihydrate in oral dosage form" represents products that must contain only amoxicillin trihydrate (not amoxicillin sodium or amoxicillin base) as the precise ingredient substance, with no other active ingredients in manufactured dose forms such as oral suspension, oral capsule (any type), oral tablet (any type). This class is not part of the international release, but may be of use in national extensions. It would be modelled in the same way as the MPF only, but would use the precise active ingredient attribute and the two additional ingredient count attributes if and when required, using the same rules as for MP precisely.

5. **Clinical Drug (CD precisely) (closed world view)**

5.1.1. Definition of CD (precisely)

An abstract representation of a medicinal product based on description of 1) its precise active ingredient substances only and explicitly, 2) the stated basis of strength substance(s) with strength, expressed as presentation strength with unit of presentation or as concentration strength as appropriate, and 3) with its manufactured dose form.

All Clinical Drugs that contain multiple *active* ingredient substances will have parent MPF and MP concepts that have the same set of active ingredient substances.

The limitation of the Clinical Drug class to the closed world view by the description of its precise active ingredient substances *only* precludes description of excipient substances such as flavours, preservatives, sweeteners etc as ingredients in a Clinical Drug. These substances can have significance for allergies etc. but can only be reliably described for individual authorised manufactured products, and as such are not within the scope of the international release.

Similarly, by limiting the the Clinical Drug class in the international release to expression of strength *either* as concentration strength *or* as presentation strength, medicinal product concepts that could usefully have *both* concentration and presentation strength will have only concentration strength in the international release. National extensions may author clinical drug concepts using the presentation strength(s) and unit(s) of presentation available in their jurisdiction if use case(s) require this. These concepts will be child concepts of the concentration clinical drug in the international release. The diagrams below illustrate this:

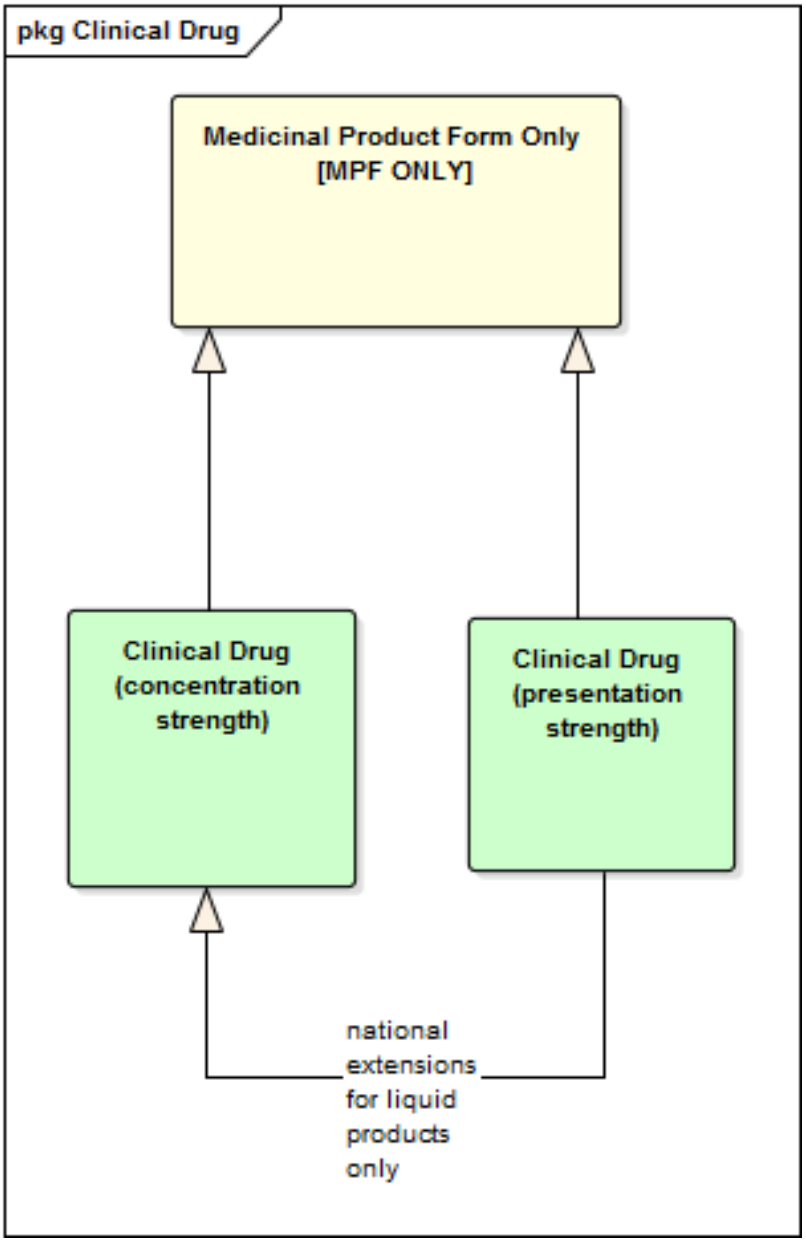


Figure 30: Clinical Drug concepts and their relationship together and to MPF only concepts

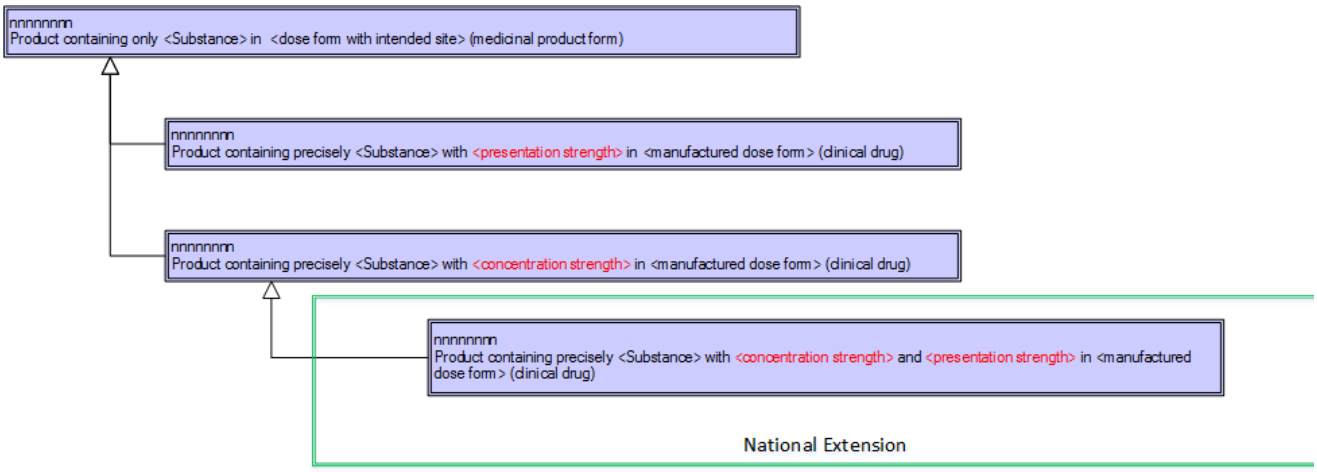


Figure 31: Clinical Drug concepts and their relationship together and to MPF only concepts in SNOMED notation, showing optional national extension concepts

Example:

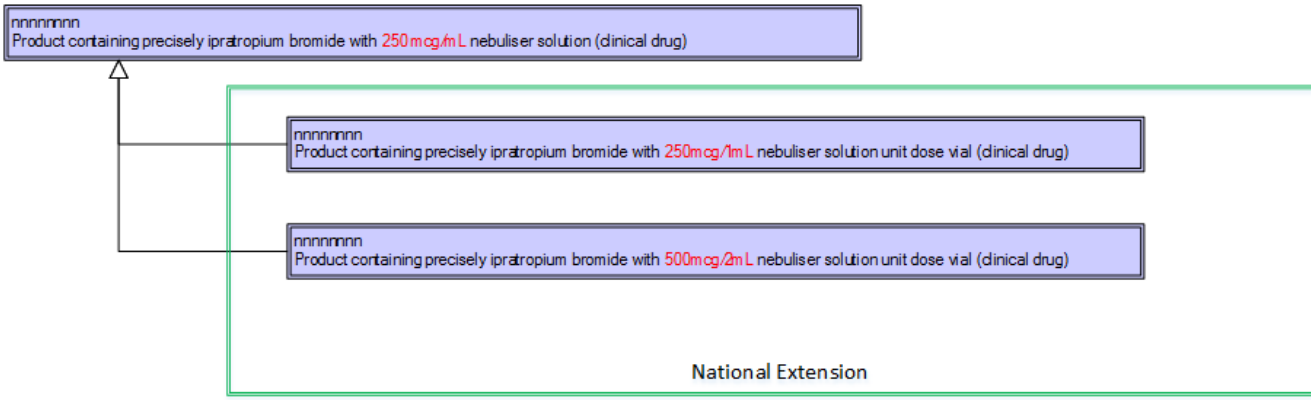


Figure 32: Clinical Drug example showing optional national extension concepts

Please also reference the National Extension specification for how to use additional model attributes to fully define concepts that can have both a concentration strength and a presentation strength such that they classify correctly.

5.1.2. Use cases supported by CD (precisely)

Use cases supported by the clinical drug concept include:

- This is the concept that most closely relates to the Manufactured Item of IDMP (see below) so this is the closest international representation of products authorised by national regulatory agencies. This is therefore the pivotal concept between the products that exist in national healthcare cultures and the international core. IDMP requires use of presentation strength whenever possible and supports explicit representation of concentration strength if required. As the abstract representation of what is authorised, the clinical drug concept is the source from which all other representation of medicinal product concepts flows
- Internationally (when cross border care delivery is supported) and nationally for many clinical purposes, such as product prescribing, adverse event reporting, formulary management, in recording medication history and in medication profiles
- Internationally and nationally in decision support and in protocols and treatment guidelines, when a more complete description of a product is required than MP or MPF
- Internationally and nationally for interoperability of patient medication information such as in patient summaries. When this more complete description of a product is available this would be the concept of choice for these use cases (see OpenMedicine report)
- In pharmacovigilance, especially for description of concomitant medication
- In analysis and research
- As a representation of what is authorised, the clinical drug concept is the source from which all other representation of medicinal product concepts flows

5.1.3. Availability of CD concepts in the international release

This class forms part of the medicinal product content provided in the international release.

5.2. **Clinical Drug (precisely) (presentation strength)**

5.2.1. Definition of Clinical Drug (precisely) (presentation strength)

An abstract representation of a medicinal product based on description of 1) its precise active ingredient substances only and explicitly, 2) the stated basis of strength substance(s) with strength, expressed as presentation strength with unit of presentation and 3) with its manufactured dose form.

This is used for product types such as tablets, capsules, pessaries, suppositories (Strength Pattern 1a below), sachets, ampoules or vials *containi ng* powders or granules etc. (solid dosage forms) and those presented with a metered dose valve such as inhalers and sprays.

5.2.2. Example diagrams for CD (precisely) presentation strength

Stated template view:

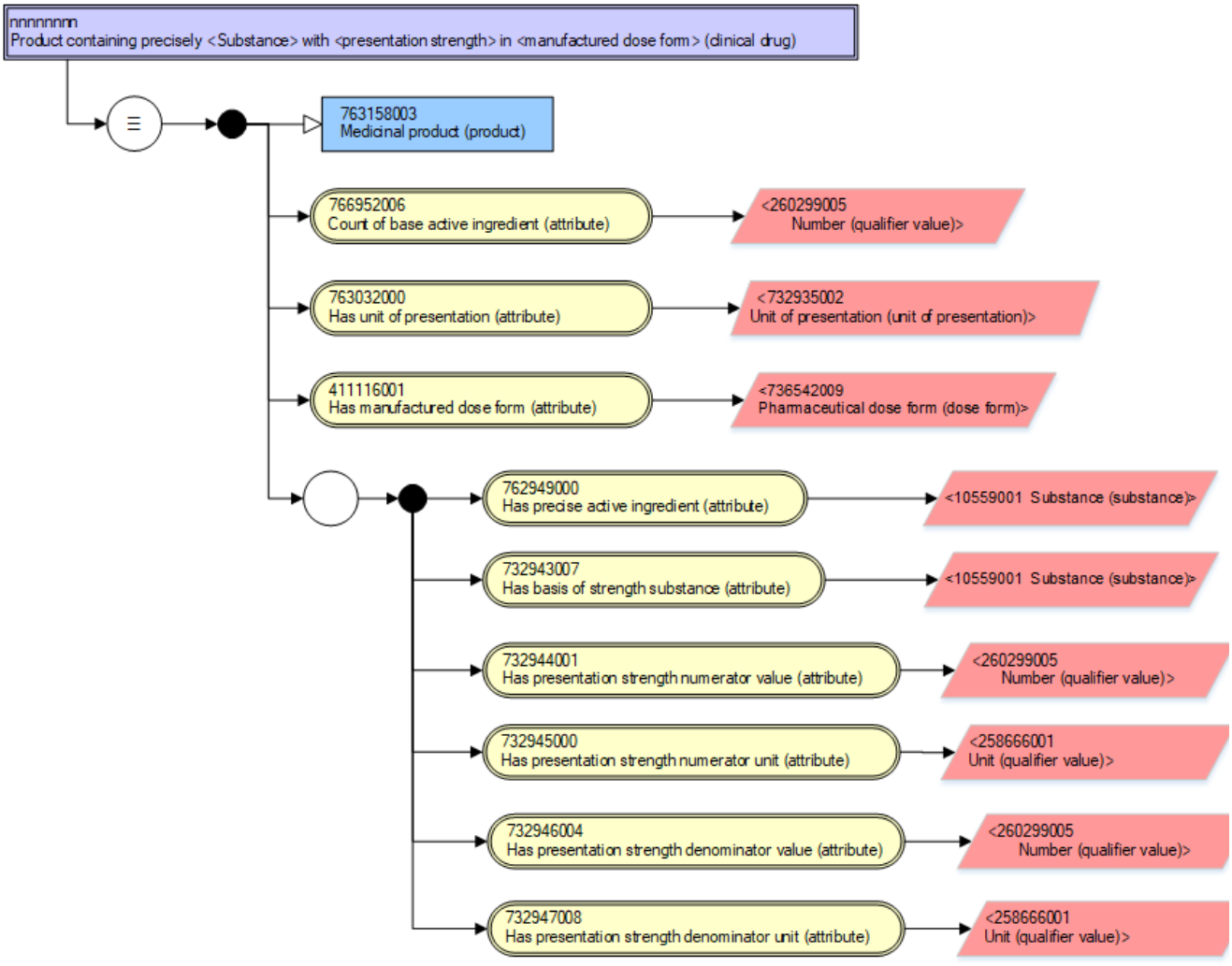


Figure 33: Clinical drug, presentation strength, stated template view

Examples: single active ingredient product: stated view followed by the inferred view that shows the parent concepts associated with the product:

