SNOMED CT Drug Model for supporting National Extension V1.0

1.Introduction

Concepts in a Medicinal Product terminology can be divided into two types:

- those concepts whose representation is abstract but which can be understood and used internationally (with sufficient language support); these are described generically using their internationally recognised constituent parts, which are:
  - active ingredient substance(s) and basis of strength substances described using their international non-proprietary names (INNs) whenever possible
  - active ingredient strength(s), described using international standards and principles such as the RTO<PQ> datatype (the ratio of physical quantities - see International Organization for Standards. Health informatics — Harmonized data types for information

interchange ISO 32090:2011) and/or UCUM units of measure or their equivalent, which in SNOMED CT is accomplished by using specific attributes for each of the numerator and denominator values and units each which can be valued with a SNOMED CT concept
        - pharmacopoeial/internationally defined dose forms
        - pharmacopoeial/internationally defined units of presentation (when appropriate)
- those concepts which describe real or actual products available for clinical use whose representation can only be fully described and understood within a jurisdiction, as they are governed by the regulations of that jurisdiction and produced by authorisation of a medicines regulatory agency responsible for that jurisdiction. This includes:
    - authorised product names (which may be brand or trademarked names); a brand name in one jurisdiction may relate to a different product than the same brand name used in another jurisdiction – although medicines regulatory agencies are trying to reduce this because of the safety issues it raises
    - proprietary dose forms including those describing a timing component (e.g. "caplets", "24-hour prolonged release tablets")
    - additional characteristics in the product name such as
        - inclusion or exclusion of particular excipients with various roles ("strawberry flavour", "sugar-free")
        - target population groups ("for children")
        - indication for use ("cough and cold")
    - packaging information
        - pack size
        - container description

SNOMED CT International Release contains concepts of the first type; those whose representation is both understandable internationally and whose use has international applicability (e.g. in support of medication information in international patient summaries, or for international pharmacovigilance). But clinical care *within* member nations usually requires both the first *and* the second type of representation for medicinal products; therefore concepts of the second type have to be authored in the extension belonging to that nation (or organisation).

2. Purpose

This document depicts an extension concept model to describe the real or actual medicinal products (sometimes described as "branded products") available for use in a particular member nation. The model is compatible with the international core model for Medicinal Products. This compatibility means that, when classified using the appropriate tooling, the correct classification results should be achieved with concepts being fully defined wherever possible. This document should therefore be read alongside the SNOMED CT Medicinal Product Model Specification which describes the classes of concepts present in the international release.

This document is a model specification, and as such it does not describe in any detail the rules and processes to be adopted for population of a national terminology; some general principles are given, but exact processes are not. These, and the terming guidelines for creation of fully specified names and additional description terms for the concepts that populate the additional model classes will need to be authored by national extensions, mindful of their own language, culture and practice considerations. These descriptive terms may be allowed to contain more information than that contained in the definitional attributes described in this specification: for example, some products may contain excipient information in their name - "without preservative" or "orange flavour", or target population information "for children"; all of this can be be reflected in the fully specified name for the relevant concept but would not be included in the value of the "product name attribute" - see section 10.1 below. In addition, national extensions may wish to author a range of synonym terms, including user interface terms, to support direct implementation. National extensions may wish to include the abstract class fully specified name within or after the fully specified name for the associated real product (for example including the full generic Clinical Drug name (either FSN or PT) in the Real Clinical Drug name: "AMOCAPS 250mg Freds Pharmaceuticals (amoxicillin 250mg oral capsules)"). However, when additional concepts for core classes of the international model (MP, MPF (if required) and CD) are authored in a national extension, the naming guidelines for the international release should be followed, for the FSN in particular.

In this document, as generally, the words 'package' and 'pack' are synonymous; 'package' is the preferred term in the documentation, although 'pack' may be used especially when short text is required.

General principles for authoring SNOMED CT extension content can be found at 5.4.1 General Authoring Principles

3. Scope

The scope of this model as documented is limited to medicinal products (pharmaceutical and biological); products that represent blood products, foods, additives, and complementary medicines (including homoeopathic products) are currently out of scope. Currently, vaccines, although they are biological medicinal products, are also out of scope.

National extensions will have to make decisions about the scope of their medicinal product terminology as they may require representation of products that are beyond the international scope, and therefore may need to author, at a minimum, Clinical Drug concepts within their extension (for example to describe national pharmacopoeial formulations). In addition, national extensions will need to set a scope for the range of medicinal products to be included; factors to consider comprise:

- Licensed medicinal products (i.e. those with a valid authorisation within the jurisdiction of the extension)
    - This may or may not include those licensed for sale or supply without an order (prescription) from a healthcare professional, depending on scope; these products are often known as "over the counter" medicines
- Unlicensed medicinal products
    - Previously licensed medicinal products (i.e. those that have, at some point in the last but which no longer hold a valid authorisation within the jurisdiction of the extension); some may continue to be available via import (see next point below)
    - Medicinal products holding a valid authorisation in a **different** jurisdiction but which are (regularly) used within the jurisdiction of the extension by practitioners on their own clinical responsibility
    - Medicinal products that are compounded according to recognised formulae; these are usually produced by authorised compounding units

- Investigational medicinal products (if and when good sources of this information become available through IDMP)

In all of the above, a reliable source of information for all the definitional attributes will be required; this may be challenging for unlicensed medicines and even for some "over the counter" medicines.

One thing that may be helpful in setting the boundary for national scope is to include those products that can be 'legally supplied'; in most healthcare cultures, compounded products, unlicensed and investigational products can be legally supplied to patients provided the terms and conditions of the jurisdiction are fulfilled. In addition, scope setting will need to bear in mind how to respond to the changes in the availability of products over time and the use case(s) for historic information for products that are no longer available in the supply chain.

This specification does not propose a model for the types of additional information that may be a useful part of a national medicinal product terminology, such as product availability or pricing. That is a matter for each jurisdiction. The principles for the status of the terminology concepts themselves should be as in the core (i.e. active - intended for terminology use; inactive - not intended for terminology use).

4. Audience

This document is written primarily for those responsible for the development and maintenance of a (national) Medicinal Product terminology within a member nation or other organisation that is managed as a module within a SNOMED CT extension.
It will also be of value to those who have a (national) Medicinal Product terminology that is not managed as a module within a SNOMED CT extension, but who wish to provide a mapping from concepts in their Medicinal Product terminology to concepts in SNOMED CT International Release Medicinal Product hierarchy.

5. National Extension Model and Concept Classes

The diagram below shows the concept classes for the extension model with, and related to, the concept classes in the international release model for medicinal products. No role or grouper concept classes that are parents of the the Medicinal Product (MP) class in the international release are shown in the diagram; it is expected that all grouping classes - based on substance structure, disposition and therapeutic role - will be inherited from the international release. For all of the classes of the national extension model for representation of medicinal products the closed world view is applied; products are defined using only the active ingredient substances as authorised by the regulatory agency in the particular jurisdiction of use; packs are defined using only the clinical drug concepts that they are composed of (contain) (see also section 8 below).