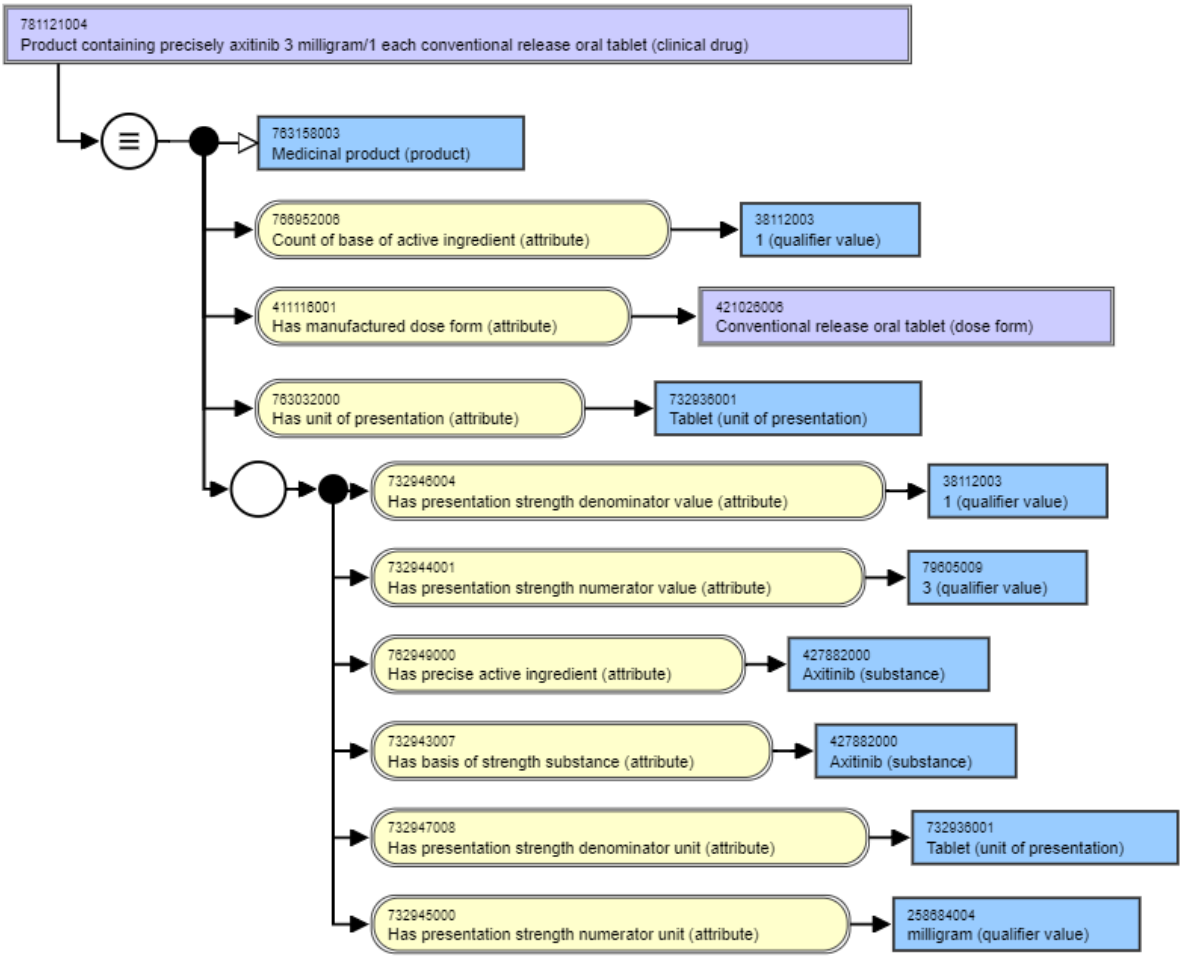


Figure 34: Clinical drug, presentation strength, example stated view

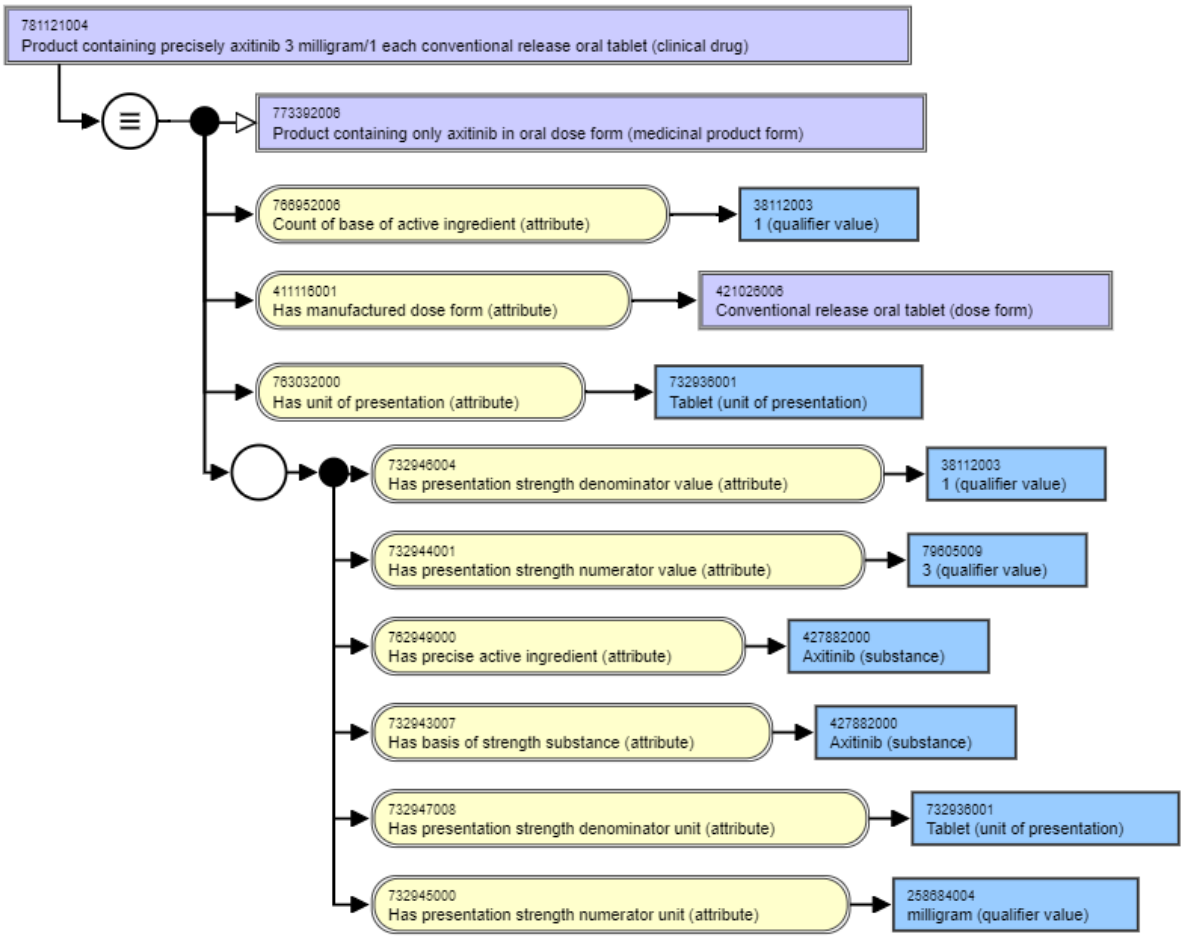


Figure 35: Clinical drug, presentation strength, example inferred view

5.2.3. Attributes of CD (precisely) (presentation strength)

The Clinical Drug (CD precisely) (presentation) concept is defined by three attributes and a set of substance/strength attributes:

Semantic tag	(clinical drug)
Definition status	900000000000073002|Sufficiently defined concept definition status (core metadata concept) • Exceptions: none identified
Attribute: **Has manufactured dose form**	• Range: 736542009 | Pharmaceutical dose form (dose form) | • Cardinality: 1..1 This is the finished dose form that a medicinal product is presented in by the manufacturer, before any transformation into an administrable dose form has taken place
Attribute: **Has unit of presentation**	• Range: < 732935002|Unit of presentation (unit of presentation)| • Cardinality: 0..1 This is the countable entity in which the clinical drug is presented. See the separate section on Unit_of_Presentation for further details, and SNOMED CT Medicinal Product Model Specification v3.0#Appendix_A for the various patterns of use of the unit of presentation concept

Attribute: **Count of base of active ingredient**	• Range: < 260299005|Number (qualifier value)| • Cardinality: 1..1 This attribute should always be present and valued
Relationship Group	One relationship group containing one instance of each of the following attributes is required for each precise active ingredient
Attribute: **Has precise active ingredient**	• Range: < 105590001|Substance (substance)| • Cardinality: 1..* This is a SNOMED CT Medicinal Product Model Specification v3.0#Prec_Act_Ing substance that the concept contains. In each group, only one precise active ingredient substance is stated
Attribute: **Has basis of strength substance**	• Range: < 105590001|Substance (substance)| • Cardinality: 1..1 This is the SNOMED CT Medicinal Product Model Specification v3.0#BoSS that the concept uses. In each group, only one precise active ingredient substance is stated. The basis of strength substance is always stated explicitly, even when it is the same as the precise active ingredient substance
Attribute: **Has presentation strength numerator value**	• Range: < 260299005|Number (qualifier value)| • Cardinality: 1..1
Attribute: **Has presentation strength numerator unit**	• Range: < 767524001 | Unit of measure (qualifier value) | • Cardinality: 1..1
Attribute: **Has presentation strength denominator value**	• Range: < 260299005|Number (qualifier value)| • Cardinality: 1..1
Attribute: **Has presentation strength denominator unit**	• Range: < 767524001 | Unit of measure (qualifier value) | • Cardinality: 1..1

For concepts that have two or more active ingredient substances that are modifications of the same base substance where MP precisely concepts are required, and for single ingredient product concepts where the active substance is an ingredient in these multiple modification multi-ingredient products, the following extra ingredient count attribute will be required:

Attribute: **Count of base and modification pair**	• Range: < 260299005|Number (qualifier value)| • Cardinality: 1..1

For concepts that have two or more active ingredient substances that are modifications of the same base active ingredient substance (i.e. parent ingredient substance) **and** where one is a further modification of the other (for example, a multi-ingredient product containing both dexamethasone phosphate and dexamethasone sodium phosphate, where the dexamethasone phosphate is a modification of dexamethasone (base) and dexamethasone sodium phosphate is a further modification of the dexamethasone phosphate) where MP precisely concepts are required, and for single ingredient product concepts where the active substance is an ingredient in these multiple modification multi-ingredient products, the following extra ingredient count attribute will be required:

Attribute: **Count of active ingredient**	• Range: < 260299005|Number (qualifier value)| • Cardinality: 1..1

As discussed above, and as described in the MRCM rules, for practical and pragmatic reasons the additional ingredient count attributes have to be applied iteratively based on requirement.

5.3. Clinical Drug (precisely) (concentration strength)

5.3.1. Definition of Clinical Drug (precisely) (concentration strength)

An abstract representation of a medicinal product based on description of 1) its precise active ingredient substances only and explicitly, 2) the stated basis of strength substance(s) with strength, expressed as concentration strength and 3) with its manufactured dose form (with the exception of some oral, usually antimicrobial, products where the administrable dose form is be used as it is the most clinically relevant - see below).

This is used for product types such as cutaneous semi-solids (without metered actuation), bulk powders and granules, topical liquids (without metered actuation) including drops, oral liquids and drops, and liquid parenteral products.

5.3.2. Example diagrams for CD (precisely) concentration strength

Stated template view:

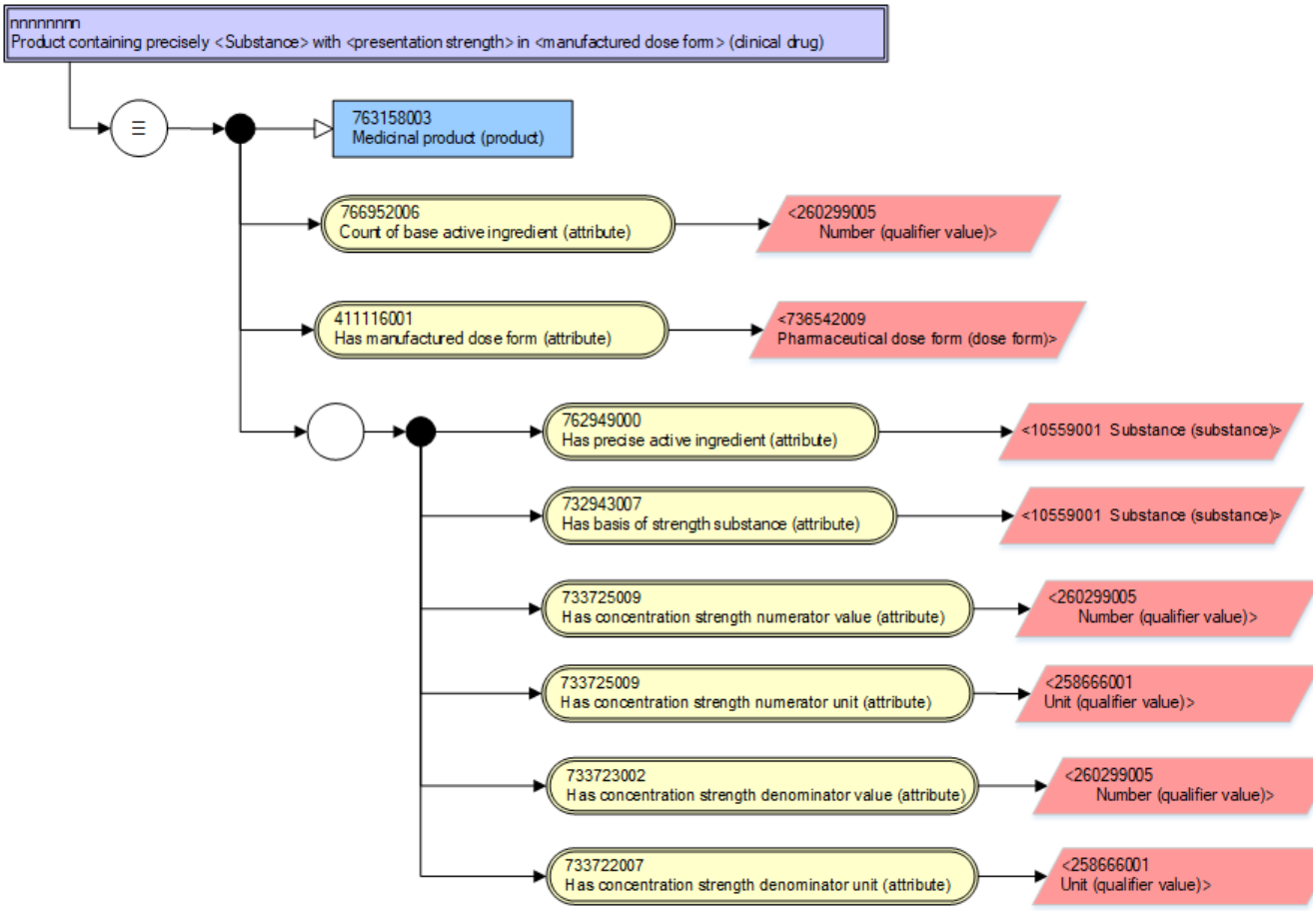


Figure 36: Clinical drug, concentration strength, stated template view

Examples: single active ingredient product: stated view followed by the inferred view that shows the parent concepts associated with the product:

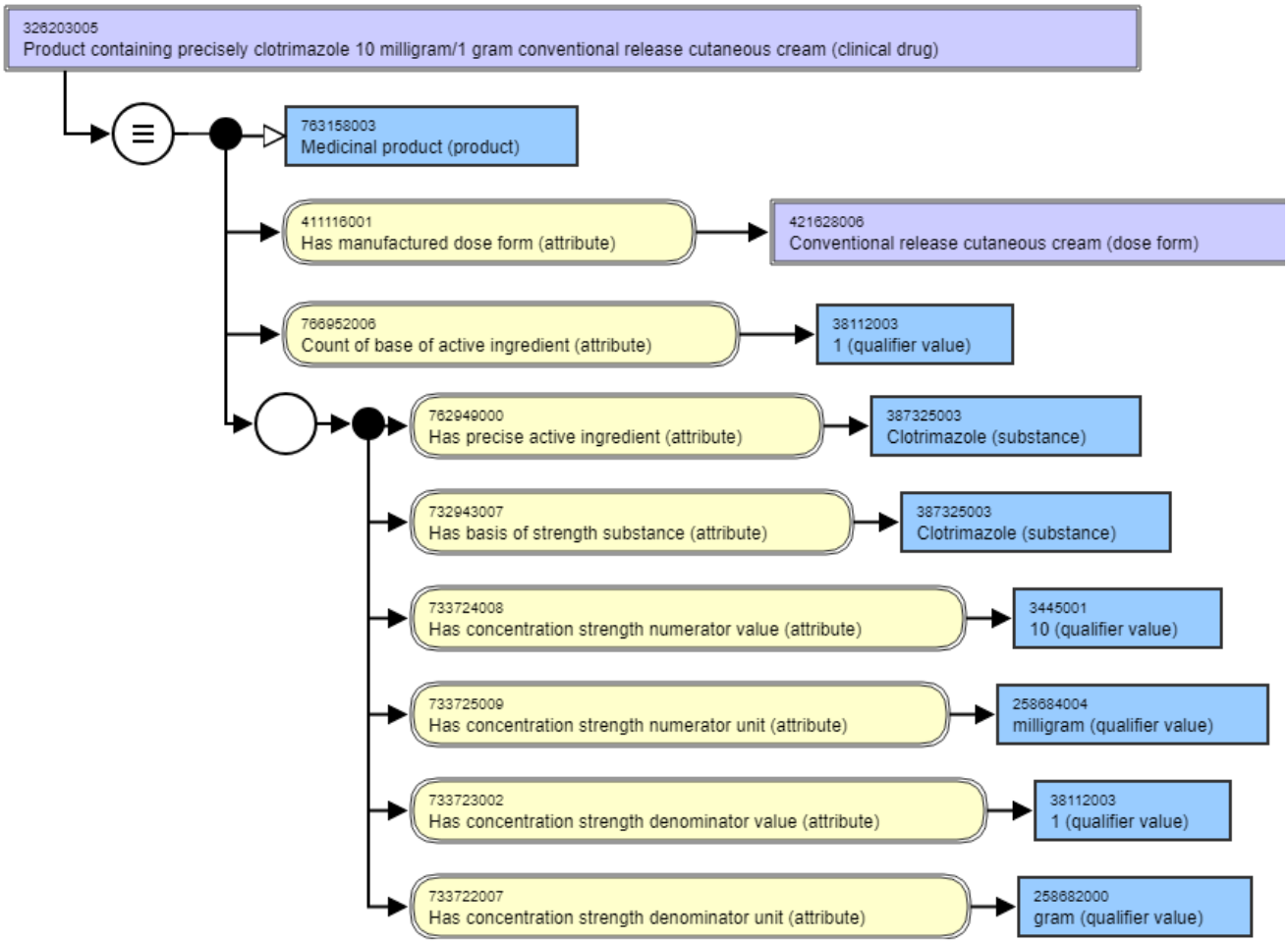


Figure 37: Clinical drug, concentration strength, example stated view

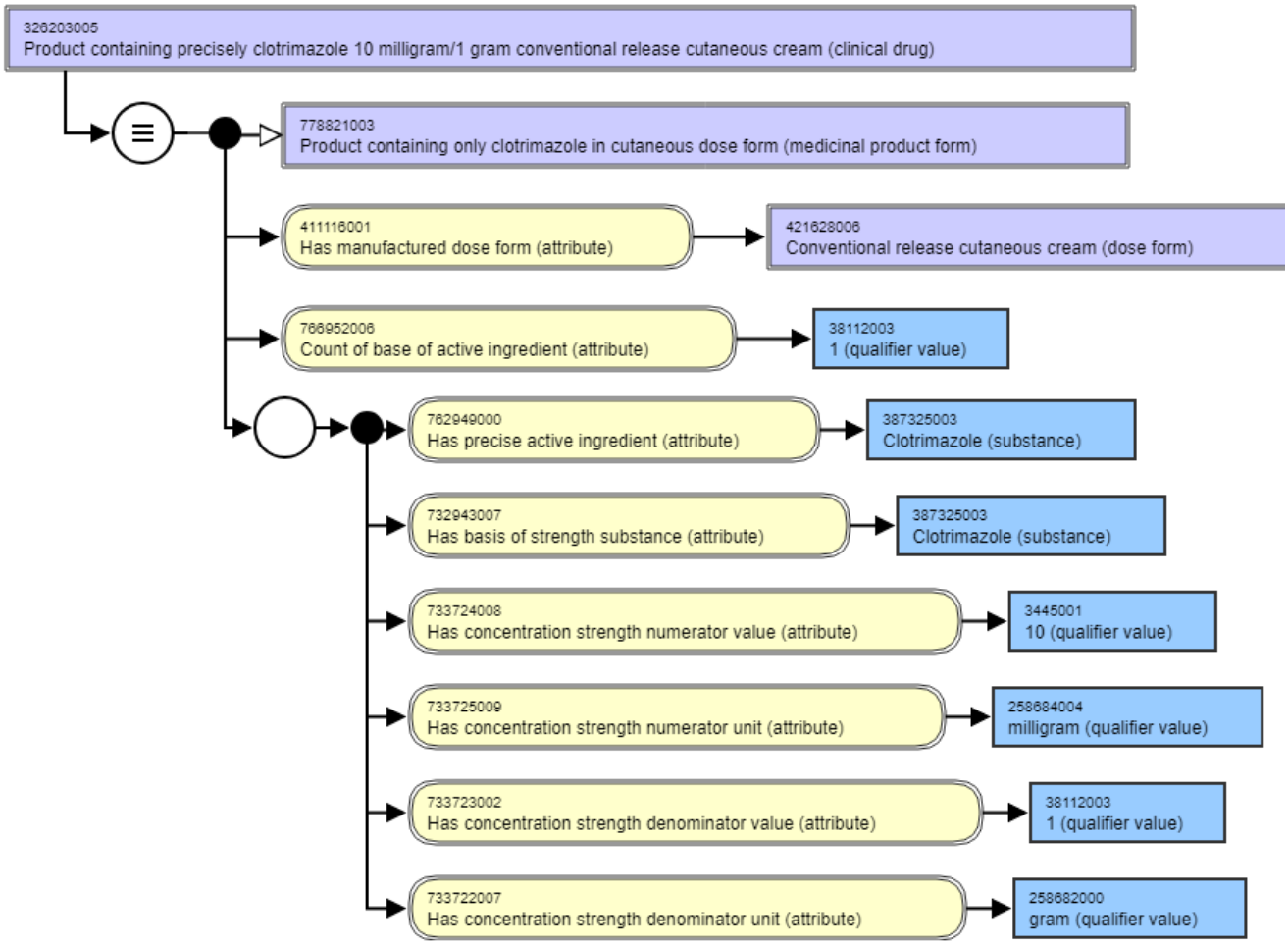


Figure 38: Clinical drug, concentration strength, example inferred view

5.3.3. Attributes of CD (precisely) (concentration strength)

The Clinical Drug (CD precisely) (concentration) concept is defined by two attributes and a set of substance/strength attributes; a Clinical Drug described only by concentration strength does not have a unit of presentation:

Semantic tag	(clinical drug)
Definition status	900000000000073002|Sufficiently defined concept definition status (core metadata concept) • Exceptions: none identified
Attribute: **Count of base of active ingredient**	• Range: < 260299005|Number (qualifier value)| • Cardinality: 1..1 This attribute should always be present and valued
Relationship Group	One relationship group containing one instance of each of the following attributes is required for each precise active ingredient
Attribute: **Has precise active ingredient**	• Range: < 105590001|Substance (substance)| • Cardinality: 1..* This is a Prec_Act_Ing substance that the concept contains. In each group, only one precise active ingredient substance is stated

Attribute: **Has basis of strength substance**	• Range: < 105590001|Substance (substance)| • Cardinality: 1..1 This is the BoSS that the concept uses. In each group, only one precise active ingredient substance is stated. The basis of strength substance is always stated explicitly, even when it is the same as the precise active ingredient substance
Attribute: **Has concentration strength numerator value**	• Range: < 260299005|Number (qualifier value)| • Cardinality: 1..1
Attribute: **Has concentration st rength numerator unit**	• Range: < 767524001 | Unit of measure (qualifier value) | • Cardinality: 1..1
Attribute: **Has concentration st rength numerator value**	• Range: < 260299005|Number (qualifier value)| • Cardinality: 1..1
Attribute: **Has concentration strength denominato r unit**	• Range: < 767524001 | Unit of measure (qualifier value) | • Cardinality: 1..1

For concepts that have two or more active ingredient substances that are modifications of the same base substance where MP precisely concepts are required, and for single ingredient product concepts where the active substance is an ingredient in these multiple modification multi-ingredient products, the following extra ingredient count attribute will be required:

Attribute: **Count of base and modification pair**	• Range: < 260299005|Number (qualifier value)| • Cardinality: 1..1

For concepts that have two or more active ingredient substances that are modifications of the same base active ingredient substance (i.e. parent ingredient substance) **and** where one is a further modification of the other (for example, a multi-ingredient product containing both dexamethasone phosphate and dexamethasone sodium phosphate, where the dexamethasone phosphate is a modification of dexamethasone (base) and dexamethasone sodium phosphate is a further modification of the dexamethasone phosphate) where MP precisely concepts are required, and for single ingredient product concepts where the active substance is an ingredient in these multiple modification multi-ingredient products, the following extra ingredient count attribute will be required:

Attribute: **Count of active ingredient**	• Range: < 260299005|Number (qualifier value)| • Cardinality: 1..1

As discussed above, and as described in the MRCM rules, for practical and pragmatic reasons the additional ingredient count attributes have to be applied iteratively based on requirement.