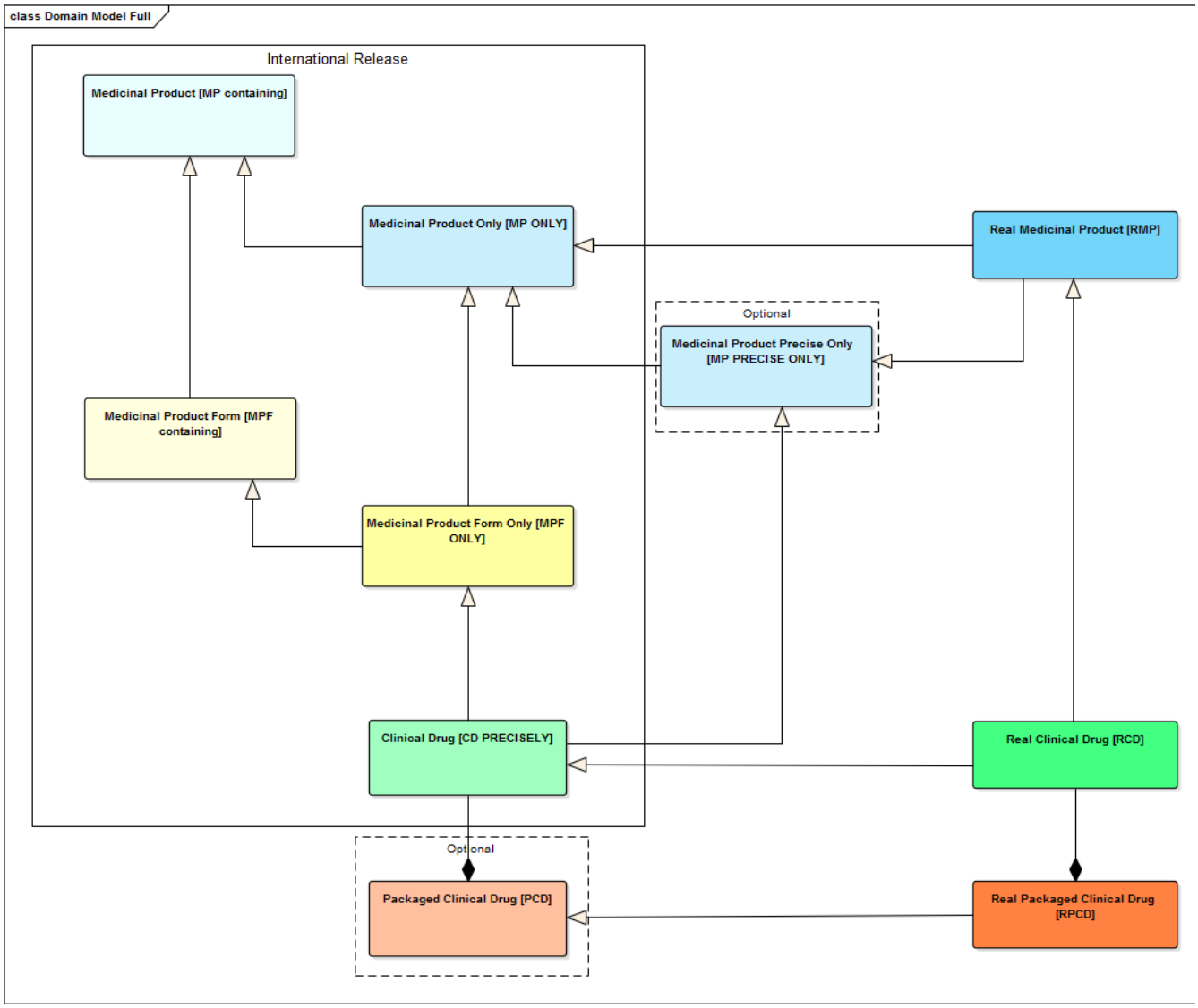


Figure 1: Diagram of the classes of the SNOMED CT national extension model for Medicinal Products

In the diagram, the MP classes are shown in shades of blue, the MPF classes in shades of yellow, the CD classes in shades of green and the PCD classes in shades of orange; the concepts represent the real world medicinal products available within a nation and described within that extension are shown in the darker shades.

5.1 Classes of National Extension Model

The five concept classes of the international release are shown on the left hand side in their three levels or groups (MP, MPF and CD), with their two representations - the "containing" and the "only" - of the open and closed world views respectively. The sixth and optional class of MP Precise Only is also shown, as an optional class that may be used in a national extension model. Definitions, descriptions and examples of concepts in these classes can be found in the SNOMED CT Medicinal Product Model Specification. No requirement has been identified to date to suggest that the MPF class from the international core requires a mirrored class in the national extension model.

The classes of the national extension model are, with the exception of the PCD, shown on the right hand side: two of the classes of the national extension model 'mirror' classes in the international model; their concepts represent the real world medicinal products available within a nation that are types of the concepts in the international release:

- the Real Medicinal Product (RMP) mirrors the Medicinal Product Only class and represents products marketed by a single organisation (supplier) under a single name (which may be a trade or brand name) and which contain the same set of active ingredient substances
- the Real Clinical Drug (RCD) mirrors the Clinical Drug class and represents a product marketed by a single organisation (supplier) under a single name (which may be a trade or brand name) which contains the same set of active ingredient substances in the same strength and which is formulated within a single dose form

Two classes of the national extension model more granular than the classes of the international model in that they represent medicinal products as they are presented into the supply chain in packages for clinical/patient use (the aggregate product packaging used in wholesaling and delivery such as boxes and pallets are excluded). These classes are

- the Real Packaged Clinical Drug (RPCD) is a representation of a packaged product marketed by a single organisation (manufacturer or supplier) under a single name (which may be a trade or brand name) which contains amounts of one or more Real Clinical Drugs within it, in set amounts
- the optional Packaged Clinical Drug (PCD) is an abstract representation of the Real Packaged Clinical Drug, in that it has no manufacturer or supplier information and therefore represents a package containing one or more Clinical Drugs within it, in set amounts

Definitions and detailed descriptions of the extension classes are given in the sections below this model introduction.

Extensions may wish to populate and use all of the classes described in the model, or they may wish to use only a subset; it is envisaged that the Clinical Drug class from the international core will be foundational, but all others may be considered optional for implementation. For example, some nations may not require Packaged Clinical Drug or Real Packaged Clinical Drug concepts, if all products are licensed and used in healthcare at the Real Clinical Drug level, whereas if a nation licenses all its products at the Real Packaged Clinical Drug level and uses those concepts in their healthcare culture, the Real Clinical Drug class may not be required , if using the Clinical Drug description for the content of the package if considered sufficient. Similarly, some nations may require the MP Precise Only concept for some classes of concepts where the precise ingredient substance can affect the clinical characteristics such as potency (e.g. glucocorticosteroids) if these concepts need to be available to support "dose based prescribing" (i.e. prescribing that specifies a medicine concept plus a route of administration, a dose quantity and a dose frequency, but does not specify a dose form or a strength so therefore not a clinical drug with its precise ingredient substance). MP Precise Only concepts can be authored in a national extension using the principles given in the international model specification (see section 3.1.3 of the International Specification). In addition, some extensions may wish to author additional Clinical Drug concepts using a presentation strength description for liquid products for which the international release has only a concentration strength representation (see section 3.3 of the International Specification). Concepts should classify correctly despite the absence of some intermediary classes, provided that they have been modelled according to the SNOMED International standards, that is using the proximal primitive parent and the relevant attributes for the concept class.

5.2 Class Relationship

The model uses the standard generalisation/specialisation relationship between the mirrored "Real" classes of the national extension and their abstract classes in the international core, and then uses a partitive relationship, shown in the diagram as the specialised composition relationship (the 'live together, die together' relationship), between the Clinical Drug and Packaged Clinical Drug classes, indicating that the Packaged Drug classes are "composed of" concepts that are themselves Clinical Drugs. The composition relationship is particularly appropriate for those packaged medicinal products that contain more than one clinical drug (often referred to as "kit products"). The combination of the generalisation relationship and partitive relationship is manageable within the SNOMED CT tooling and will be applicable for description of other types of product concepts within the overall scope of SNOMED CT such as medical devices, which are often composed of more than one type of entity (e.g drug eluting stents). The use of the composition relationship between Clinical Drugs and Packaged Clinical Drugs means that if implementations wish to display Packaged Clinical Drugs "under" the Clinical Drugs and they wish to transfer information such as the therapeutic role from the Clinical Drug to the Packaged Clinical drug that they are related to, this composition relationship and the 'contains clinical drug' attribute must to be used to facilitate that.