5.4. **Other Clinical Drug Grouping Concepts not present in this model or in the international release**

A grouping of Clinical Drugs may be constructed by disregarding solvation and hydration, so for example grouping together all products containing only atorvastatin calcium 40mg oral tablets and therefore including concepts representing products with precise active ingredient substance of atorvastatin calcium propylene glycol solvate and those with precise active ingredient substance of atorvastatin calcium. A Clinical Drug grouping concept of this nature would be a "Clinical Drug containing Only" concept as opposed to a "Clinical Drug containing Precisely" concept.

Clinical Drug concepts in the international release are defined by their precise active ingredient substance(s) and their basis of strength substance, as described above. A concept that grouped clinical drugs by their strength and basis of strength substance only (i.e. disregarding the precise active ingredient substance) may be appropriate in some contexts in national extensions (e.g. 'amlodipine 10mg conventional release oral tablet' as a concept with three child concepts 'amlodipine (as amlodipine besiliate) 10mg conventional release oral tablet' and 'amlodipine (as amlodipine mesiliate) 10mg conventional release oral tablet' 'amlodipine (as amlodipine maleate) 10mg conventional release oral tablet'. A Clinical Drug grouping concept of this nature would be a "Basis of Strength Subatance Clinical Drug" concept as opposed to a "Clinical Drug containing Precisely" concept.

SImilar to the BoSS-based CD, an additional grouping of Clinical Drugs might disregard all types of modification, thereby describing only the active moiety, especially in cases where the modifications have little clinical significance and strengths are the same even though the BoSS is the same as the precise ingredient substance. For example a concept might group together both 'promethazine teoclate 25mg conventional release oral tablet' and 'promethazine hydrochloride 25mg conventional release oral tablet' concepts to give a concept such as "Product containing only promethazine 25mg oral tablet".

5.5. **IDMP Compatibility**

Both CD (only) presentation and CD (only) concentration concepts are directly compatible with the IDMP Manufactured Item concept since both presentation strength and concentration strength can be represented in the IDMP model. Note however that the Manufactured Item is not an "identified" class in IDMP (no identifier attribute within it) and therefore having the CD presentation and CD concentration concepts within SNOMED CT provides identified concepts that are in addition to the IDMP concepts, giving value beyond IDMP to support the clinical drug use cases. The diagram (from IDMP 11615 Ingredient Substance and Strength and TS 20443 Implementation Guide, Section 9.7.2) below shows the Manufactured Item concept using the blue box:

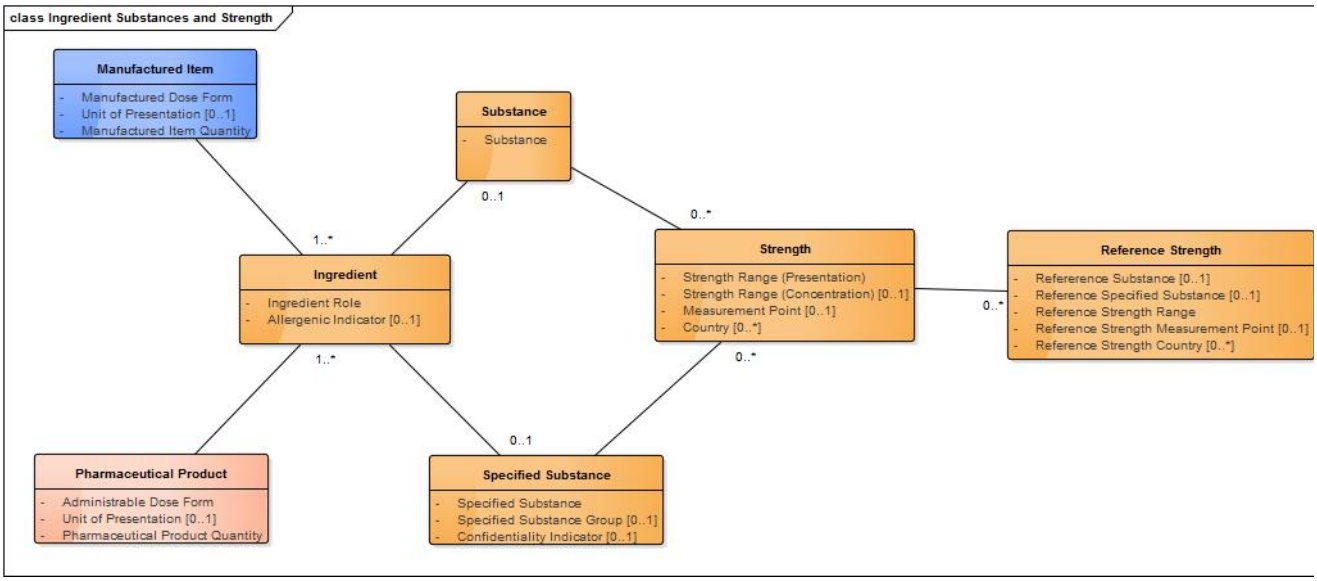


Figure 39: Manufactured Item in ISO 11615, showing presentation and concentration strength and reference strength (BoSS)

The distinction between Substance and Specified Substance in IDMP is thus: as substance is "any matter of defined composition that has discrete existence, whose origin may be biological, mineral or chemical" whereas a Specified Substance is one that is "defined by groups of elements that describes multi-substance materials or specifies further information on substances relevant to the description of Medicinal Products". Specified substances are substances like simeticone, which are mixture substances, or substances that are defined by pharmacopoeial specification (like water for injection) or substance where a particular manufacturing process is specified (as for biosynthetic insulins). For SNOMED CT, all such substances, with the possible exception of 'water for injection') can be present in the Substance hierarchy and are candidate concepts to be used in the ingredient role attributes of the Medicinal Product hierarchy; as such the IDMP distinction between Substance and Specified Substance has no material effect. In IDMP, the precise ingredient substance would be the substance with the (precise) ingredient role in the Ingredient Class; the Basis of Strength Substance would be described in the reference strength class. IDMP also allows additional description of strength (e.g. using units instead of mg) using the reference strength class.

6. **Supporting Concepts: the Attributes of the classes in the Medicinal Product Hierarchy**

The following sections discuss the detail of the concepts that are used as attributes for the classes of representation in the Medicinal Product Hierarchy.

6.1. **Describing Ingredient Substances**

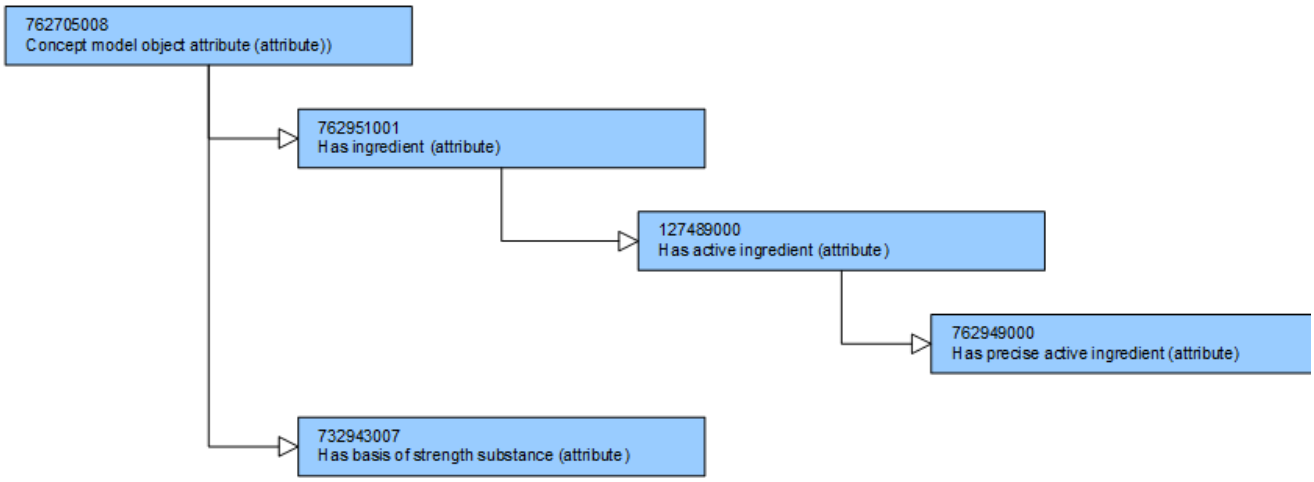


Figure 40: Ingredient role attributes

The diagram above shows the relationship of the various attribute roles that a substance can play in the definition of MP, MPF and CD description of medicinal products. Any concept from the Substance hierarchy may play one or more of these roles within a product. In all of the descriptions below, when the phrase "a set of substances" is used, the set may have only one member.

6.1.1. Has ingredient

A medicinal product concept has a set of substances that are combined to manufacture the medicinal product, that can be described using the "has ingredient" attribute. However, each substance(s) in the "has ingredient" set will have more specific ingredient role that should be described using that more specific concept. Therefore, this is a grouping concept that is not used for definition of medicinal product concepts in the Medicinal Product hierarchy; it is a parent concept and it provides scope for further child concepts to be added to support future use cases, such as the description of inactive ingredient substances in products in a national extension. The physical presence or otherwise of the ingredient substance in the finished product is not explicitly part of the definition; for example substances that play a role in the manufacturing process, such as solvents etc. are deemed "ingredients" for the product; their presence may or may not remain in the manufactured item. As such, basis of strength substance could be considered as a child concept of the Has ingredient concept, although it is not modelled in that way currently.

6.1.2. Has active ingredient

A medicinal product concept has a set of active ingredient substance(s) responsible for providing the therapeutic effect of the medicinal product and which are described using the clinically relevant part or whole of the substance that is intended to have a therapeutic action on or within the body. In the majority of cases, this description excludes modifiers such as esters, salts or other non-covalent derivatives (such as a complex, chelate etc.), but may include them in the minority of cases when clinically significant. This is therefore usually an abstract representation of the active ingredient substance(s) and is used in more abstract representations of medicinal products, such as MP (some).

Note that "clinical significance" can be described as "something that as a practical, demonstrable effect on the treatment and condition of the patient". For example: different modifiers of a particular active moiety have clinical significance if they affect the potency of the therapeutic action of the moiety (and therefore have an affect on the dose quantities to be used). See Kazdin, E The Meanings and Measurement of Clinical Significance *Journal of Consulting and Clinical Consulting* 67 (3): 332–9[2]
This is the attribute role that is used in the definition of the MP concept (containing and only) and the MPF concept.
Examples of substances playing the role of active ingredient in a medicinal product:

- azithromycin where the precise active ingredient may be azithromycin dihydrate, azithromycin hemiethanolate monohydrate, azithromycin isopropanolate monohydrate
- haloperidol where the precise active ingredient may be haloperidol hydrochloride, haloperidol decanoate, haloperidol lactate
- esomeprazole where the precise active ingredient may be esomeprazole magnesium dihydrate, esomeprazole magnesium trihydrate, esomeprazole sodium
- oxybutynin where the precise active ingredient may be oxybutynin chloride or oxybutynin xinafoate
- diclofenac where the precise active ingredient may be diclofenac sodium, diclofenac potassium, diclofenac diethylamine
- axitnitib where the precise active ingredient substance is also axitinitib

6.1.3. Has precise active ingredient

A medicinal product concept has a set of precise active ingredient substance(s), those substance(s) that provides the therapeutic effect of the medicinal product and which are described using the fullest and most specific description of the substance *as it is used in the product(s) that the concept represents* (as they are presented by the manufacturer in the manufactured dose form, before any dilution or transformation). The precise active ingredient substance may include various modifiers, such as salts, esters, polymers (e.g. pegylation), and/or solvates (including waters of hydration); not all substances, even when used as the precise active ingredient substance, have a modification (see axitnitib). This is the attribute role that is used in the definition of the MP (precisely) concept, and in the definition of the CD (precisely).
Examples:

- azithromycin hemiethanolate monohydrate

- haloperidol decanoate
- esomeprazole magnesium dihydrate
- oxybutynin chloride
- paroxetine hydrochloride isopropyl solvate
- dexamethasone sodium phosphate
- sorafenib tosylate
- axitinib

The precise active ingredient attribute will use the Substance hierarchy as a flat list (without role chaining), so that a Clinical Drug containing a modified substance is not subsumed under a clinical drug containing the unmodified substance, thereby unintentionally adding more recursion to the clinical drug class (for example: so that a morphine (base) precise clinical drug does not subsume a clinical drug containing precisely morphine sulphate). This highlights the difference between the semantic of "contains precisely" which explicitly and exclusively describes the full modified substance in the medicinal product concept and "contains only" which inclusively describes the therapeutically active moiety which may be manifest in one or more substance modifications of itself.

Examples:

- "contains dexamethasone only" means that a product will contain only dexamethasone as its active ingredient; that dexamethasone may be present as dexamethasone base, as dexamethasone phosphate, dexamethasone sodium phosphate, as dexamethasone acetate, as dexamethasone palmitate etc.
- "contains dexamethasone phosphate only" means that a product can contain either dexamethasone phosphate or dexamethasone sodium phosphate (which is a modification of dexamethasone phosphate) as its active ingredient; but it will not contain dexamethasone acetate or dexamethasone palmitate etc.
- "contains dexamethasone phosphate precisely" means that a product will contain exclusively dexamethasone phosphate; dexamethasone sodium phosphate will not be present

See also the subsection below "Using the ingredient roles" which provides a diagram further describing the use of role chaining with the active ingredient role and that there is no role chaining for the precise active ingredient role.

6.1.4. Basis of strength substance

A medicinal product clinical drug concept has one or more substances that have the role of being the substance against which the strength quantity(s) of the product(s) are measured. There will be a basis of strength substance stated for each active ingredient substance present in a multi-ingredient clinical drug product.

Examples:

- azithromycin - in an oral suspension containing azithromycin hemiethanolate monohydrate, where the strength is 100 mg per 5 mL of azithromycin
- haloperidol in a solution for injection containing haloperidol decanoate, where the strength is 250 mg per 5 mL of haloperidol
- esomeprazole - in a prolonged release tablet containing esomeprazole magnesium dihydrate, where the strength is 20 mg per tablet of esomeprazole
- oxybutynin chloride – in an oral tablet containing oxybutynin chloride, where the strength is 5 mg per tablet of oxybutynin chloride
- paroxetine – in an oral tablet containing paroxetine hydrochloride isopropyl solvate, where the strength is 10 mg per tablet of paroxetine
- dexamethasone phosphate – in a solution for injection containing dexamethasone sodium phosphate, where the strength is 4 mg per 1 mL of dexamethasone phosphate
- diclofenac sodium – in a gastro-resistant tablet containing diclofenac sodium, where the strength is 25 mg per tablet of diclofenac sodium
- sorafenib – in an oral tablet containing sorafenib tosylate, where the strength is 200 mg per tablet of sorafenib

Almost always, the basis of strength substance is either the active ingredient substance or the precise active ingredient substance; very occasionally products are licensed using a "reference" basis of strength substance (e.g. a product containing diclofenac diethylammonium as its precise active ingredient substance having its strength expressed in terms of diclofenac sodium).

6.1.5. Using the ingredient role

The Medicinal Product and Medicinal Product Form use the active ingredient attribute, which will have a role chain attached to it, so that it can use the Substance hierarchy as a hierarchy through the "is modification" relationship. This will allow the classifier to make the appropriate relationships between MPs, MPFs and CDs based on their active ingredient substances. The role chain is a characteristic that is not inherited, so the precise active ingredient attribute does not inherit this characteristic. The Clinical Drug uses the precise active ingredient attribute /relationship which will use the Substance hierarchy as a flat list without role chaining, so that a clinical drug containing a modified substance is not subsumed under a clinical drug containing the unmodified substance, thereby unintentionally adding more recursion to the clinical drug class (for example: so that a morphine (base) precise clinical drug does not subsume a clinical drug containing precisely morphine sulphate).

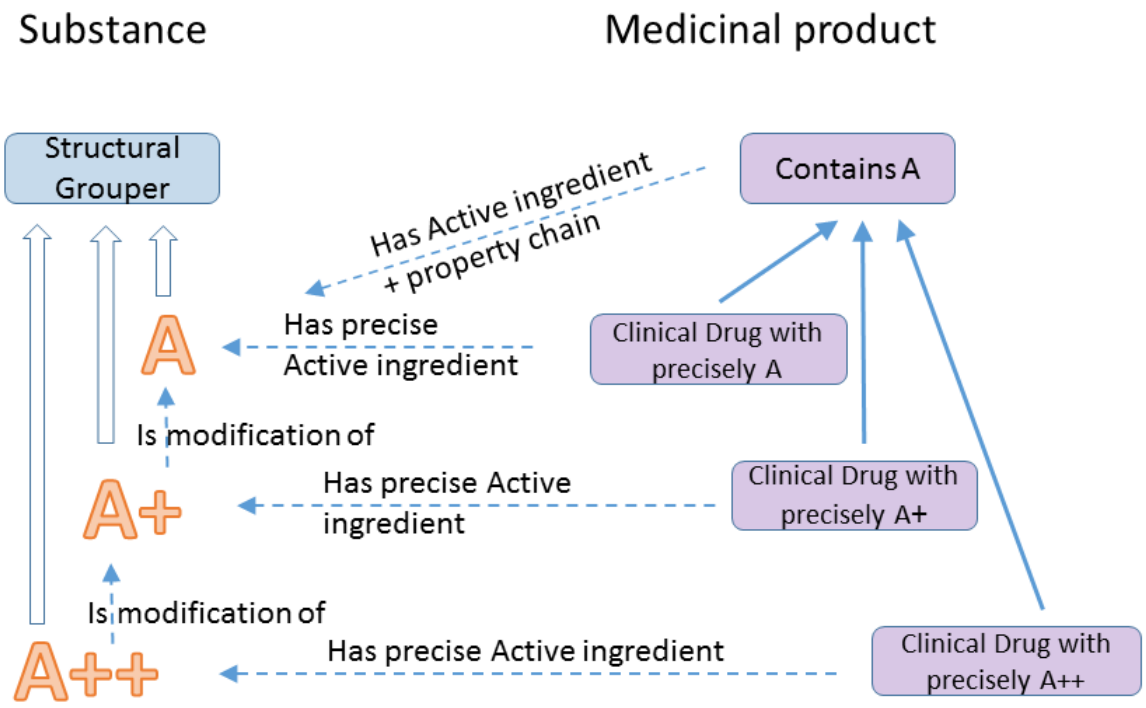


Figure 41: Ingredient role chaining

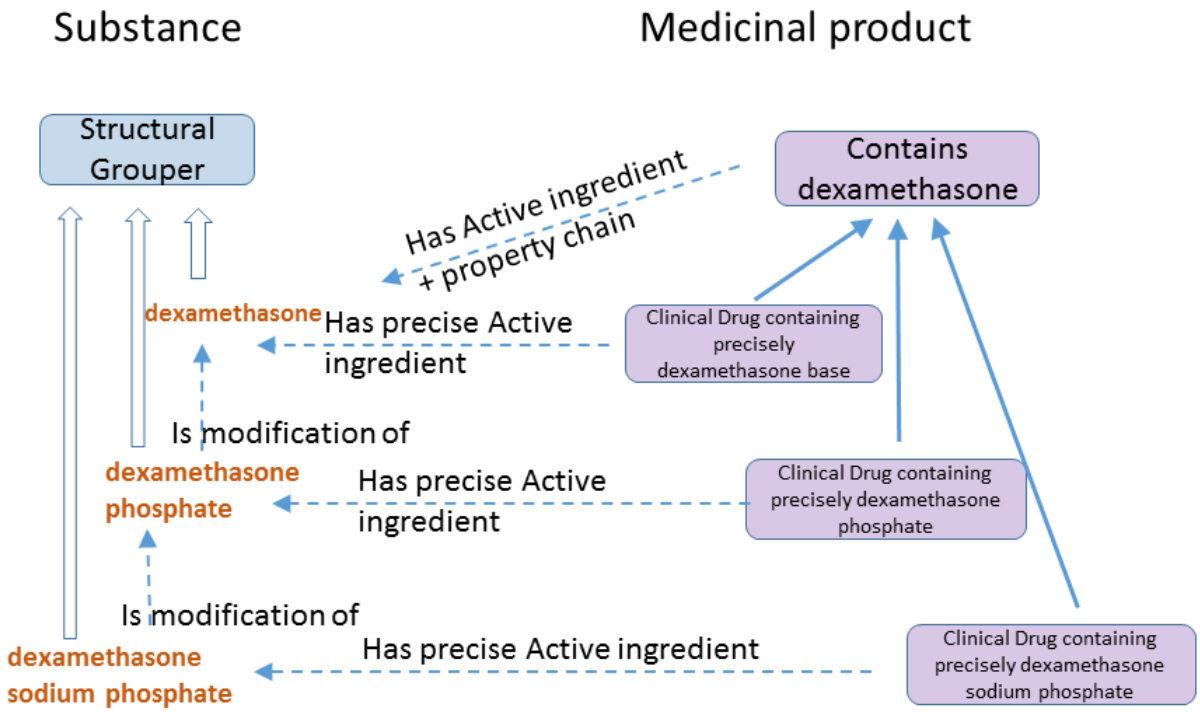


Figure 42: Ingredient role chaining example

6.1.6. IDMP Compatibility

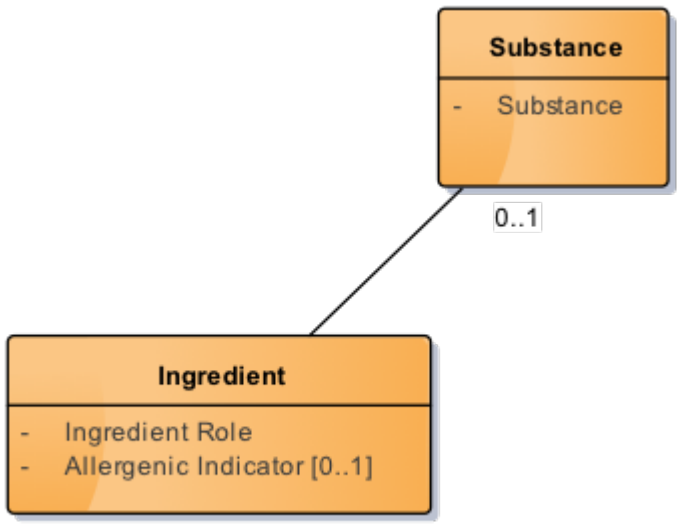


Figure 43: Ingredient role in ISO 11615 of IDMP

Ingredient role is a specific attribute in ISO 11615 in IDMP, but no vocabulary/value set was specified in the conceptual standard for the ingredient roles. Examples that have been given include "active", "inactive" and "adjuvant". This supports the regulatory listing of all the substances present in a product, with their basic role (therapeutic or otherwise).
The explicit use of ingredient roles in the Medicinal Product model is compatible with the IDMP conceptual model; however, the relationship of ingredient role to substance strength is still being elucidated in IDMP. Note that the (role) concept of "basis of strength substance", in the very few cases where it is not actually a substance present in the product, is managed by the use of the Reference Substance class in IDMP (SNOMED CT Medicinal Product Model Specification v3.0_Medicinal_Product_Strength).
See also IDMP Compatibility for Clinical Drug (above).

6.2. **Ingredient Count**

Ingredient count is the mechanism that the SNOMED CT concept model is using as a proxy to implement a "closed world" view of medicinal products such that a medicinal product concept can be represented as containing only substance X as its active ingredient, and that all more granular child medicinal product concepts also containing only substance X subsume under the correct parent concept(s).

Three count attributes are available for use, but only one is mandatory for all "only" concepts; i.e. MP (only), MP (precisely), MPF (only) and CD). The additional ingredient counts have to be applied iteratively, if and when they are required based on the presence of multi-ingredient concepts which contain active ingredient substances that have modifications of the same base. For new concepts, the count attribute is first authored for Clinical Drug concepts, which have their precise ingredient substance described; the more abstract classes can then be populated upwards using the base (or parent) active ingredient substance if different.

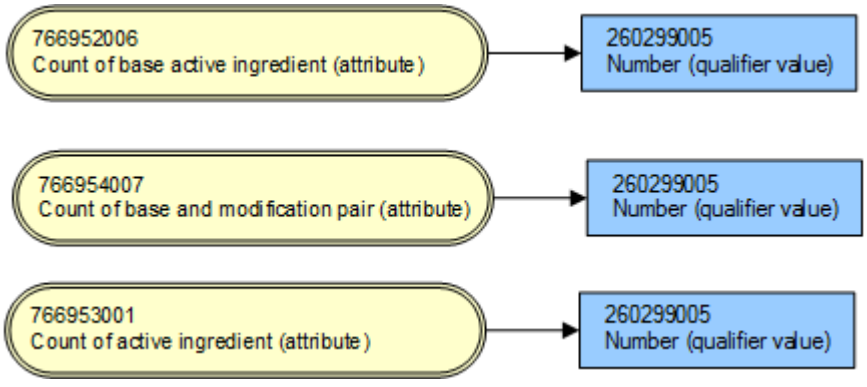


Figure 44: Ingredient count attributes

6.2.1. Count of base of active ingredient - mandatory for the closed world view

This count is the number of base (or root or main parent) active ingredient substance(s) (as described in the SNOMED CT Substance hierarchy) present in the medicinal product. Base ingredient substances can be identified from their modifications through the relation "is modification of", traversed iteratively if necessary, until reaching a substance that is not a modification of any other substance.

For all single ingredient products and for the majority of multi-ingredient products, this is the only count information that needs to be described in order to support correct subsumption.

Example:

Precise active ingredient substance(s)	Base active ingredient substance(s)	Count of base of active ingredient
Amlodipine besylate	Amlodipine	1
Atorvastatin calcium trihydrate	Atorvastatin	1
Amlodipine besylate and Atorvastatin calcium trihydrate	Amlodipine and Atorvastatin	2

The tooling uses these values to produce the correct subsumption hierarchy, as shown diagrammatically below:

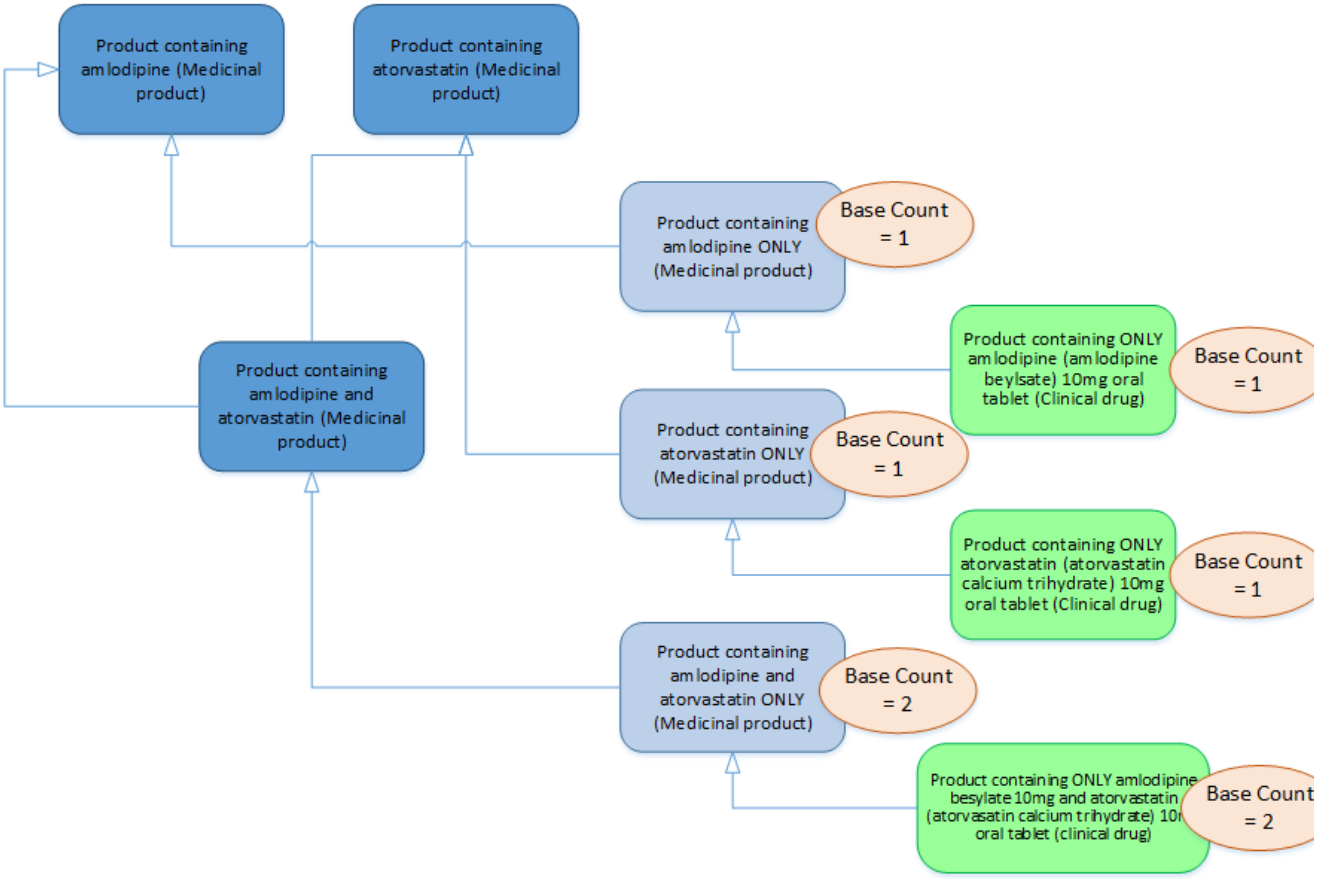


Figure 45: Ingredient count attributes simple multi-ingredient example

The base count facilitates the correct subsumption relationship between the "Product containing only Amlodipine and Atorvastatin" and the Clinical Drug that contains only Amlodipine and Atorvastatin. It avoids the "Product containing only Amlodipine and Atorvastatin" being incorrectly subsumed by the concept "Product containing only Amlodipine" or by the concept "Product containing only Atorvastatin" since a concept of a base count of 1 will not subsume a product with a base count of 2. Similarly the Clinical Drug concepts containing only Amlodipine or only Atorvastatin, both of which have a base count of 1, are prevented from being subsumed by the "Product containing only Amlodipine and Atorvastatin" which has a base count of 2.

6.2.2. Count of base and modification pair (closed world view) - optional - to be used in certain circumstances

This count is used for multi-ingredient products where the two (or more) active ingredient substances share the same base active ingredient substance. This will only occur when at least one of the active ingredient substances is a modification of a base active ingredient substance. The count used in addition to the base active ingredient substance count. The count is of how many pairs of base + modification substances are present in the medicinal product; this draws from the Substance hierarchy where concepts are managed using the pattern of base substance with related concepts being modifications (salts, esters, chelates) of the base substance; each modification is therefore a "pair".

Example:

Precise active ingredient substance (s)	Base active ingredient substance(s)	Count of base of active ingredient	Base + modification pair	Count of Base + modification pair
Betamethasone sodium phosphate	Betamethasone	1	Betamethasone + sodium phosphate	1
Betamethasone acetate	Betamethasone	1	Betamethasone + acetate	1
Betamethasone sodium phosphate and Betamethasone acetate	Betamethasone	1	Betamethasone + sodium phosphate Betamethasone + acetate	2

Betamethasone sodium phosphate and betamethasone acetate are both modifications of the betamethasone: a phosphorylation and an acetate esterification; however neither are modifications of each other.

The tooling uses these values to produce the correct subsumption hierarchy, as shown diagrammatically below:

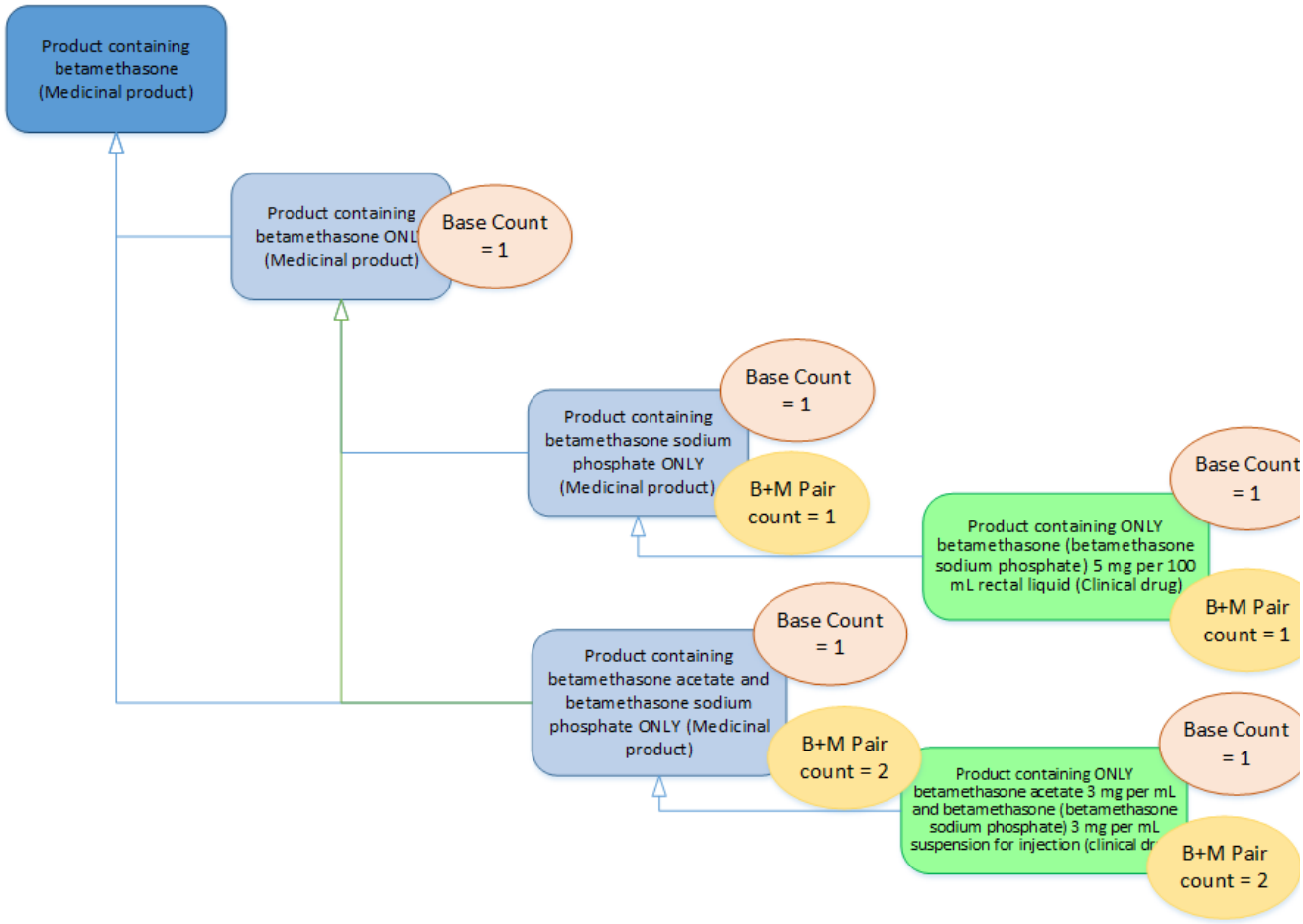


Figure 46: Ingredient count attributes complex multi-ingredient example with multiple modification of a single base active ingredient requiring two ingredient count attributes

Base count alone would not prevent the incorrect subsumption of the "Clinical Drug containing precisely Betamethasone sodium phosophate and Betamethasone acetate" to the parent Medicinal product concepts containing Betamethasone sodium phosophate only (or Betamethasone acetate only - not shown on the above diagram). By adding in the Count of Base + modification pair, that incorrect subsumption is avoided and the "Clinical Drug containing precisely Betamethasone sodium phosophate and Betamethasone acetate" is correctly subsumed by just the one parent Medicinal Product, that "containing only Betamethasone sodium phosophate and Betamethasone acetate".The (grand)parent medicinal product concept "Product containing betamethasone only" does not (cannot) have a Count of Base + modification pair, since it does not have any active ingredient modification described; therefore it can correctly parent medicinal product concepts containing only Betamethasone sodium phosophate, containing only Betamethasone acetate (not shown) and containing "only Betamethasone sodium phosophate and Betamethasone acetate", because they all share a Base count of 1, relating to Betamethasone.