Other options for the relationships between the classes of the national extension model were discussed; these are described in an Appendix, for reference.

The relationships in the diagram are shown only in terms of their semantics; no cardinality is given. National extensions may populate those classes for which they have use cases; for example, if a nation has no requirement for the Real Medicinal Product class, it does not have to be populated.

5.3 Relationship between content in the international release and in national extensions

The international core content of SNOMED CT will provide all the **attribute relationships** (see detail below) needed to define medicinal product concepts in a national extension. These will be suitably defined according to SNOMED machine-readable concept model (MRCM) principles and available for use in the tooling. However, not all the concepts to provide the **values** for those attributes can be present in the core (the product names for the Real Medicinal Product etc. and the supplier organisations) and as such, this specification cannot provide ranges for those attributes; however supertype concepts will be available to support extension authoring.

For various reasons, not all the individual Medicinal Product and Clinical Drug concepts that a nation requires may be present in the international core; some may require authoring in the nation's own extension. However all the substance, strength, dose form and pack unit concepts to value the attributes should be available in the core content to satisfy the interoperability use cases for the medicinal product hierarchy.

All concepts in the classes of the national extension model should be modelled using the proximal primitive parent modelling pattern and be fully defined wherever possible, using the attribute relationships and values from the core the substance, strength and dose form concepts and values from the national extension for product names and manufacturer/supplier organisations, but it is accepted that some primitive concepts may have to be authored.

6. Real Medicinal Product (RMP) (closed world view)

Definition: The representation of a medicinal product marketed by a single organisation (supplier) in a single jurisdiction under a single name (which may be a trade or brand name) and which contains the same set of active ingredient substances, regardless of any modification of those active ingredient substances. It is a subtype of and real world equivalent to the Medicinal Product Only (MP only) class in the international core.

Discussion with examples:

Single ingredient substance branded products:

The RMP "Lipitor product" shown in Figure 2 below presents products marketed by Pfizer under a single name (Lipitor) and containing only atorvastatin as the base active ingredient substance:

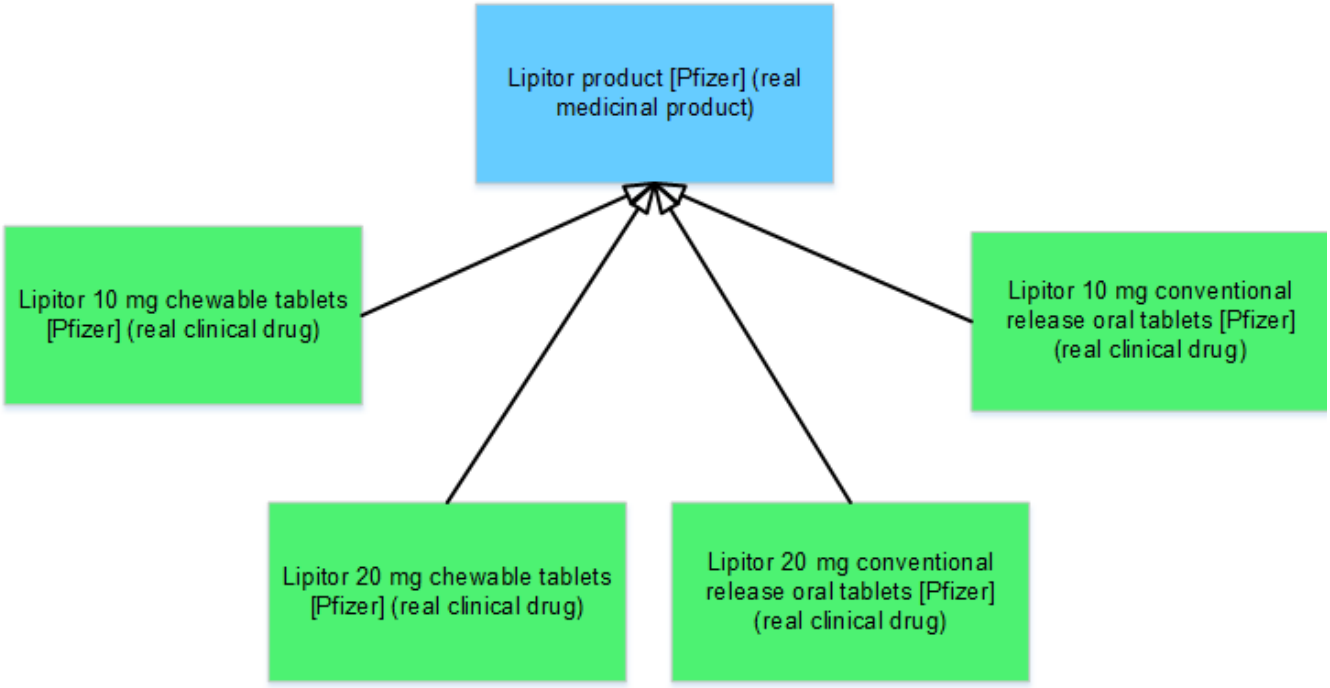


Figure 2: Diagram showing a branded single ingredient substance real medicinal product and its supporting real clinical drug concepts (note, not all possible real clinical drug concepts shown)

Single ingredient "generic" products:

For those products without a unique (i.e. invented) product name (i.e. so called "generic products"), extensions may choose not to populate the Real Medicinal Product class, as shown below:

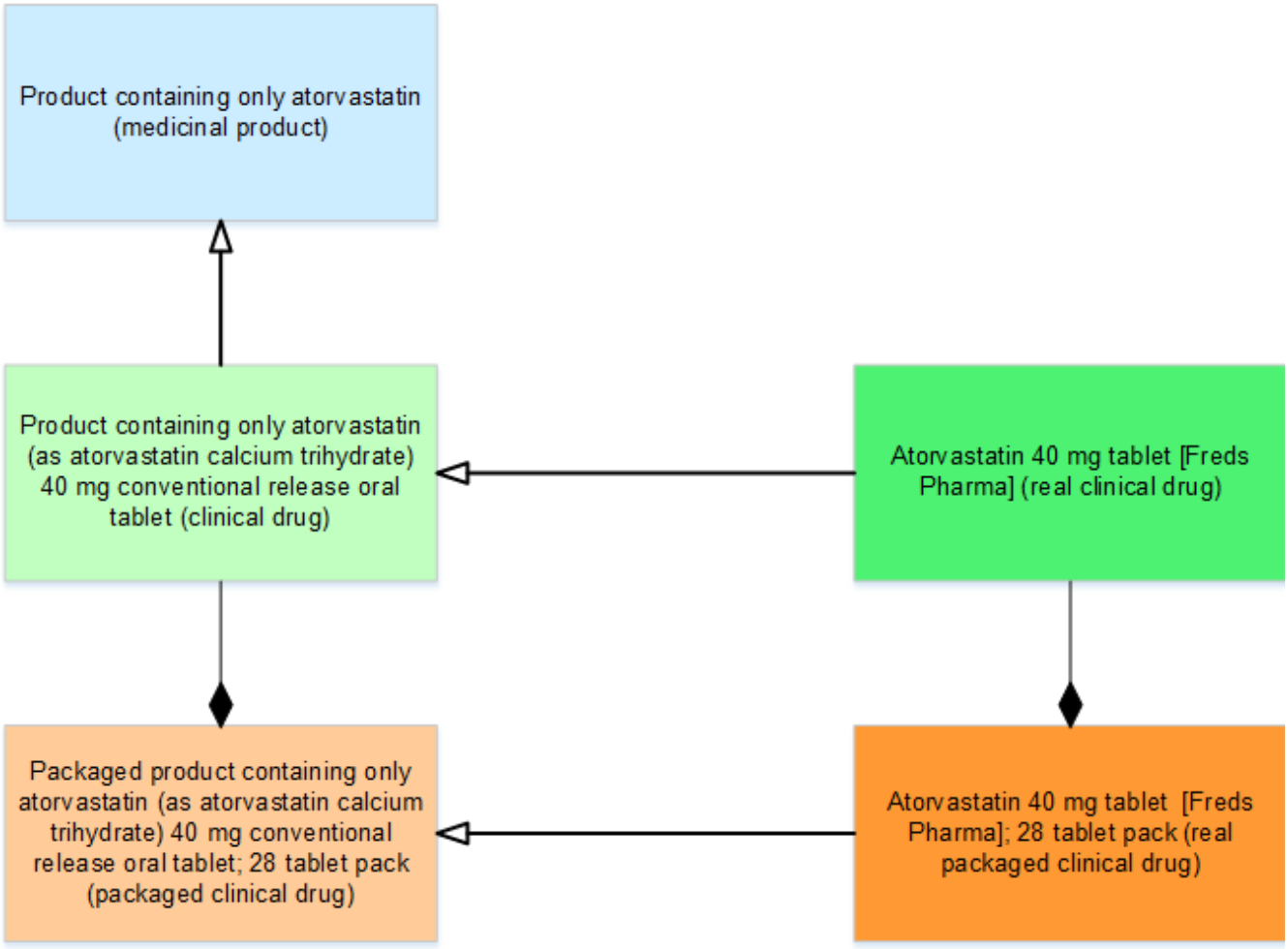


Figure 3: Example of authorised "generic" products where a real medicinal product concept has not be authored

Alternatively, for "generic products" a national extension may choose to populate the Real Medicinal Product using the generic name, since with the manufacturer/supplier organisation, this gives a unique concept, as shown below:

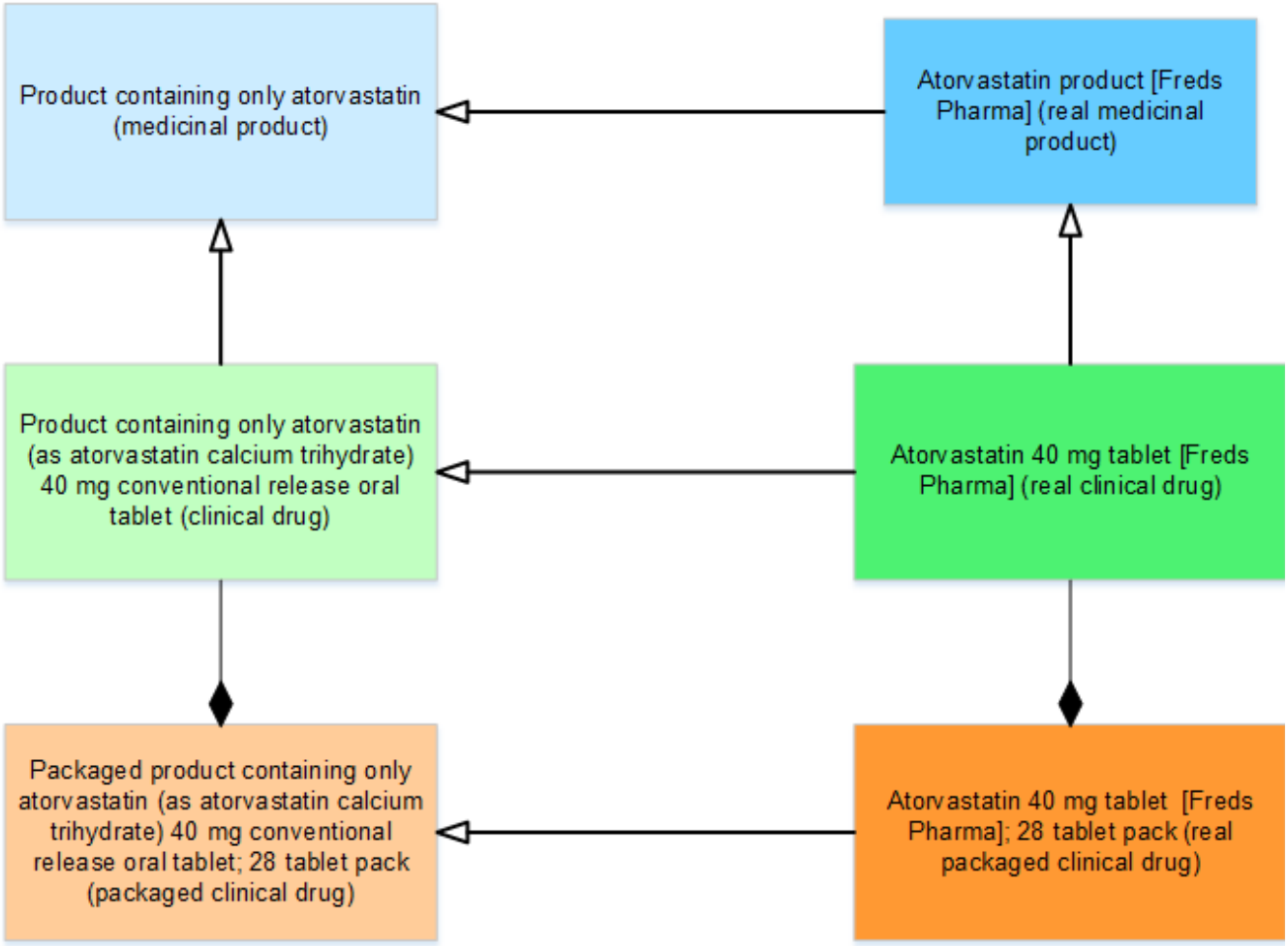


Figure 4: Example of authorised "generic" products where a real medicinal product concept has been authored using product and manufacturer name

Multi-Ingredient substance branded products

One of the definitional attributes for a Real Medicinal Product is that it represents a single set of active ingredient substances. Therefore not all medicinal products that share the same (invented) product name will relate to a Real Medicinal Product, especially for over the counter (OTC) medicines, where a commercial "brand family" may contain products with different active ingredient sets which would therefore have different MP only representations. For example: some cough and cold product ranges span expectorant products, cough suppressants, antipyretics and decongestant products, with different sets of active ingredients in each, but all sharing the same brand name.

In the example below, the three real clinical drug products all share the same product name ("Benylin®") in one jurisdiction but they do not relate to a single real medicinal product because they each relate to different Medicinal Products due to differences in their active ingredient substances.