6.2.3. Count of active ingredient (closed world view) - optional - to be used in certain circumstances

This count is used for the fairly rare cases of multi-ingredient products where the two (or more) precise active ingredient substance(s) share the same base active ingredient substance and one of those precise active ingredient substances is a modification of another; it is used in addition to the base count and the base + modification pair count. The count is of how many precise active ingredient substance(s) are present in the product (and therefore can be a count of the number of precise active ingredient attributes are present on a concept).

Example:

Precise active ingredient substance (s)	Base active ingredient substance(s)	Count of base of active ingredient	Base + modification pair	Count of Base + modification pair	Count of (precise) ingredient substance(s)
Insulin aspart	Insulin	1	Insulin + aspart	1	1
Insulin aspart protamine	Insulin	1	Insulin + aspart protamine	1	1
Insulin aspart and Insulin aspart protamine	Insulin	1	Insulin + aspart Insulin + aspart protamine	1	2

Insulin aspart and insulin aspart protamine are both modifications of insulin; but since Insulin aspart protamine is itself a modification of Insulin aspart, the Base + modification pair count is only equal to 1 (insulin plus 1 modification - the aspart). To get correct subsumption between the Clinical Drug and Medicinal Product concepts in these types of situations, the third count, that of precise active ingredient substance, must be used as well.

The tooling uses these values to produce the correct subsumption hierarchy, as shown diagrammatically below:

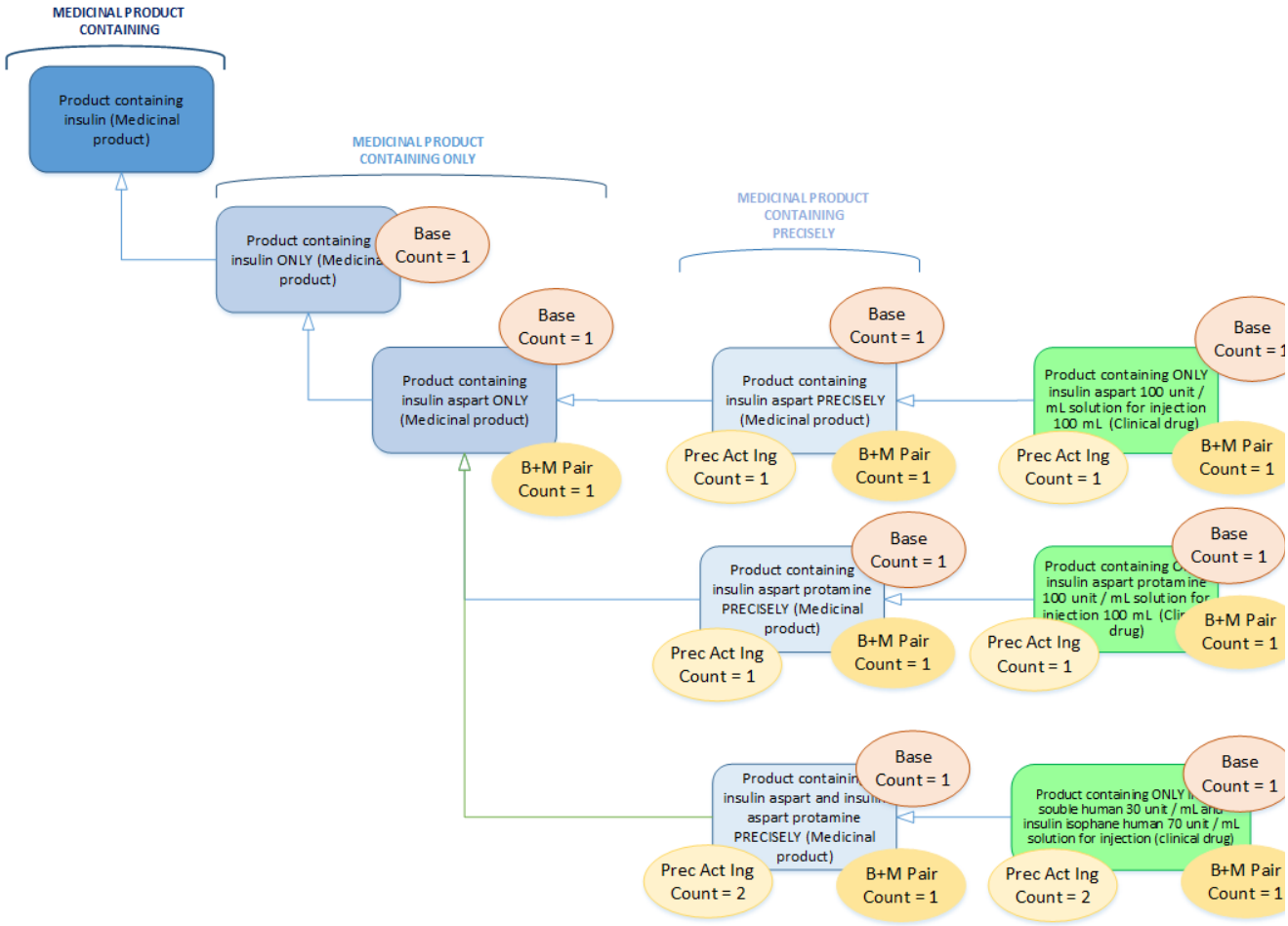


Figure 47: Ingredient count attributes complex multi-ingredient example with multiple modification of a single base active ingredient re quiring three ingredient count attributes

Neither base count alone nor base count and base + modification pair count would prevent the incorrect subsumption of the "Clinical Drug containing precisely Insulin aspart and insulin aspart protamine" because both give a count of 1. The differentiation comes from the counting the precise active ingredient substances. This then gives the (optional in the international release) intermediate parent concepts of "Medicinal product containing precisely" either "insulin aspart", "insulin aspart protamine" or "insulin aspart and insulin aspart protamine" with their correct Clinical Drug concepts as children. The MP (precisely) concepts are then correctly subsumed to the (grandparent) MP (only) concept of insulin aspart only, on the basis of the base count of 1.

6.3. **Describing Dose forms**

A clinical drug concept has a pharmaceutical dose form, the physical manifestation of a medicinal product that contains the active ingredient substance(s) and inactive ingredient substances that are intended for administration for the patient. The clinical drug concept in the international release is defined by its manufactured dose form, the dose form as the item is presented by the manufacturer into the supply chain. This may be the same as the administrable dose form, which is the dose form that can be given to the patient after any necessary transformation (such as dissolution or dispersion) has taken place. or it may be different. Examples of the relationship between manufactured and administrable dose forms and transformation are given below. Note that both manufactured dose forms and administrable dose forms are types of pharmaceutical dose form.

Manufactured dose form	Administrable dose form	Transformation
conventional release oral tablet	conventional release oral tablet	none
tablet for conventional release oral solution (synonym "soluble oral tablet")	oral solution	dissolve
conventional release cutaneous cream	conventional release cutaneous cream	none
powder for prolonged-release suspension for injection	prolonged-release suspension for injection	disperse

The exception to the principle of using the manufactured dose form to describe clinical drugs in the international release is for oral antimicrobial liquid products (solutions, suspensions) that are supplied by the manufacturer as powders but that undergo dissolution or dispersion prior to dispensing for administration. The exception is present because of the need to describe these products using a clinically relevant strength reflecting the concentration of the administered liquid.

See also the Dose Form Model - Description of Model & Editorial Guidelines for Modeling and Terming and the pages underneath this header page.

6.4. Describing Medicinal Product Strength - Presentation and Concentration Strength

"Medicinal product strength" is not well defined in standards. It is closely aligned with "potency" which in pharmacology describes the measurement or calculation of the therapeutic activity of the medicine; this is expressed in terms of the amount of medicine required to produce an effect of given intensity.
Strength is a ratio type concept: expressing the amount of something against another amount of something, which in practical terms is expressed fractionally using the numerator and denominator quantities and their relevant units. The numerator represents how much of the active ingredient substance there is, and the denominator represents the "whole" that the numerator amount is present in.
For a medicinal product, therefore, the strength is:
the amount of (active) substance (in the form of) the basis of strength substance ***in one instance of "a whole" of medicinal product***

It is the "*one instance of "a whole" of medicinal product*" that causes the difficulty. It is not possible to have a single pattern for what this means for all types of medicinal products. Therefore, the consensus for all medicinal product terminology is to define the pattern for each type of product and apply it consistently. In addition, because historically, there has been a difference in how to develop and apply these patterns, a differentiation has developed between two types of representation "presentation strength" and "concentration strength", which are best expressed explicitly.

- **Presentation strength**

Presentation strength is the amount of the basis of strength substance present in the unit of presentation of or in the volume (or mass) of the single clinical drug being represented.

- **Concentration strength**

Concentration strength is the amount of the basis of strength substance present per unitary amount (volume, mass) of the single clinical drug being represented.

These two options may be used separately, as they are in this international model specification but can also be used together (as may be used in national extensions), thereby producing three patterns for how medicinal product strength can be described. The place of unit of presentation to provide the "bounding" and to support the description of "a whole" for the medicinal product is described in detail in its own section below.

6.4.1. Use of concentration strength and presentation strength

Description of strength is a safety issue. Mindful that SNOMED core is a reference terminology not an interface terminology, it is still important that the description of product strength should be that which is least confusing for national extensions to use and build out from. Presentation strength is deemed by patient safety agencies to be the least confusing for the majority of types of products so should be provided whenever possible. However, to avoid combinatorial explosion and to have realistic maintenance processes for the international core content, some types of products that could be described with both presentation and concentration strength will be described with concentration strength only.

6.4.2. Table of Strength Patterns

Strength Pattern	Product Types	Unit of Presentation	Presentation Strength (logical)	Presentation Strength (usual description)	Concentration Strength	Example (not necessarily to SNOMED FSN pattern)
Pattern 1a Unit of presentation draws from /bounded as the basic dose form	tablets, capsules, pessaries, suppositories etc.	The basic solid dose form e.g. "tablet"	Mass amount per 1 unit of presentation e.g. "5 mg per tablet	Mass amount only; the “per” is implicit e.g. "5 mg"	The weight of one finished dose form (including excipients) is rarely known so concentration strength is not usually available Not deemed of any clinical significance	Bendroflumethiazide 5mg conventional release oral tablet
Pattern 1b Unit of presentation bounds as a continuous basic solid dose form	sachets, ampoules or vials *containing* powders or granules etc.	The "intimate container" e.g. "vial"	Mass amount per 1 unit of presentation e.g. "2 g per vial"	Mass amount, with the “per” either implicit or explicit e.g. "2 g per vial" or just "2 g"	The concentration strength is not usually available (total amount of solid, including excipients not known) Not deemed of any clinical significance	Cefotaxime 2g (per vial) powder for solution for injection

Pattern 1c Unit of presentation bounds continuous basic dose form using a metered dose valve	pressurised inhalers, cutaneous sprays, nasal sprays etc.	Actuation	Mass amount per 1 unit of presentation e.g. "100 mcg per actuation"	Mass amount, with the “per” explicitly stated e.g. "100 mcg per actuation"	The concentration of product (usually liquid) inside the metered delivery system may be known (to the regulatory agency) but is Not deemed of any clinical significance	Beclometasone dipropionate 100 mcg per actuation pressurised inhalation
Pattern 2a - *not used in the international release, may be used in national extensions* Unit of presentation bounded by the intimate container, which contains a volume of a liquid dose form	parenteral liquids, unit dose nebuliser solutions etc.	The "intimate container "e.g. "ampoule"	Mass amount per volume contained in the unit of presentation e.g. "100 mg per 20 mL"	Mass amount per volume the “per” is explicitly stated e.g. "100 mg per 20 mL"	Mass amount per unitary volume e.g. "5 mg per (1) mL"	Metoclopramine hydrochloride 100 mg per 20 mL solution for injection ampoule
Pattern 2a - *not used in the international, may not be used in national extensions either, depending on culture and use case(s)* Unit of presentation is an "external volume delivery device" (as opposed to a metering valve that is integral to the presentation of the medicinal product)	oral liquids	"Volume delivery device" e.g. "5 mL (medicine spoon)"	Mass amount per volume contained in the unit of presentation e.g. "100 mg per 5 mL"	Mass amount per volume the “per” is explicitly stated e.g. "100 mg per 5 mL"	Mass amount per unitary volume e.g. "40 mg per (1) mL"	Aciclovir 200mg/5mL oral suspension
Pattern 3a Unit of presentation exists, but clinically relevant strength is concentration strength (as a proxy for rate)	transdermal patches	The "intimate container" e.g. "patch"	Mass amount per unit of presentation e.g. "20.4 mg per patch" Not deemed of any clinical significance	NA	Mass amount per unitary volume/time e.g. "100 mcg per (1) hour"	Fentanyl 100 mcg per hour transdermal patch
Pattern 3a Unit of presentation exists, but clinically relevant strength is concentration strength	insulins	The "intimate container" e.g. "cartridge"	Mass amount per unit of presentation e.g. "150 units per cartridge" Not deemed of any clinical significance	NA	Mass amount per unitary volume e.g. "100 unit per (1) mL"	Insulin human soluble 100 unit / mL solution for injection
Pattern 3a Unit of presentation exists, but clinically relevant strength is concentration strength	bulk parenteral solutions	The "intimate container" e.g. "bag"	Mass amount per unit of presentation e.g. "450 mg per 500 mL" Not deemed of any clinical significance	NA	Mass amount per unitary volume e.g. "9 mg per 1 mL" *Synonym: 0.9% w/v*	Sodium chloride 0.9% solution for infusion
Pattern 3a Unit of presentation exists, but is not stated, concentration strength used	parenteral liquids, unit dose nebuliser solutions etc.	The "intimate container "e.g. "ampoule"	Mass amount per volume contained in the unit of presentation e.g. "100 mg per 20 mL"	Mass amount per volume the “per” is explicitly stated e.g. "100 mg per 20 mL"	Mass amount per unitary volume e.g. "5 mg per (1) mL"	Metoclopramide hydrochloride 5 mg per 1 mL solution for injection ampoule
Pattern 3b Continuous presentation; no unit of presentation exists	cutaneous semi-solids (without metered actuation)	Does not exist			Mass amount per unitary mass/volume e.g."10 mg per 1 g" *Synonym: 1 % w/w*	Hydrocortisone 1% cutaneous cream
Pattern 3b Continuous presentation; no unit of presentation exists	bulk powders and granules	Does not exist			Mass amount per unitary mass/volume e.g."620 mg per 1 g" *Synonym: 62 % w/w*	Sterculia 62% oral granules
Pattern 3b Continuous presentation; no unit of presentation exists	topical liquids (without metered actuation)	Does not exist			Mass amount per unitary mass/volume e.g."5 mg per 1 mL" *Synonym: 0.5 % w/v*	Chloramphenicol 0.5% eye drops
Pattern 3b Continuous presentation; no unit of presentation exists	oral liquids /drops	Does not exist			Mass amount per unitary mass/volume e.g."50 mcg per 1 mL"	Digoxin 50 mcg per 1 mL oral drops, solution

6.4.3. Use of Product Strength patterns for Clinical Drug concepts in the international release

Clinical drug concepts using pattern 1 will be present in the international release as will clinical drugs using strength pattern 3. Clinical drugs using strength pattern 2 may be authored in national extensions.

6.4.4. IDMP Compatibility

IDMP (and in particular (ISO 11615 section 9.7.2.4) is clear that strength "can be expressed in two ways: strength (presentation) and strength (concentration)" and it uses both in parallel within the standard. Presentation strength is generally required for description of manufactured items, whereas concentration strength may be optionally provided. When describing the strength of a pharmaceutical product that has undergone a transformation (e.g. dissolution or dispersion), the strength is specified as it would occur "when the transformation undertaken exactly in accordance with the regulated product information". It is not clear whether, if the regulated product information provides alternative transformations, more than one pharmaceutical product would be authored. Since the Medicinal Product model does not intend to represent a transformed product using the administrable dose form when this is different, primarily because of this type of uncertainty, this issue can be put aside.
IDMP has the concept of "Reference Strength" to explicitly describe the difference between the precise active ingredient substance and the basis of strength substance, or to support description of strength in alternative units. The Medicinal Product model supports basis of strength substance explicitly, and therefore is compatible with IDMP, and because alternative descriptions (synonyms) are a core part of the SNOMED structure, alternative strength representations could be provided if required (e.g. adrenaline 1:1000 rather than 1 mg per mL).

See also the IDMP Compatibility part of the Clinical Drug section.

6.4.4.1. Measurement Point

ISO 11615 in IDMP introduces the concept of "measurement point" for strength in some products, usually those with a metered dosage value system, for example the strength of the active ingredient substance in some inhaler products is measured at a particular distance from the point of aerosolisation. Using a strength measurement point is currently something that is country-specific (although regulation may change to make it more standardized as its use becomes more widespread). In the international core, it may become important to specify the measurement point for the strength of some products to allow national extensions to select the correct concept for their use, since it would appear that differences in measurement point between otherwise similar products can be clinically significant. Measurement point is currently not explicitly described in the international release. This is a developing area and will be kept under review.