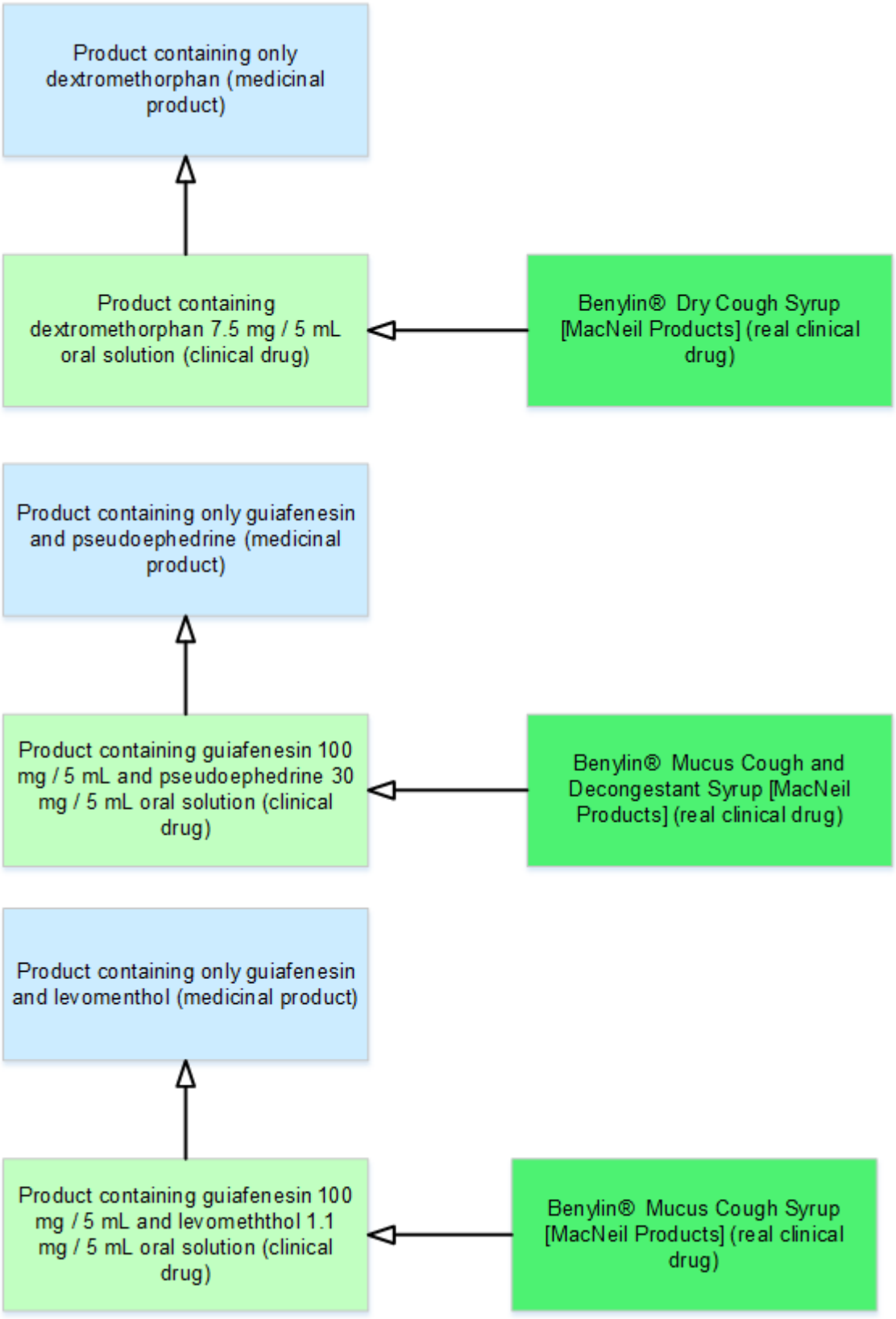


Figure 5: Example of branded real clinical drug products sharing the same product name but not relating to a Real Medicinal Product

A national extension may choose to populate RMPs for "brand families" that contain products with different active ingredient sets by extending the product name concept to include enough detail to scope just a single active ingredient set, as shown below:

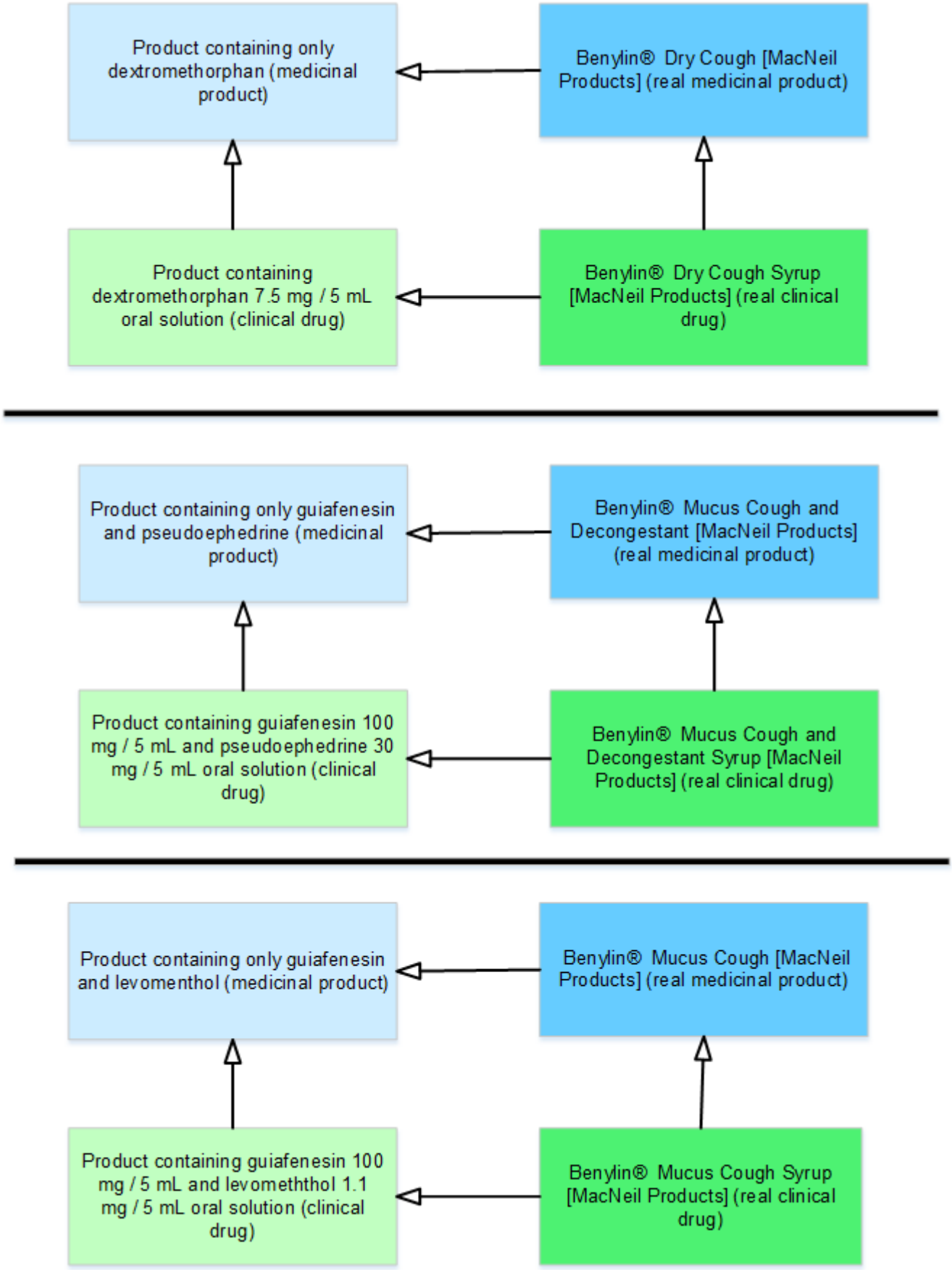


Figure 6: Example of branded real clinical drug products relating to a Real Medicinal Product by alternative authoring of product name

Existing national terminology equivalents for real medicinal product:

- Trade family in NHS dm+d
- Trade Product (TP) in AMT/NZULM (possibly – AMT appears to allow strength and dose form modifiers)
- Brand Name (BN) in RxNorm (possibly)

6.1 Attributes of Real Medicinal Product (RMP)

The Real Medicinal Product concept class has two attributes inherited from the Medicinal Product (only) class in the international core and two additional attributes.