6.5. Unit of Presentation

A unit of presentation is a qualitative concept that describes a countable entity in which the clinical drug is presented, or in which it is bounded. It is used to support expression of presentation strength, where it provides the denominator for the strength ratio, and to differentiate different clinical drug products when the "intimate container" (see below) is clinically important (e.g. differentiating pre-filled syringes from ampoules for a solution for injection product).
As described in the Strength section above and detailed further in an Appendix, there are various patterns for describing how unit of presentation and expression of strength relate together, based on whether the unit of presentation relates to the basic dose form or the intimate container (which is therefore the countable unit) of the medicinal product. As the countable entity for a medicinal product, unit of presentation is also important in describing packages, which although out of scope of the international release, may be of major importance for national extensions describing medicinal products. There are three types of unit of presentation:

- **those that are basic solid dosage forms: e.g. tablets, capsules, suppositories, pessaries etc.**
  - in this type, the solid dosage form, because of its discrete nature, is the countable unit; it provides the physical boundary in which the active ingredient substance(s) of the medicinal product are presented
- **those that are created by metered dosing valves: e.g. the "actuation" of inhalers, sprays etc.**
  - in this type, the countable unit is the "actuation" provided by the metering valve; it is the valve that determines (bounds) the physical amount of the active ingredient substance(s) of the medicinal product are presented
- **those that are intimate containers: e.g. ampoules, vials, sachets, cartridges etc.**
  - see below for detail

6.5.1. Intimate container

The "intimate container" of a medicinal product is the receptacle or vessel used to contain (or bound) liquid and some solid or semi-solid medicinal products into countable entities. A medicinal product presented in an intimate container will almost always have at least one layer of additional packaging added to it in order to make it into a packaged medicinal product; this external packaging is not described in the international release. For example: an ampoule is an intimate container to present a solution for injection dosage form; the ampoule will always be supplied in a box or a moulded carton, possibly additionally with a blister strip as intermediate packaging. Particularly for liquid parenteral products and for nebuliser liquids, the intimate container/unit of presentation may have clinical significance: providing a patient heparin in a pre-filled syringe is different from supplying that same concentration of heparin in a (multi-dose) vial. Similarly, hormone replacement gels may be supplied in single dose sachets to provide the correct administration amount.

6.5.2. IDMP Compatibility

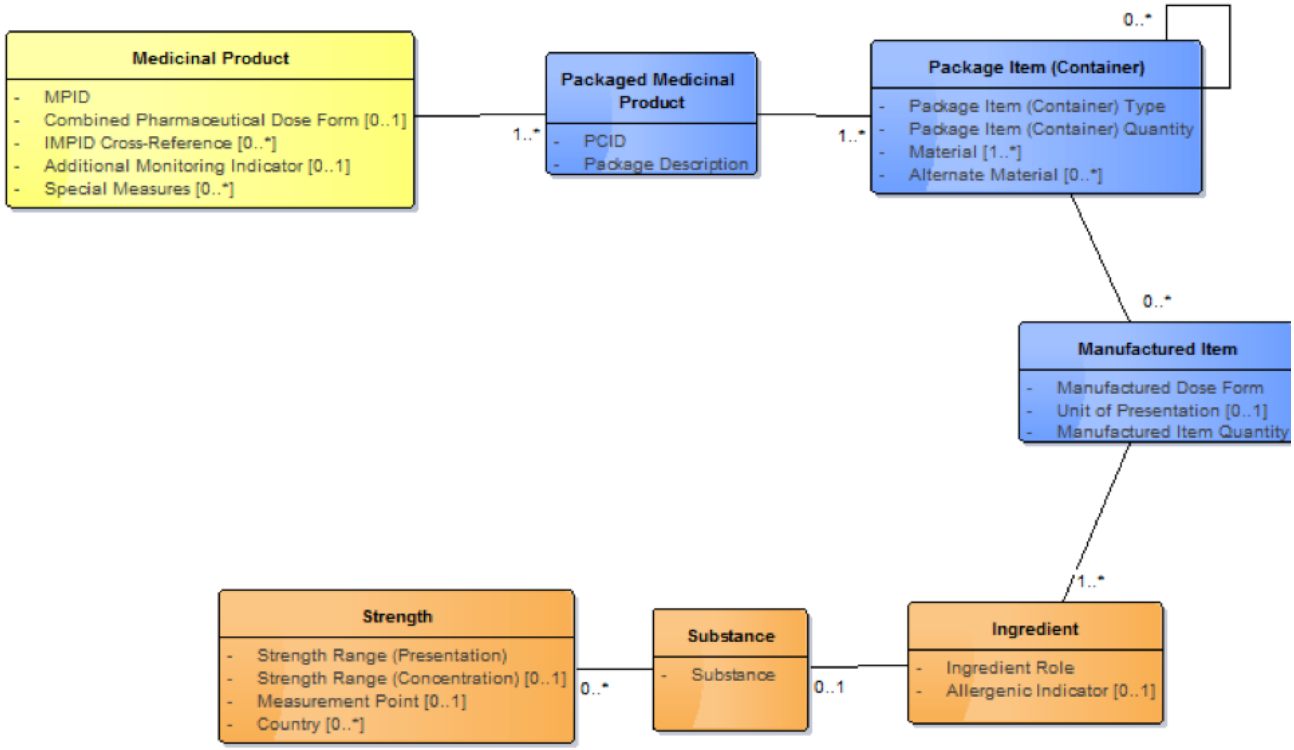
In IDMP, the "*one countable instance of a whole of medicinal product*" is managed through the information model: it is (generally) one instance of the Manufactured Item, with its manufactured dose form and unit of presentation or one instance of the Pharmaceutical Product (with its administrable dose form and unit of presentation). The Manufactured Item is therefore the concept/class that most closely resembles the SNOMED CT Clinical Drug, but both Manufactured Item and Pharmaceutical Product contain the key "unit of presentation" attribute. The unit of presentation in IDMP is what specifies the "real world" units in which the quantity of the manufactured item is described. The unit of presentation can be specified in accordance with ISO 11239 and ISO/TS 20440 and its resulting terminology [implemented through EDQM].
IDMP goes on to state: "For items where their quantity is a measured quantity of weight or volume, the "unit of presentation" shall not be given since it is the same as the units of that quantity (that is ml, mg or %). For solid dose forms and other items that are measured by counting integer quantities, the unit for quantity shall be "unit" and the "unit of presentation" shall be the item that is counted."
In EDQM, unit of presentation is defined as the "Qualitative term describing the discrete countable entity in which a pharmaceutical product or manufactured item is presented, in cases where strength or quantity is expressed referring to one instance of this countable entity."

> **EXAMPLE 1:** To describe strength: "Contains 100 mg per tablet" ('tablet' is the unit of presentation).
> **EXAMPLE 2:** To describe quantity: "Contains 100 mL per bottle" ('bottle' is the unit of presentation).

Unit of Presentation is therefore sometimes known as "the countable unit".

7. Appendix A: Product Patterns

To correctly interpret "*one countable instance of a whole of medicinal product*", it is important that this is seen in the context of the overall description of a medicinal product, which is always presented from the manufacturer in as a "packaged medicinal product". Note that description of packaged medicinal products is outside the scope of the international release but may be included within a national extension. The IDMP Medicinal Product model describes this, showing how the Manufactured Item is related to the Packaged Medicinal Product via the Package Item (Container); this is a recursive class that represents both the package as supplied by the manufacturer (and, for example, labelled with the GTIN, the batch number and the expiry), and through a recursive relationship, with any sub-packages inside the outer pack.

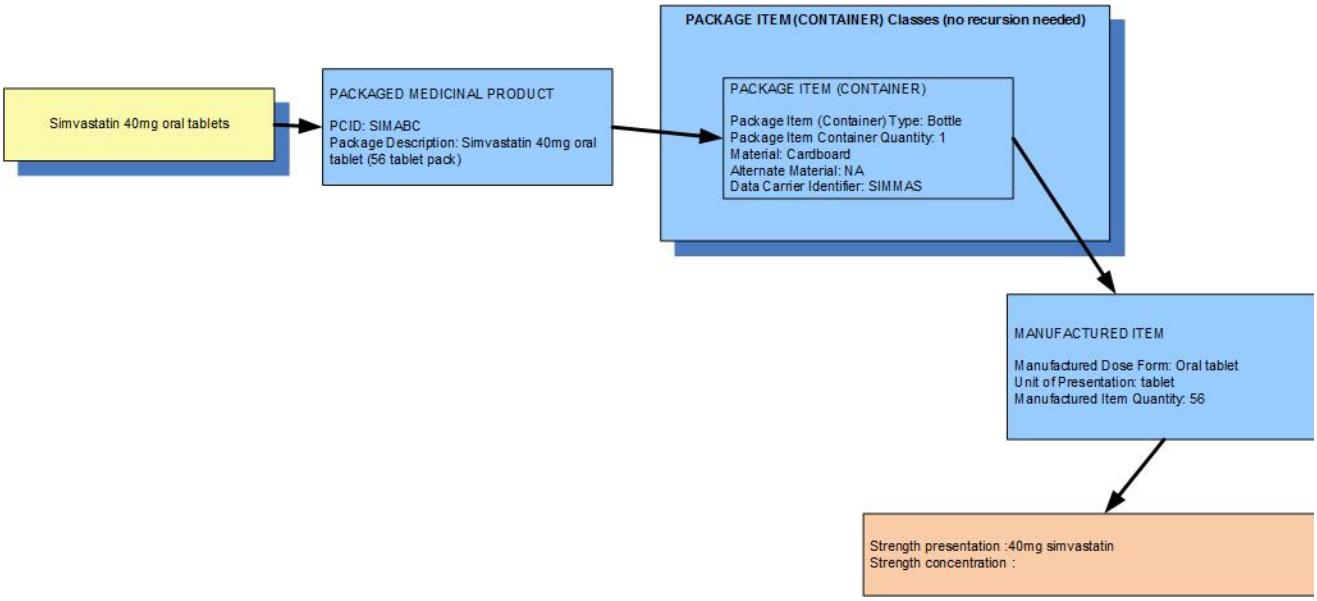


By describing the various standard patterns of products with their basic dose forms and intimate containers, consistent representation of strength based on unit of presentation can be maintained.Note: in all the patterns described below, although pack size may be mentioned, this is to show how information is sourced from "what is". Description of pack size is out of scope for the international release, although it will be in scope for the national extension model, as some nations may require medicinal products that include description of pack size for their national terminology; therefore it is useful to have it shown here for informational purposes only.

7.1. Discrete manufactured dose form; similar unit of presentation

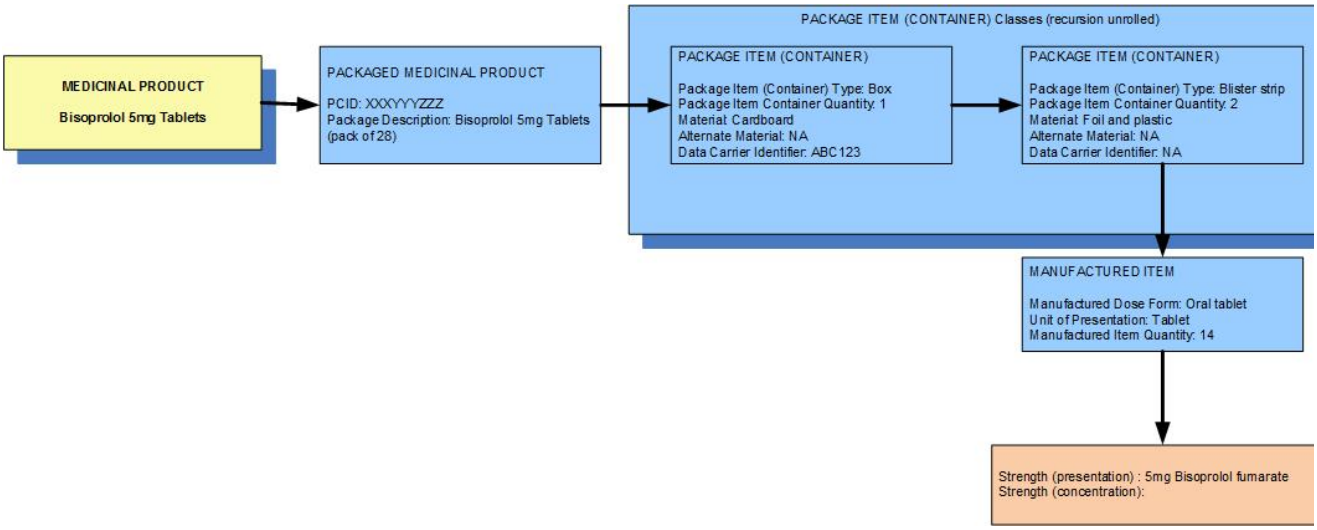
Examples: various tablets, capsules, cachets, pessaries, suppositories, tampons
The unit of presentation is usually a less granular term than the manufactured dose form, and often corresponds to the basic dose form.
Strength is expressed as "per one unit of presentation" and the presentation strength and the concentration are exactly the same.

7.1.1.1.1. Example 1: A bottle of 56 simvastatin 40mg oral tablets



Manufactured dose form	Oral tablet	
Unit of presentation	Tablet	
[Pack size]	*56 tablets in the container*	
Precise active ingredient	simvastatin	
Basis of strength substance	simvastatin	
Presentation strength (logical)	40 mg per 1 unit of presentation	
Presentation strength	40 mg [per 1 tablet]	UCUM: 40 mg [per 1 each]
Concentration strength		The weight of the tablet is not usually known so concentration strength is not usually available and is not deemed clinically significant

7.1.1.1.2. Example 2: A pack of 28 bisoprolol 5 mg oral tablets contains two blister strips each with 14 tablets

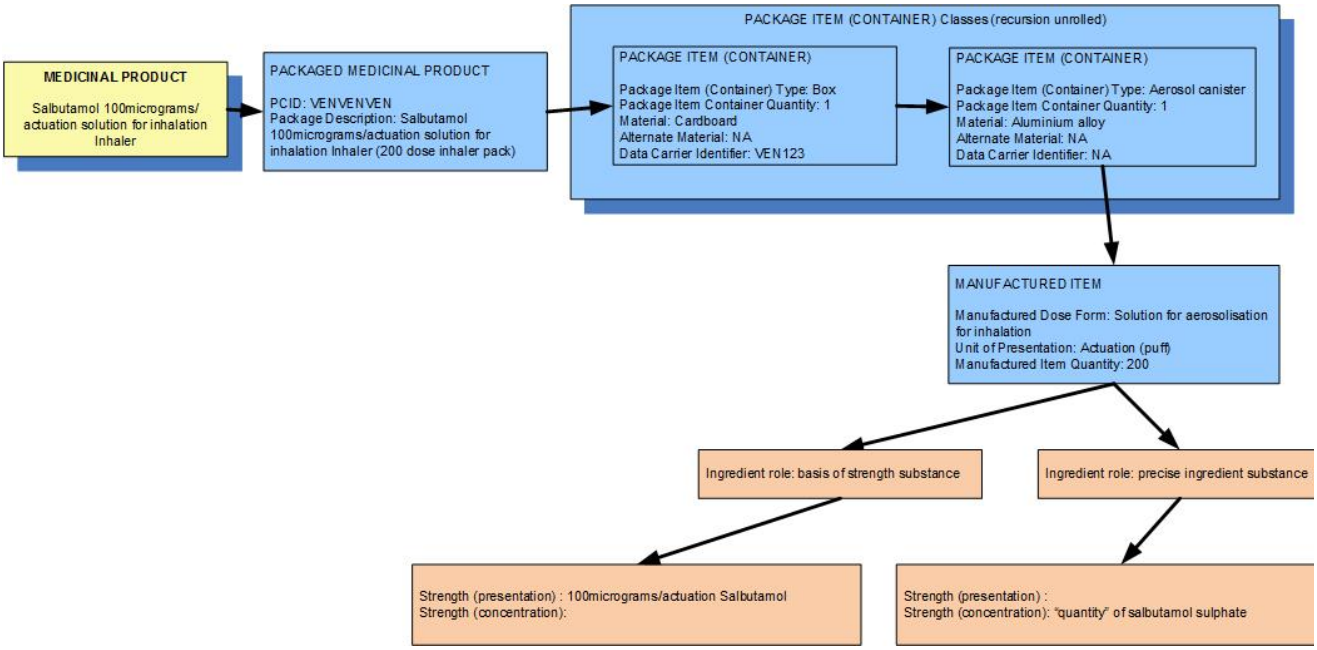


Manufactured dose form	Oral tablet	
Unit of presentation	Tablet	
[Pack size]	*14 tablets in the blister strip2 blister strips in the box*	*28 tablets in the outer container*
Precise active ingredient	bisoprolol fumarate	
Basis of strength substance	bisoprolol fumarate	
Presentation strength (logical)	5 mg per 1 unit of presentation	
Presentation strength	5 mg [per 1 tablet]	UCUM: 5 mg [per 1 each]
Concentration strength		The weight of the tablet is not usually known so concentration strength is not usually available and is not deemed clinically significant

7.2. **Continuous presentation: Metered dose unit of presentation**

Examples: various inhalers, nasal sprays, some cutaneous sprays/foamsThe unit of presentation is the actuation, the “single operation of a metered-dose pump, valve or other equivalent dosing mechanism” [EDQM].Strength is expressed as “per one unit of presentation” and the presentation strength and the concentration are exactly the same.

Example: A single inhaler containing a total of 200 actuations worth of salbutamol, 100 micrograms per actuation, packaged in a box

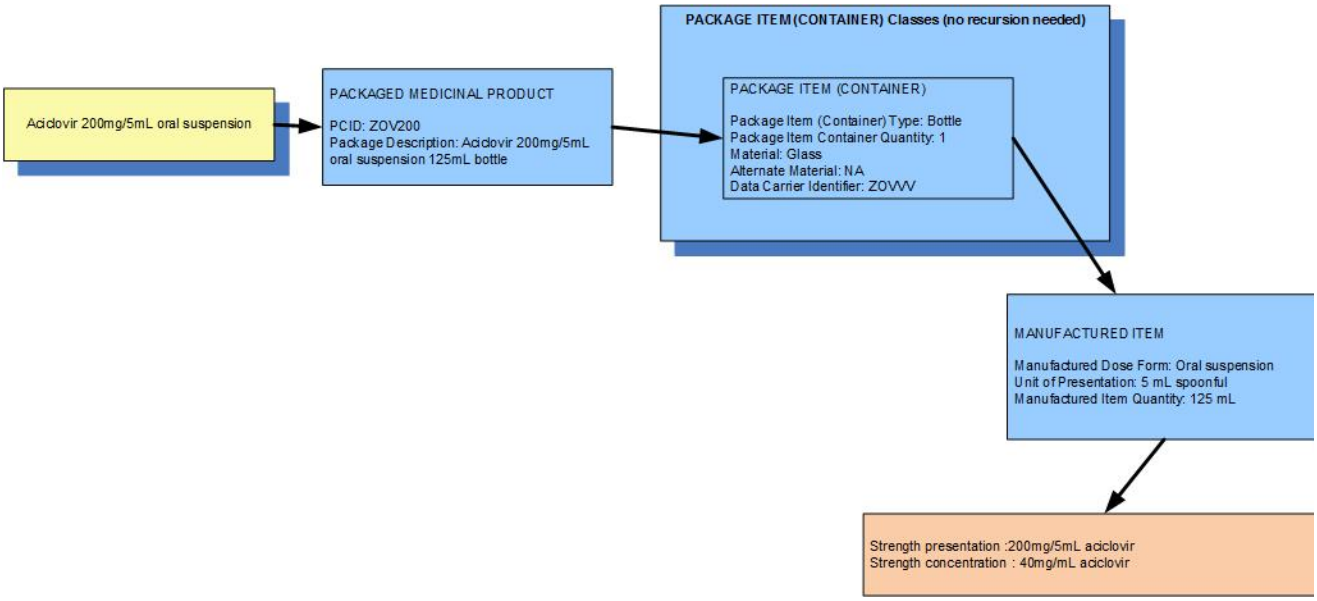


Manufactured dose form	Solution for aerosolisation	
Unit of presentation	Actuation	
[Pack size]	*200 actuations in the inhaler*	
Precise active ingredient	salbutamol sulphate	
Basis of strength substance	salbutamol	
Presentation strength (logical)	100 mcg per 1 unit of presentation	
Presentation strength	100 mcg per 1 actuation	UCUM: 100 mcg per 1 each
Concentration strength		The concentration of salbutamol sulphate in the inhalant solution inside the inhaler container is probably known to the regulatory agency but is not deemed clinically significant

7.3. **Continuous presentation: Oral liquids designed for administration by "metered" medicine spoon**

Examples: oral solutions, suspensions, emulsions, syrups. This is a variation on the metered dose presentation; the unit of presentation supplied by the manufacturer to provide the “metered dose” is the 5mL spoonful, since this represents “the quantity of product that is administered by filling a single spoon administration device” [EDQM]. Strength is expressed as “per one unit of presentation” (per 5 mL [spoonful]) BUT the presentation strength and the concentration are NOT the same, since these are continuous liquids, so the concentration strength of “per 1 mL” will usually be a different value. Note that explicit representation of the medicine spoon would be as an administration device, and is therefore out of scope of the international Medicinal Product hierarchy. National extensions may wish to represent the inclusion of a medicine spoon (or indeed any other administration device such as an applicator) in the package description (as in IDMP, for example) should the use case(s) require.