Stated parent concept	763158003|Medicinal product (product) • Exceptions: none identified
Semantic tag	(real medicinal product)
Definition status	900000000000073002|Sufficiently defined concept definition status (core metadata concept) Note: This can only be the case if extensions author concepts to represent product names and manufacturer/supplier organisations
Attribute: **Has active ingredient**	• Range: 105590001|Substance (substance) - descendants only, excluding concepts representing structural groupers, dispositions, or combined substances • Cardinality: 1..* The attribute value should represent the base of BoSS of the descendant (real clinical drug) concepts unless explicitly identified as an exception. • Exceptions: none identified
Attribute: **Count of base of active ingredient**	• Range: 260299005 |Number (qualifier value)| - descendants only • Cardinality: 1..1
Attribute: **Has product name**	• Range: Extensions must author product name concepts within their extension using the root of 774167006| Product name (product name)| from the Qualifier hierarchy • Cardinality: 1..1 The attribute value should represent the (authorised) product name; this may (or may not) be a trademarked name, and is often referred to as the "brand name" (see section 10.1 below)
Attribute: **Has supplier**	• Range: Extensions must author concepts to value supplier organisation information within their extension using the root of 774164004| Supplier (supplier)| from the Qualifier hierarchy • Cardinality: 1..1 The attribute value should represent the holder of the marketing authorisation or authorisation for supply; this may or may not be the organisation responsible for the actual manufacture of the product (see section 10.2 below)

Note: the cardinalities given in the above table are the business cardinalities; the MRCM will have different (usually more relaxed) cardinalities for its own purposes.

6.2 Examples

Stated template view:

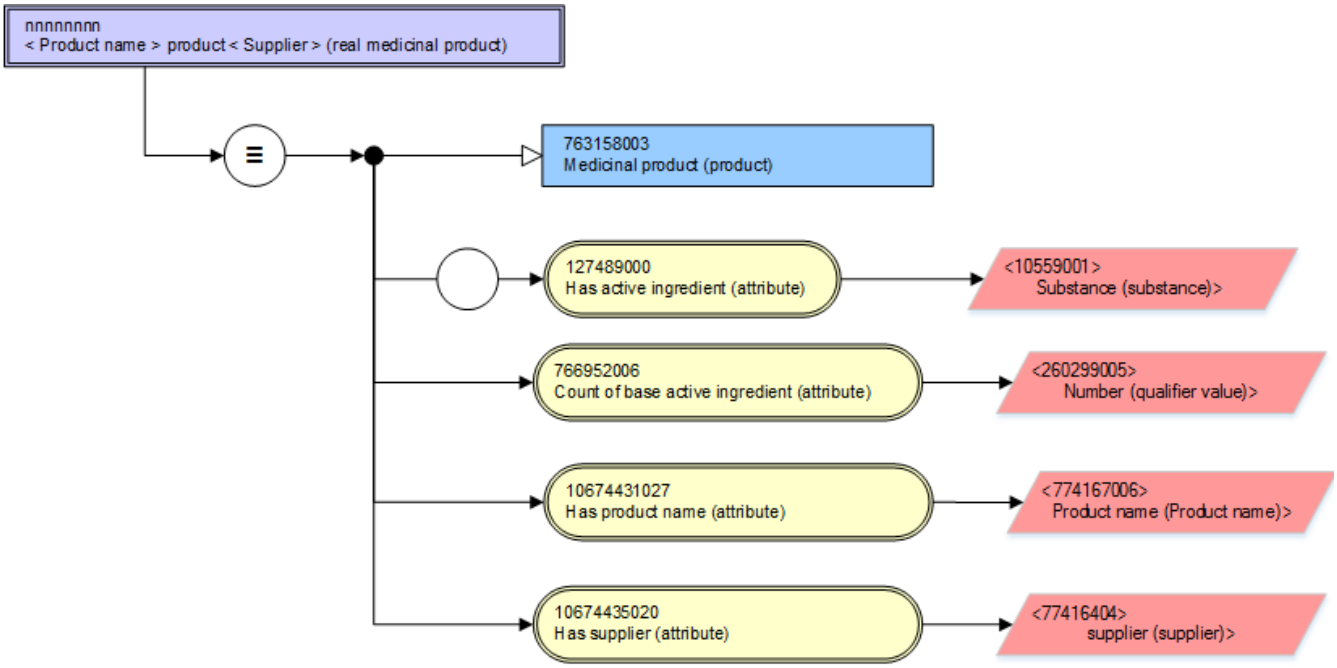


Figure 7: Template for a real medicinal product

Example (stated view):

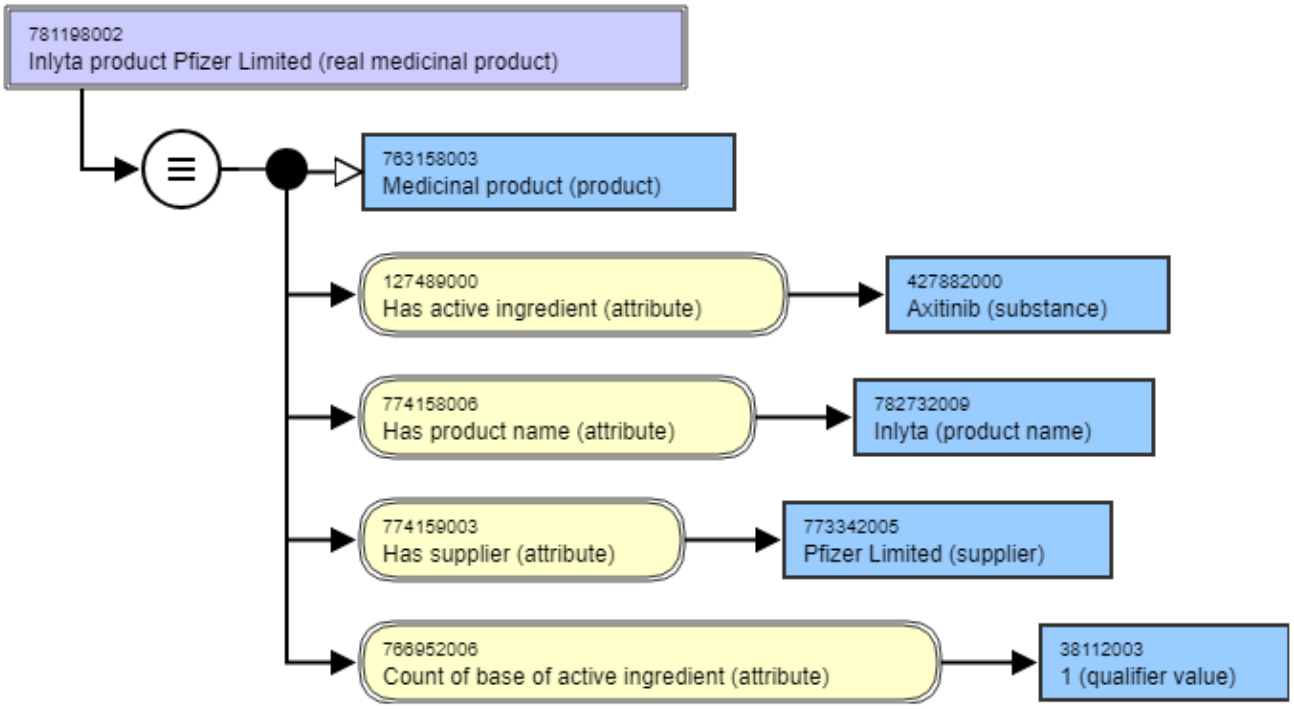


Figure 8: Example of a real medicinal product - stated view

Example (inferred view):