7.3.1.1.1. **Example: A bottle of 125 mL of aciclovir oral suspension 200mg/5mL**

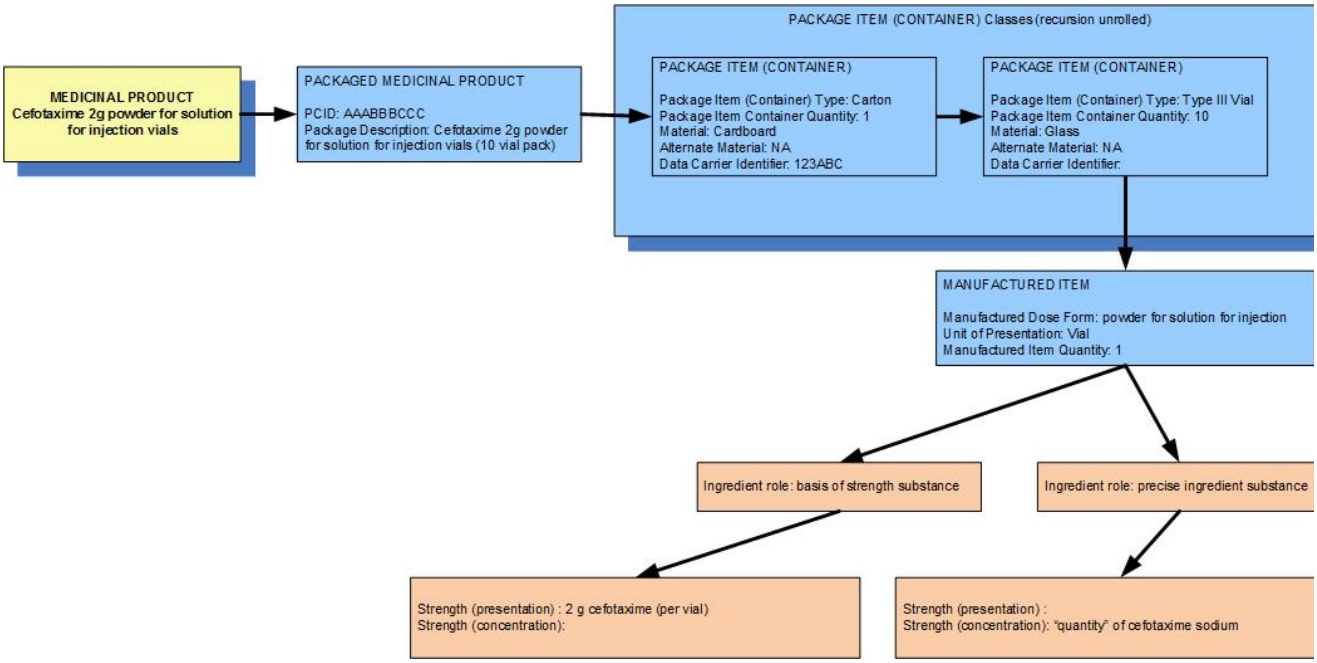


Manufactured dose form	Oral suspension	
Unit of presentation	5 mL [spoonful]	
[Pack size]	*125 mL in the bottle*	*Not usually expressed as 25 spoonfuls!*
Precise active ingredient	aciclovir	
Basis of strength substance	aciclovir	
Presentation strength (logical)	200 mg per 1 unit of presentation	
Presentation strength	200 mg per 5 mL	
Concentration strength	40 mg per 1 mL	

7.4. **Continuous presentation: bounded by unit of presentation; solid dose forms**

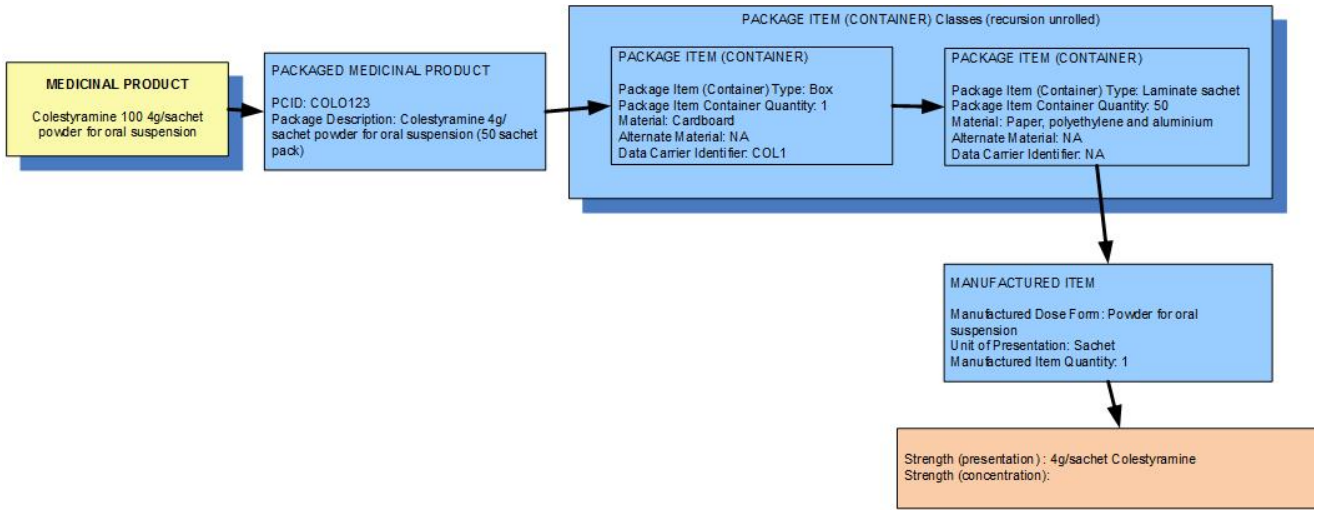
Examples: vials, ampoules, sachets, containing solid dose forms such as powders or granules which may or may not be dissolved before administration
The unit of presentation usually either uses the same word (even though it is a different concept) as the (package item) container, or the (package item) container is a more granular concept and the unit of presentation uses a less granular term.
Strength is expressed as "per one unit of presentation" and the presentation strength and the concentration are exactly the same.

7.4.1.1.1. **Example 1: A pack of 10 vials each containing 2g cefotaxime powder for solution for injection**



Manufactured dose form	Powder for solution for injection	
Unit of presentation	vial	The vial "bounds" the 2g of the dose form
[Pack size]	*10 vials in the carton*	
Precise active ingredient	cefotaxime sodium	
Basis of strength substance	cefotaxime	
Presentation strength (logical)	2 g per 1 unit of presentation	
Presentation strength	2 g [per 1 vial]	UCUM: 2 g per 1 each
Concentration strength		The concentration of cefotaxime in the powder inside the vial is known to the regulatory agency but is not deemed clinically significant

7.4.1.1.2. **Example 2: A pack of 50 sachets containing 4g of colestyramine powder for oral solution**

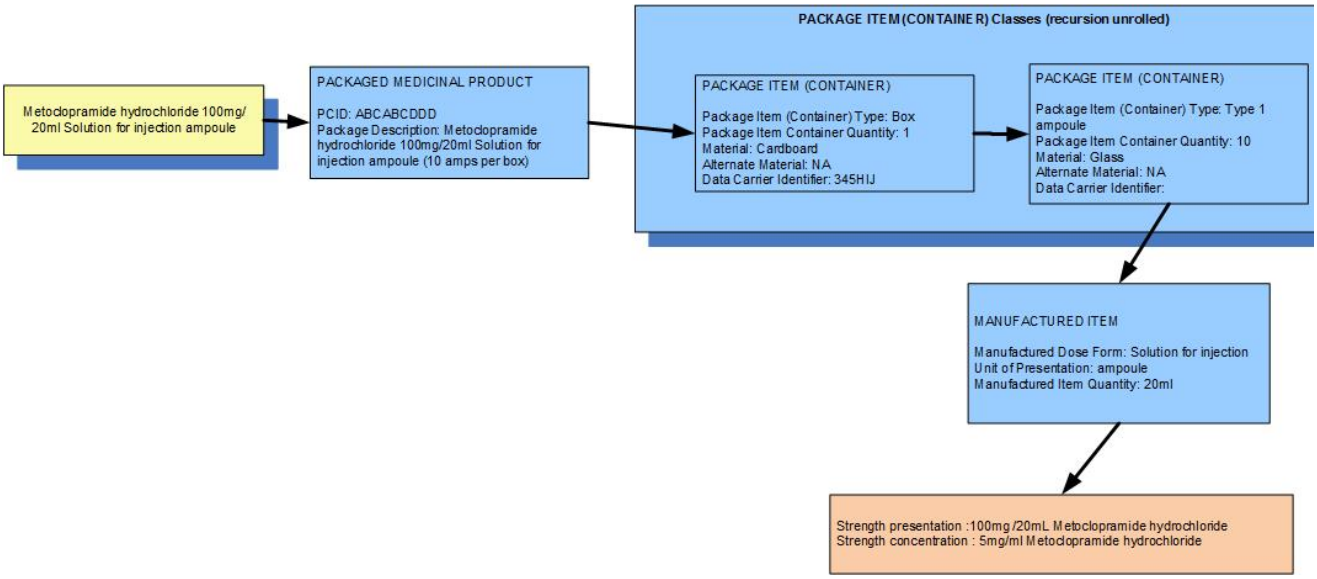


Manufactured dose form	Powder for oral suspension	
Unit of presentation	Sachet	**The sachet "bounds" the 4g of the dose form**
[Pack size]	*50 sachets in the box*	
Precise active ingredient	colestyramine	
Basis of strength substance	colestyramine	
Presentation strength (logical)	4 g per 1 unit of presentation	
Presentation strength	4 g per 1 sachet	**UCUM: 4 g per 1 each**
Concentration strength		**The concentration of colestyramine in the powder inside the sachet is known to the regulatory agency but not deemed clinically significant**

7.5. **Continuous presentation: bounded by container; liquid dose forms**

Examples: parenteral solutions, unit dose nebuliser solutions
The unit of presentation usually either uses the same word (even though it is a different concept) as the (package item) container, or the (package item) container is a more granular concept and the unit of presentation uses a less granular term.
Presentation strength is expressed as "per the amount of liquid bounded by the unit of presentation" but concentration strength is per mL (and therefore is often different).

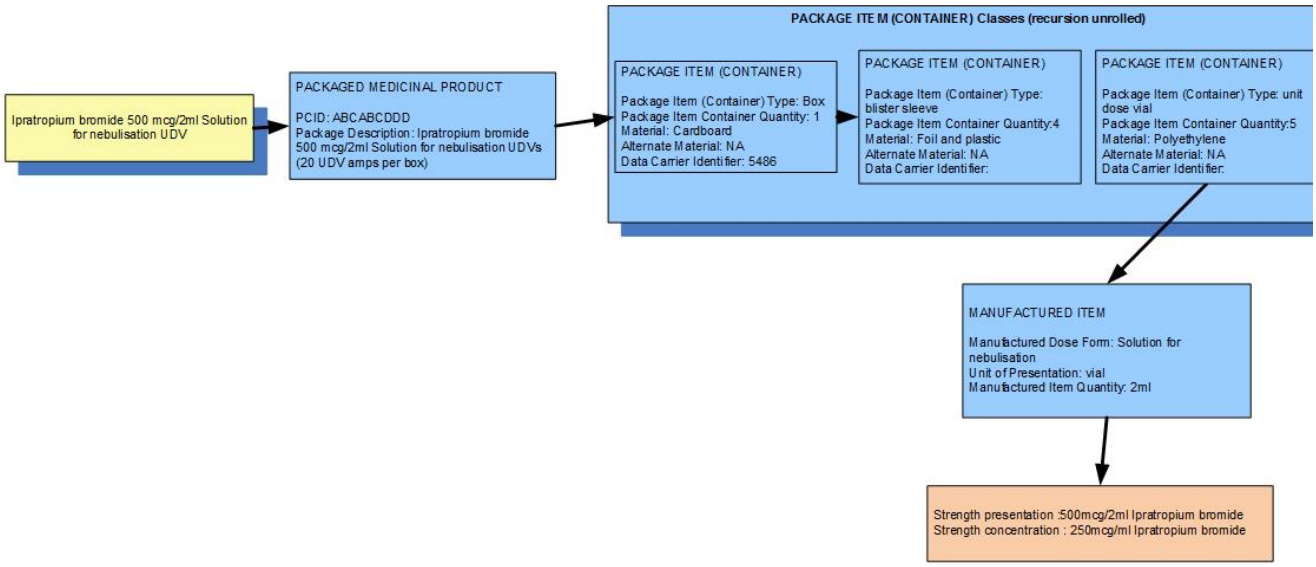
7.5.1.1.1. **Example 1: A pack of 10 ampoules each containing 20mL of metoclopramide hydrochloride for solution for injection**



Manufactured dose form	Solution for injection	
Unit of presentation	Ampoule	The ampoule "bounds" the liquid
[Pack size]	*10 ampoules in the box*	
Precise active ingredient	metoclopramide hydrochloride	
Basis of strength substance	metoclopramide hydrochloride	

Presentation strength (logical)	100 mg per volume contained in the unit of presentation	The amount of the dose form bounded in the unit of presentation
Presentation strength	100 mg per 20 mL	
Concentration strength	5 mg per 1 mL	

7.5.1.1.2. Example 2: A pack of 20 UDVs each containing 2mL of ipratropium bromide for solution for nebulisation

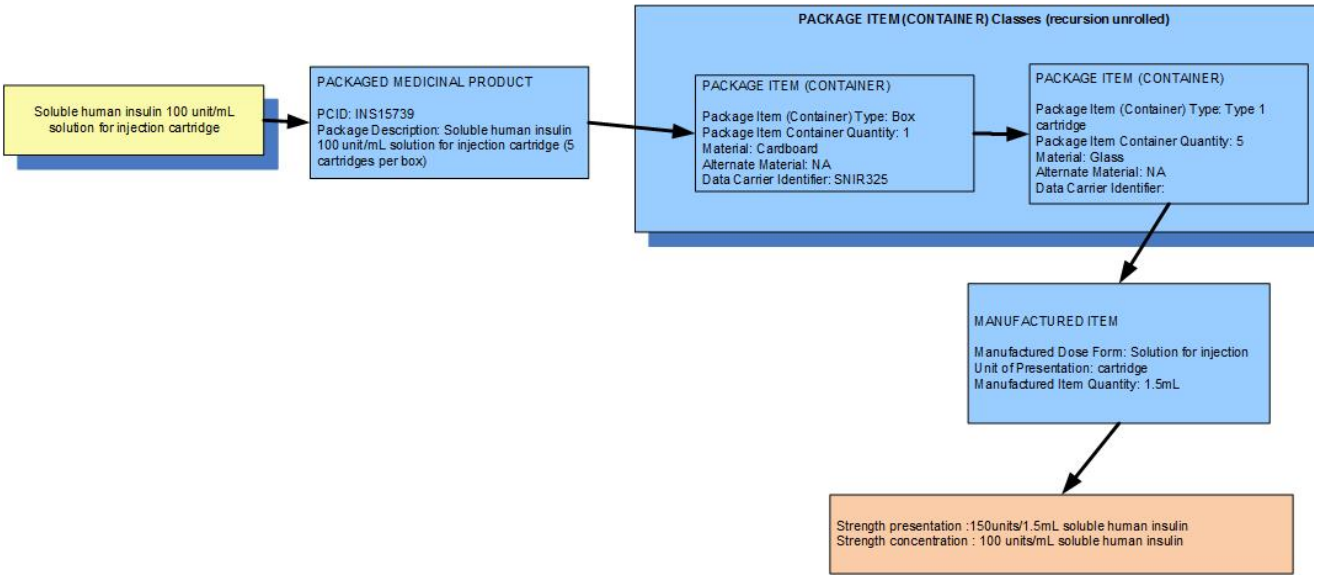


Manufactured dose form	Solution for nebulisation	
Unit of presentation	Unit dose vial	The vial "bounds" the liquid
[Pack size]	*5 vials in a sleeve, 4 sleeves in the box*	
Precise active ingredient	ipratropium bromide	
Basis of strength substance	ipratropium bromide	
Presentation strength (logical)	500 mcg per volume contained in the unit of presentation	The amount of the dose form bounded in the unit of presentation
Presentation strength	500 mcg per 2 mL	
Concentration strength	250 mcg per 1 mL	

7.6. Continuous presentation: bounded by container; liquid/semi-solid dose forms; concentration strength required

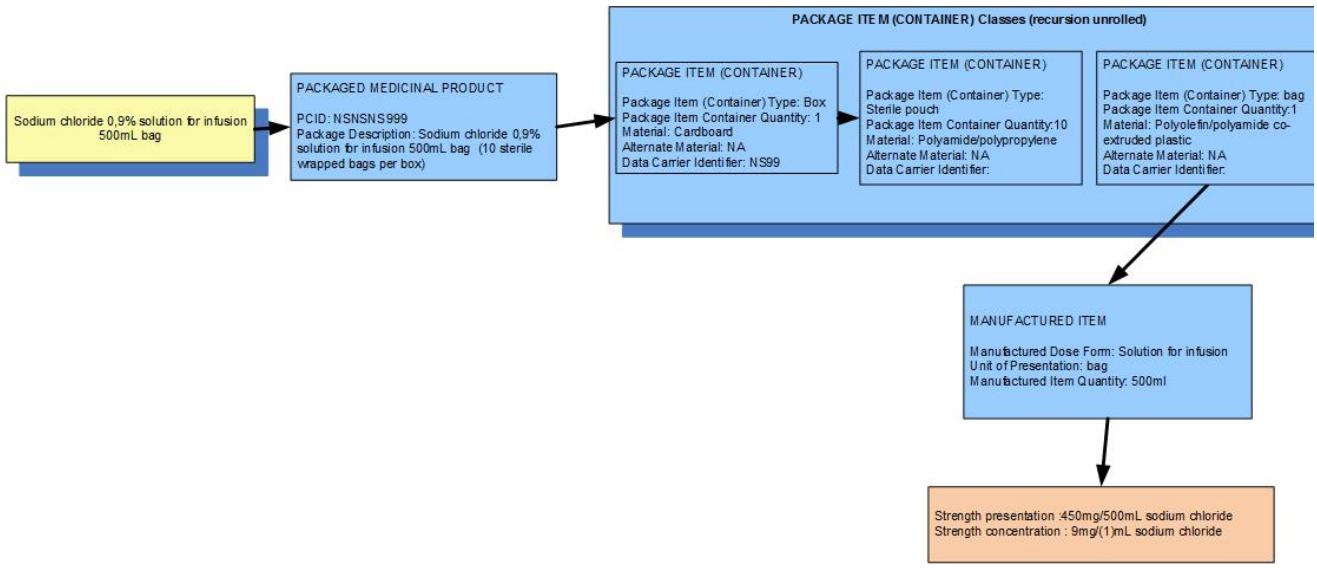
Examples: bulk parenteral solutions, insulins, patches
The unit of presentation usually either uses the same word (even though it is a different concept) as the (package item) container, or the (package item) container is a more granular concept and the unit of presentation uses a less granular term.
However, although presentation strength is expressed as "per one unit of presentation" the clinically relevant strength is the concentration strength as almost all are used in individually calculated and variable amounts.
Note that the unit of presentation is likely to be useful in description of the medicinal product concept at some level; insulin presented in a multi-dose vial will be used/administered differently from insulin presented in a cartridge for use within a "pen device".

7.6.1.1.1. Example 1: A pack of 5 cartridges each containing 1.5mL soluble human insulin 100 units/mL solution for injection



Manufactured dose form	Solution for injection	
Unit of presentation	Cartridge	The vial "bounds" the liquid
[Pack size]	*5 cartridges in a sleeve,1 sleeve in the box*	
Precise active ingredient	insulin soluble human	
Basis of strength substance	insulin soluble human	
Presentation strength (logical)	150 units per volume contained in the unit of presentation	The amount of the dose form bounded in the unit of presentation
Presentation strength	150 units per 1.5 mL	Not a clinically safe expression of strength
Concentration strength	100 units per 1 mL	

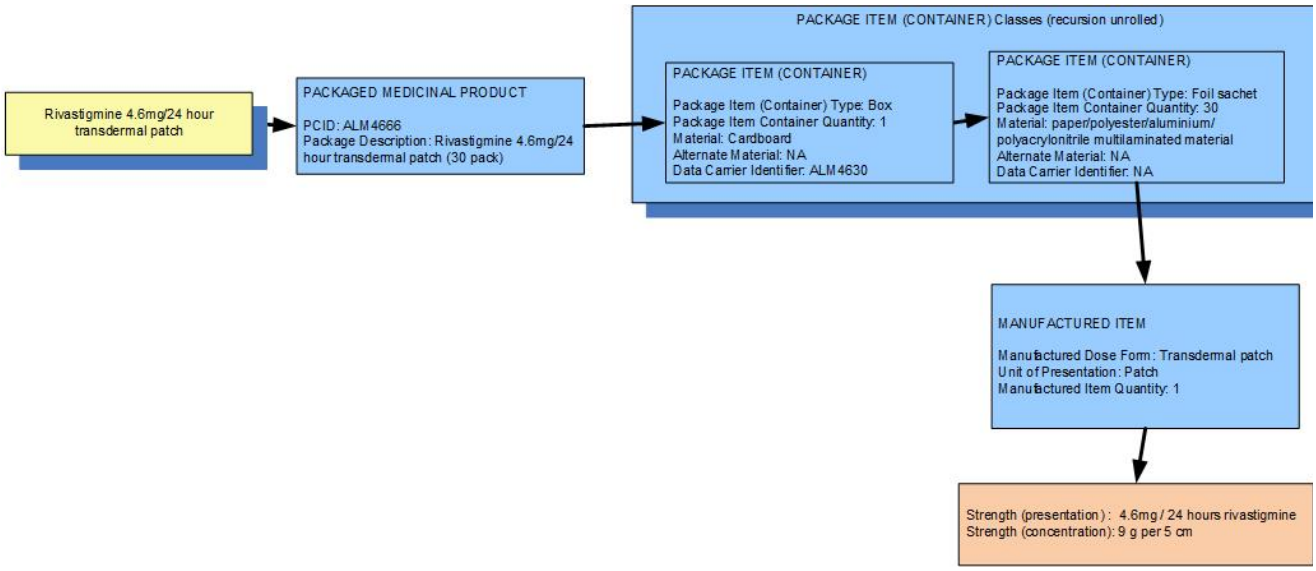
7.6.1.1.2. Example 2: A box of 10 bags of Sodium chloride 0.9% solution for infusion 500mL



Manufactured dose form	Solution for injection	
Unit of presentation	Bag	The bag "bounds" the liquid

[Pack size]	*1 bag in a sterile pouch,10 pouches in the box*	
Precise active ingredient	sodium chloride	
Basis of strength substance	sodium chloride	
Presentation strength (logical)	450 mg per volume contained in the unit of presentation	The amount of the dose form bounded in the unit of presentation
Presentation strength	450 mg per 500 mL	Not a clinically safe expression of strength
Concentration strength	9 mg per 1 mL	Synonym: 0.9% w/v

7.6.1.1.3. **Example 3: A pack of 30 sachets each containing a transdermal patch delivering 4.6mg per 24 hours of rivastigmine**

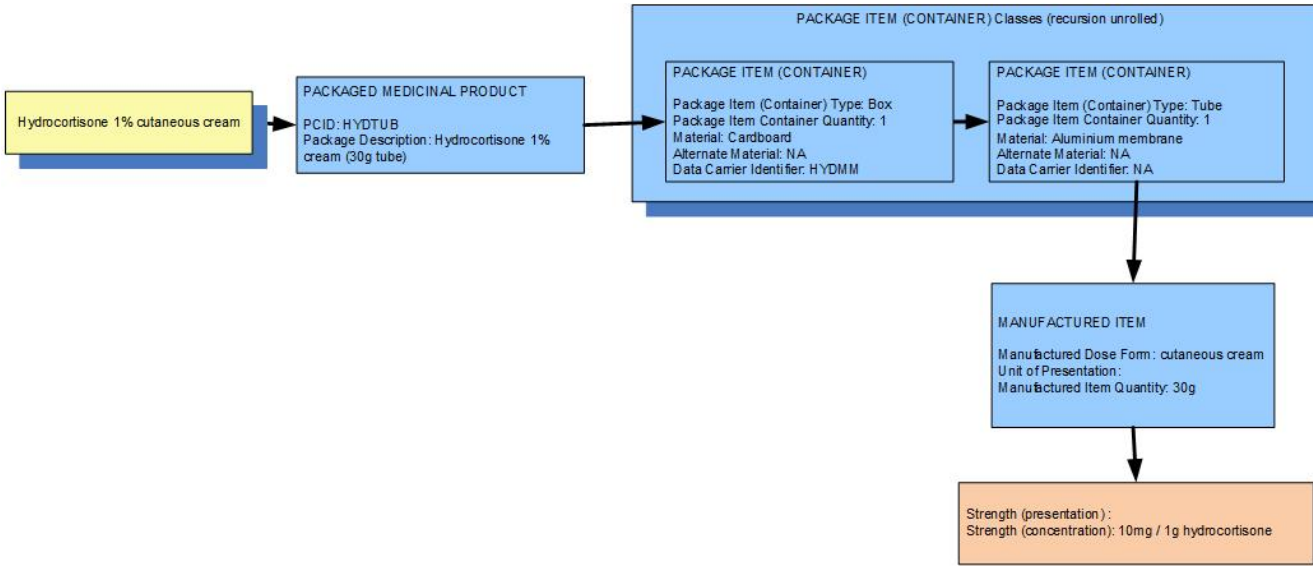


Manufactured dose form	Transdermal patch	
Unit of presentation	Patch	The patch "bounds" the dose form that delivers the medication
[Pack size]	*1 patch in sachet, 30 sachets in the box*	
Precise active ingredient	rivastigmine	
Basis of strength substance	rivastigmine	
Presentation strength (logical)	9 g per volume contained in the unit of presentation	The amount of the dose form bounded in the unit of presentation
Presentation strength	9 g per (5cm) patch	Not a clinically safe expression of strength
Concentration strength	4.6 mg per 24 hours	This is a "rate" strength

7.7. **Continuous presentation: unbounded by container**

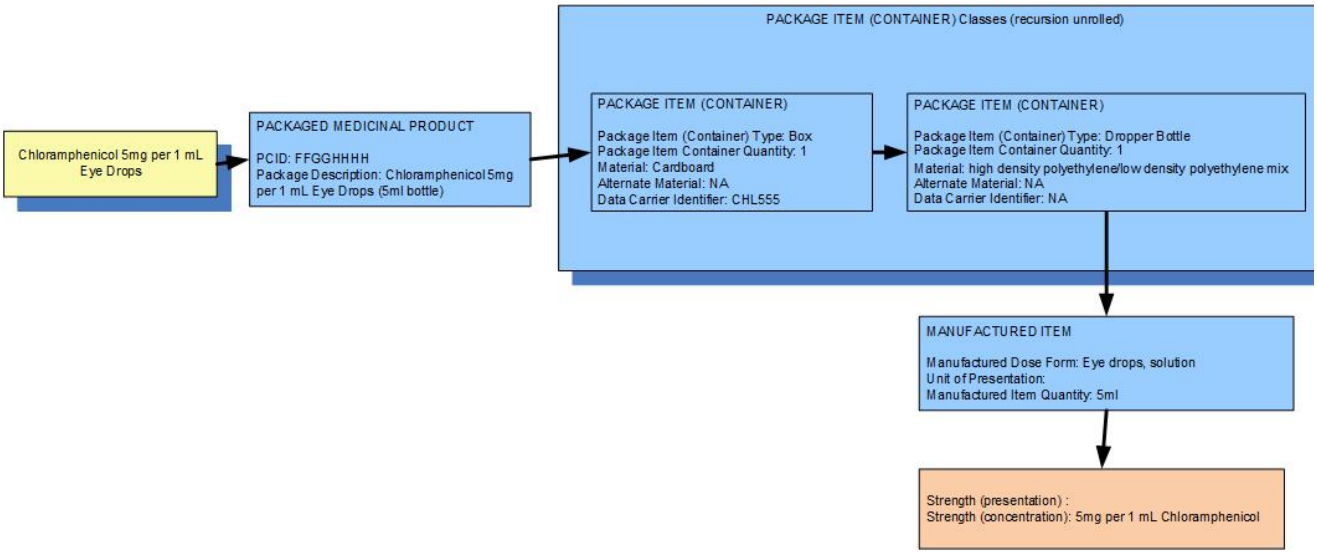
Examples: bulk powders and granules, bulk liquids, semi-solids
These presentations are not particularly bound by their container in any way that is meaningful in terms of their use or administration; the Manufactured Item is a continuous presentation and almost all are used in individually calculated and variable amounts. For example, hydrocortisone cream for cutaneous use is contained in a tube, but its use is based on how much is squeezed out and applied to the skin; chloramphenicol eye drops are presented in a dropper bottle, but they are administered drop by drop and although the dropper bottle aims to deliver a roughly uniform sized drop to the eye, they are not "metered dose containers" in the way that containers with valves are.
A unit of presentation is not usually given for these products. The pack size (not relevant for SNOMED international model) is given as the Manufactured Item quantity.
Strength is expressed as a concentration and as such the presentation strength and the concentration are exactly the same.

7.7.1.1.1. Example 1: A 30g tube of hydrocortisone 1% cutaneous cream w/w in an outer box



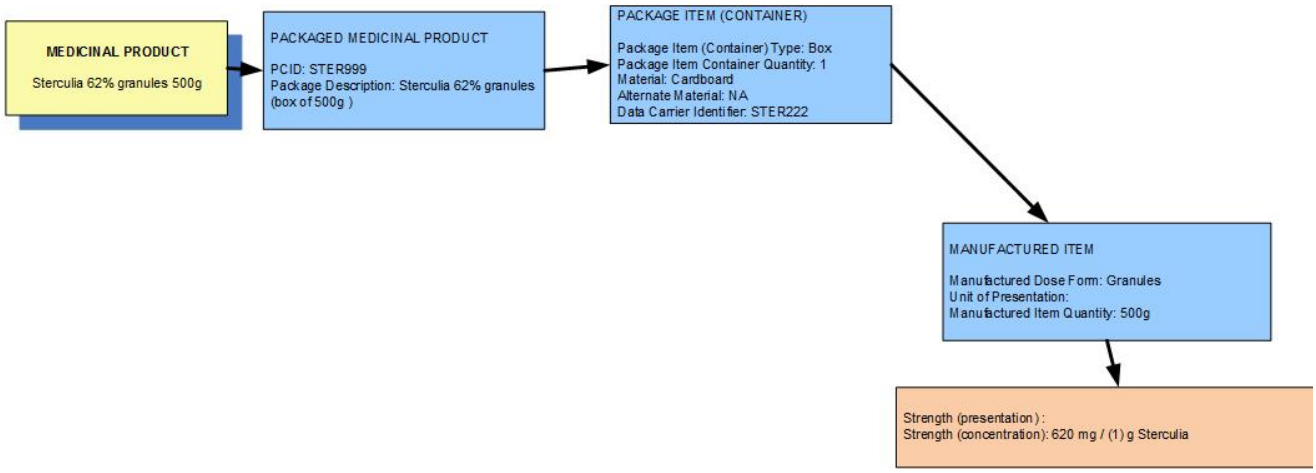
Manufactured dose form	Cutaneous cream	
Unit of presentation	NOT VALUED	There is nothing that really "bounds" the dose form that delivers the medication "per dose"
[Pack size]	*30 g in the tube,1 tube in the box*	
Precise active ingredient	hydrocortisone	
Basis of strength substance	hydrocortisone	
Presentation strength (logical)	300 mg per 30 g	Not a clinically safe or recognisable expression of strength
Presentation strength		
Concentration strength	10 mg per 1 g	Synonym: 1.0 % w/w

7.7.1.1.2. Example 2: A bottle of 5 mL of chloramphenicol eye drops 0.5% w/v in an outer box



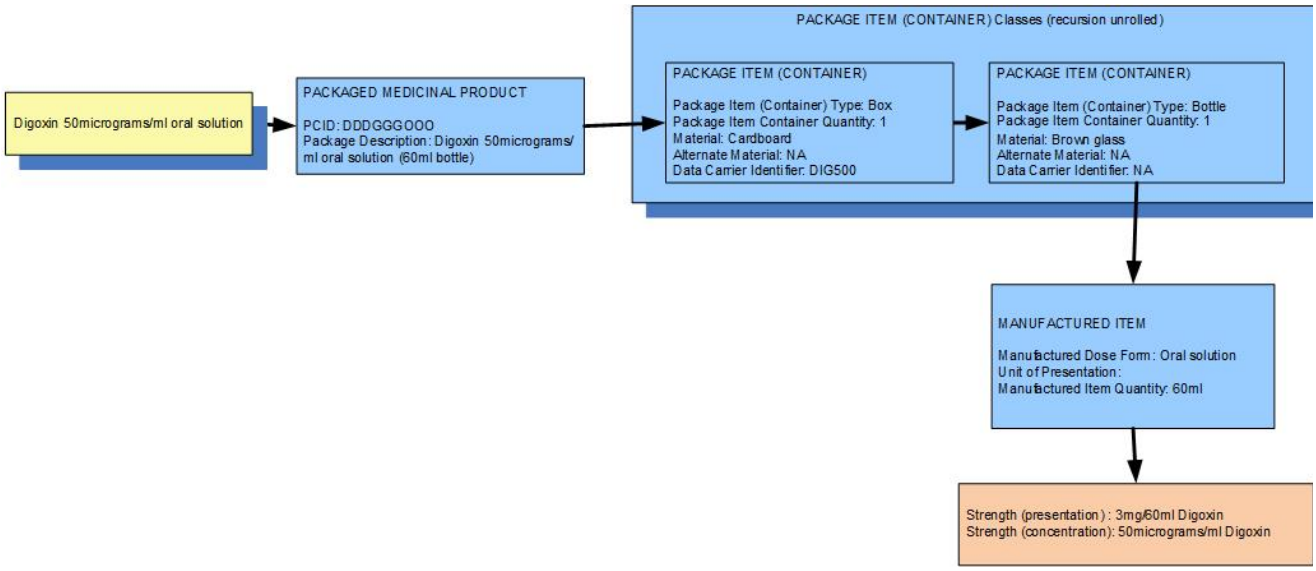
Manufactured dose form	Eye drops, solution	
Unit of presentation	NOT VALUED	There is nothing that really "bounds" the dose form that delivers the medication "per dose"
[Pack size]	*5 ml in the dropper bottle,1 bottle in the box*	
Precise active ingredient	chloramphenicol	
Basis of strength substance	chloramphenicol	
Presentation strength (logical)	25 mg per 5 mL	Not a clinically safe or recognisable expression of strength
Presentation strength		
Concentration strength	5 mg per 1 mL	Synonym: 0.5 % w/v

7.7.1.1.3. Example 3: A pack of 500g of sterculia 62% w/w granules (EDQM –"granules" = "oral granules")



Manufactured dose form	Oral granules	
Unit of presentation	NOT VALUED	There is nothing that really "bounds" the dose form that delivers the medication "per dose"
[Pack size]	*500 g in the box*	
Precise active ingredient	sterculia	
Basis of strength substance	sterculia	
Presentation strength (logical)	310 g per 500 g	Not a clinically safe or recognisable expression of strength
Presentation strength		
Concentration strength	620 mg per 1 g	Synonym: 62 % w/w

7.7.1.1.4. Example 4: A bottle of 60 mL of digoxin oral solution 50mcg/mL in an outer box (which has an oral syringe in it)



Manufactured dose form	Oral solution	
Unit of presentation	NOT VALUED	There is nothing that really "bounds" the dose form that delivers the medication "per dose"
[Pack size]	*60 ml in the bottle,1 bottle in the box*	
Precise active ingredient	digoxin	
Basis of strength substance	digoxin	
Presentation strength (logical)	3 mg per 60 mL	Not a clinically safe or recognisable expression of strength
Presentation strength		
Concentration strength	50 mcg per 1 mL	Synonym: 0.5 % w/v