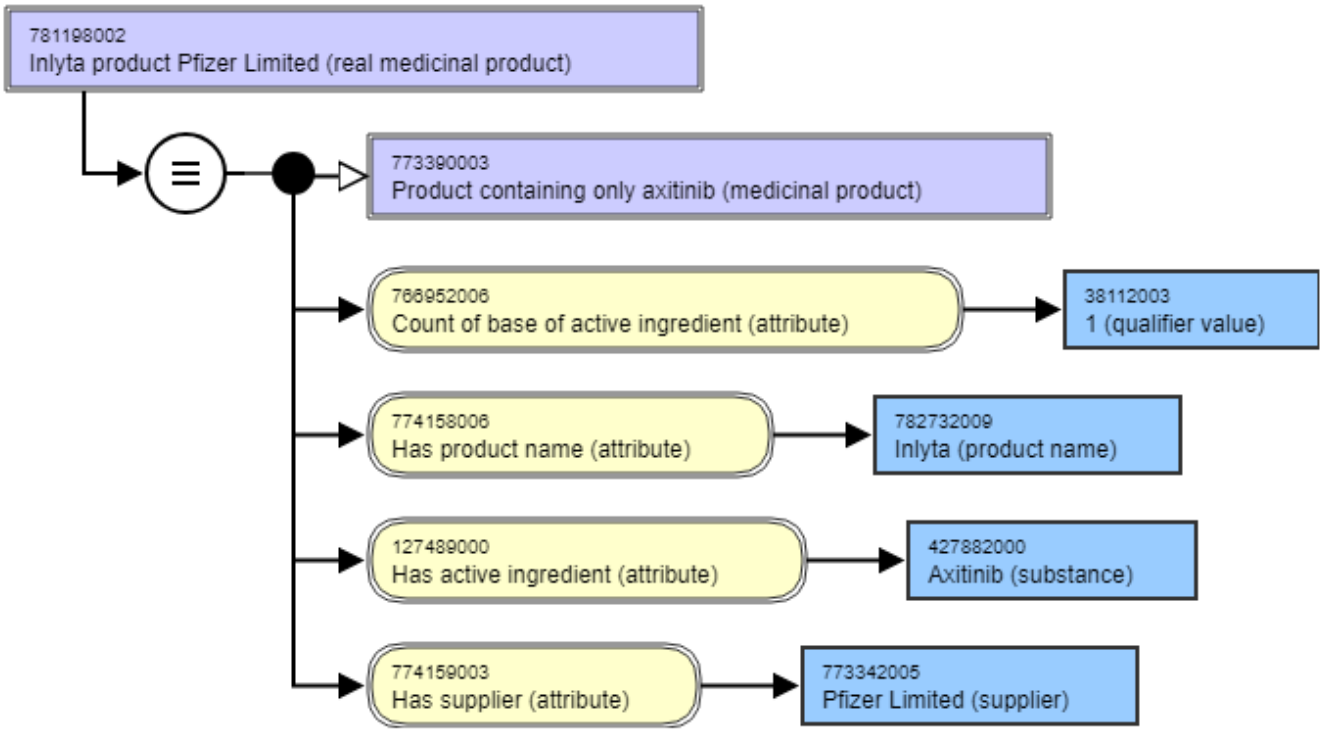


Figure 9: Example of a real medicinal product - inferred view

6.3 Use cases supported by Real Medicinal Product

The following use cases are supported by the Real Medicinal Product concept class:

- Describing medication statements for a medication profile when the detail of the exact product used is not known; e.g. "patient states they used Ventolin for 5 years in childhood"
- Decision support and protocol management may have a use case for this class (for example to change presentation within a product family)
- Pharmacovigilance (abstract representation of a manufactured medicinal product)

6.4 IDMP Compatibility

There is no identified representation of a class similar to the Real Medicinal Product concept class in IDMP, despite there being (a possible) pharmacovigilance use case for this class.

7. Real Clinical Drug (RCD) (closed world view)

Definition: The representation of a medicinal product marketed by a by a single organisation (supplier) in a single jurisdiction under a single name (which may be a trade or brand name) and which contains the same set precise active ingredient substances and strengths in a single manufactured dose form. It is a subtype of and real world equivalent to the Clinical Drug (CD precisely) class in the international core.

Most but not all regulatory authorities license products at this level, then the individual packaged products that are marketed into the supply chain in any jurisdiction are included within that authorisation. A small number of regulatory authorities license each package of a medicinal product separately. Since this class represents real products as authorised in a jurisdiction, description of additional non-defining information, such as excipient substances (flavours, preservatives, sweeteners etc.) or details about the product name parts or product authorisation information and product availability information can be attached to Real Clinical Drug concepts, should a national extension wish to do this. For further details, see section 7.3

Concentration and Presentation Strength:

Clinical Drug concepts may have their strength expressed as “presentation strength” and/or as “concentration strength” as appropriate for different types of product (see Appendix A of the international specification). In the international release, Clinical Drug concepts are authored *either* using presentation strength (for discrete dose forms) *or* using concentration strength (for liquid dose forms and patches etc.). In national extension terminology this may be sufficient, or their may be a requirement to represent liquid dose form products using both concentration and presentation strength, either for the the abstract Clinical Drug or for the Real Clinical Drug, or for both. This is shown in the diagram below:

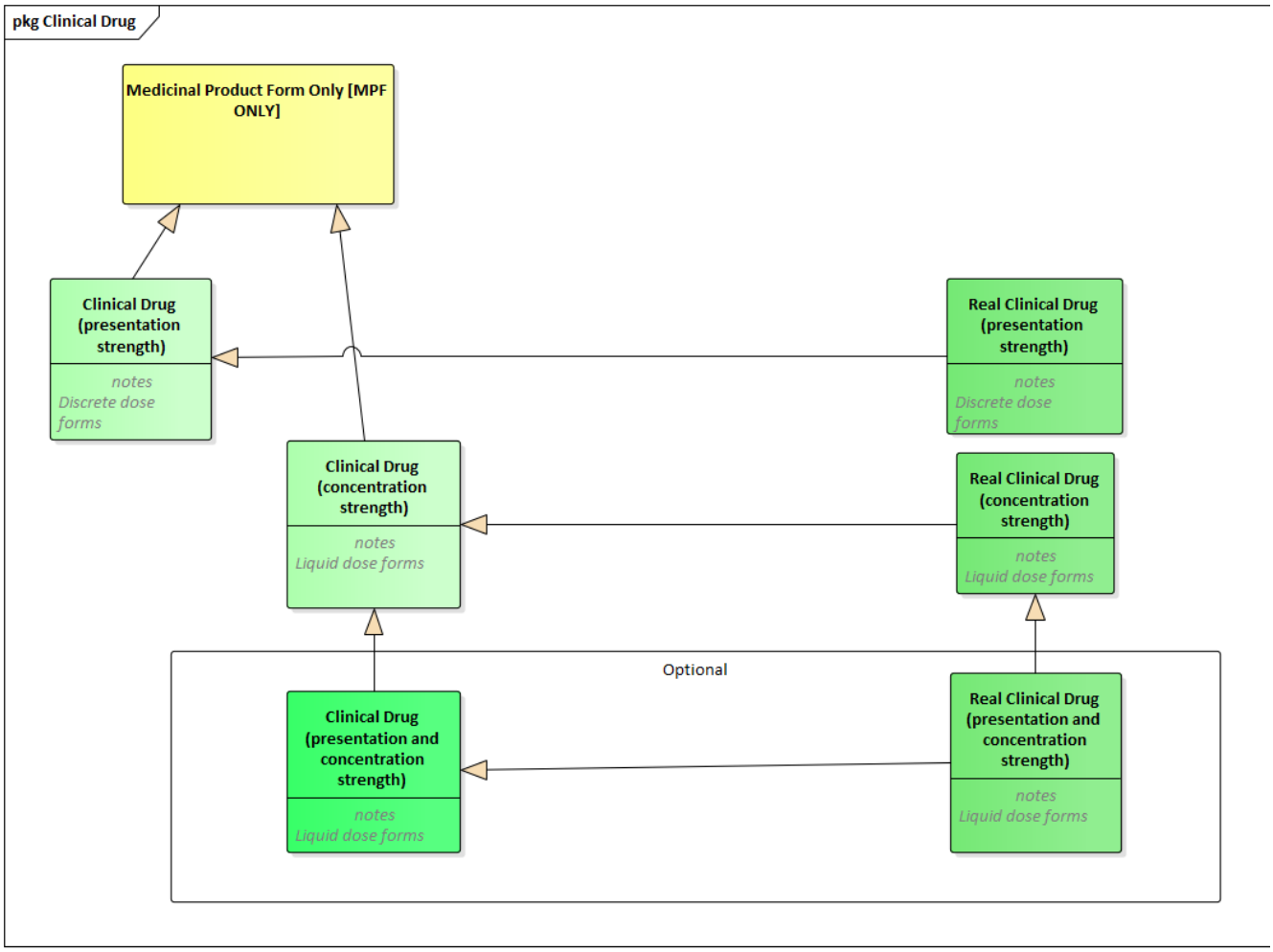


Figure 10: Diagram of relationships and optionality for presentation strength and concentration strength Clinical Drug and Real Clinical Drug

Even within a single jurisdiction, authorisations are not always consistent in dealing with presentation and concentration strength. Some regulatory agencies have or are moving to licensing all parenteral liquid products using presentation strength (with the exception of not insulins and some large volume parenteral fluid replacement products and bulk use vials etc.); other agencies have been are using this pattern for some products (e.g. pf syringes) and may change for others as IDMP takes effect. Some national terminologies are working to normalise the patterns (particularly for safety considerations; others are dealing with the mixed economy that exists "as is". Therefore this international specification allows for all options by having the different patterns for both Clinical Drugs and Real Clinical Drugs.

Existing national terminology equivalents:

- Actual Medicinal Product in NHS dm+d and Belgian SAM
- Trade Product Unit of Use in in AMT/NZULM
- Semantic Branded Drug (SBD) in RxNorm
- HPK class in the Dutch Z-Index
- Medicinal Product (MP) class in CCDD, the Canadian Clinical Drug Dataset

7.1 Attributes of Real Clinical Drug

The Real Clinical Drug class has attributes inherited from the Clinical Drug (precisely) class in the international core and attributes inherited from the Real Medicinal Product class.
In the following table, two relationship groups (marked with an *) are described: one for presentation strength and one for concentration strength; the appropriate relationship group type(s) should be selected based on the real product being described and the national editorial guidelines. In order to support correct classification, a liquid product being described using a presentation strength will also need its concentration strength attributes authored. For all those concepts where a presentation strength is described, the unit of presentation attribute should also be valued.

Semantic tag	(real clinical drug)

Definition status	900000000000073002|Sufficiently defined concept definition status (core metadata concept) This can only be the case if extensions author concepts to represent product names and manufacturer/supplier organisations
Attribute: **Has manufactured dose form**	• Range: 736542009|Pharmaceutical dose form (dose form) - descendants only • Cardinality: 1..1 This is the finished dose form that the manufactured product is presented in by the manufacturer, before any transformation into an administrable dose form has taken place.
Attribute: **Count of base of active ingredient**	• Range: 260299005 |Number (qualifier value)| - descendants only • Cardinality: 1..1
Attribute: **Has unit of presentation**	• Range: 732935002 | Unit of presentation (unit of presentation) - descendants only • Exceptions: none identified • Cardinality: 0..1 • Not valued for those real clinical drugs that can only be described using concentration strength (e.g. semi-solids)
*** Relationship group** **- for presentation strength**	One relationship group containing only the following six attributes is required for each active ingredient • Cardinality: 1..*
• **Attribute:** • **Has active ingredient**	• Range: 105590001|Substance (substance) - descendants only, excluding concepts representing structural groupers, dispositions, and combined substances • Cardinality: 1..1 (per relationship group) This should be the precise active ingredient substance present in the real clinical drug
• **Attribute:** • **Has basis of strength substance**	• Range: 105590001|Substance (substance) - descendants only, excluding concepts representing structural groupers, dispositions, and combined substances • Cardinality: 1..1 (per relationship group)
Attribute: • **Has presentation strength numerator value**	• Range: 260299005|Number (qualifier value) - descendants only • Cardinality: 1..1 (per relationship group)
Attribute: • **Has presentation strength numerator unit**	• Range: 258666001|Unit (qualifier value) - descendants only • Cardinality: 1..1 (per relationship group)
Attribute: • **Has presentation strength denominator value**	• Range: 260299005|Number (qualifier value) - descendants only • Cardinality: 1..1 (per relationship group)
Attribute: • **Has presentation strength denominator unit**	• Range: 258666001|Unit (qualifier value) - descendants only • Cardinality: 1..1 (per relationship group)
*** Relationship group** **- for concentration strength**	One relationship group containing only the following six attributes is required for each active ingredient • Cardinality: 1..*

• **Attribute:** • **Has active ingredient**	• Range: 105590001|Substance (substance) - descendants only, excluding concepts representing structural groupers, dispositions, and combined substances • Cardinality: 1..1 (per relationship group) This should be the precise active ingredient substance present in the real clinical drug
• **Attribute:** • **Has basis of strength substance**	• Range: 105590001|Substance (substance) - descendants only, excluding concepts representing structural groupers, dispositions, and combined substances • Cardinality: 1..1 (per relationship group)
• **Attribute:** • **Has concentration strength numerator value**	• Range: 260299005|Number (qualifier value) - descendants only • Cardinality: 1..1 (per relationship group)
• **Attribute:** • **Has concentration strength numerator unit**	• Range: 258666001|Unit (qualifier value) - descendants only • Cardinality: 1..1 (per relationship group)
• **Attribute:** • **Has concentration strength denominator value**	• Range: 260299005|Number (qualifier value) - descendants only • Cardinality: 1..1 (per relationship group)
• **Attribute:** • **Has concentration strength denominator unit**	• Range: 258666001|Unit (qualifier value) - descendants only • Cardinality: 1..1 (per relationship group)
Attribute: **Has product name**	• Range: Extensions must author product name concepts within their extension using the root of 774167006| Product name (product name)| from the Qualifier hierarchy • Cardinality: 1..1 The attribute value should represent the (authorised) product name; this may (or may not) be a trademarked name, and is often referred to as the "brand name" (see section 10.1 below)
Attribute: **Has supplier**	• Range: Extensions must author concepts to value supplier organisation information within their extension usin g the root of 774164004| Supplier (supplier)| from the Qualifier hierarchy • Cardinality: 1..1 The attribute value should represent the holder of the marketing authorisation or authorisation for supply; this may or may not be the organisation responsible for the actual manufacture of the product (see section 10.2 below)

Note: the cardinalities given in the above table are the business cardinalities; the MRCM will have different (usually more relaxed) cardinalities for its own purposes.

7.2 Examples

Stated template view:

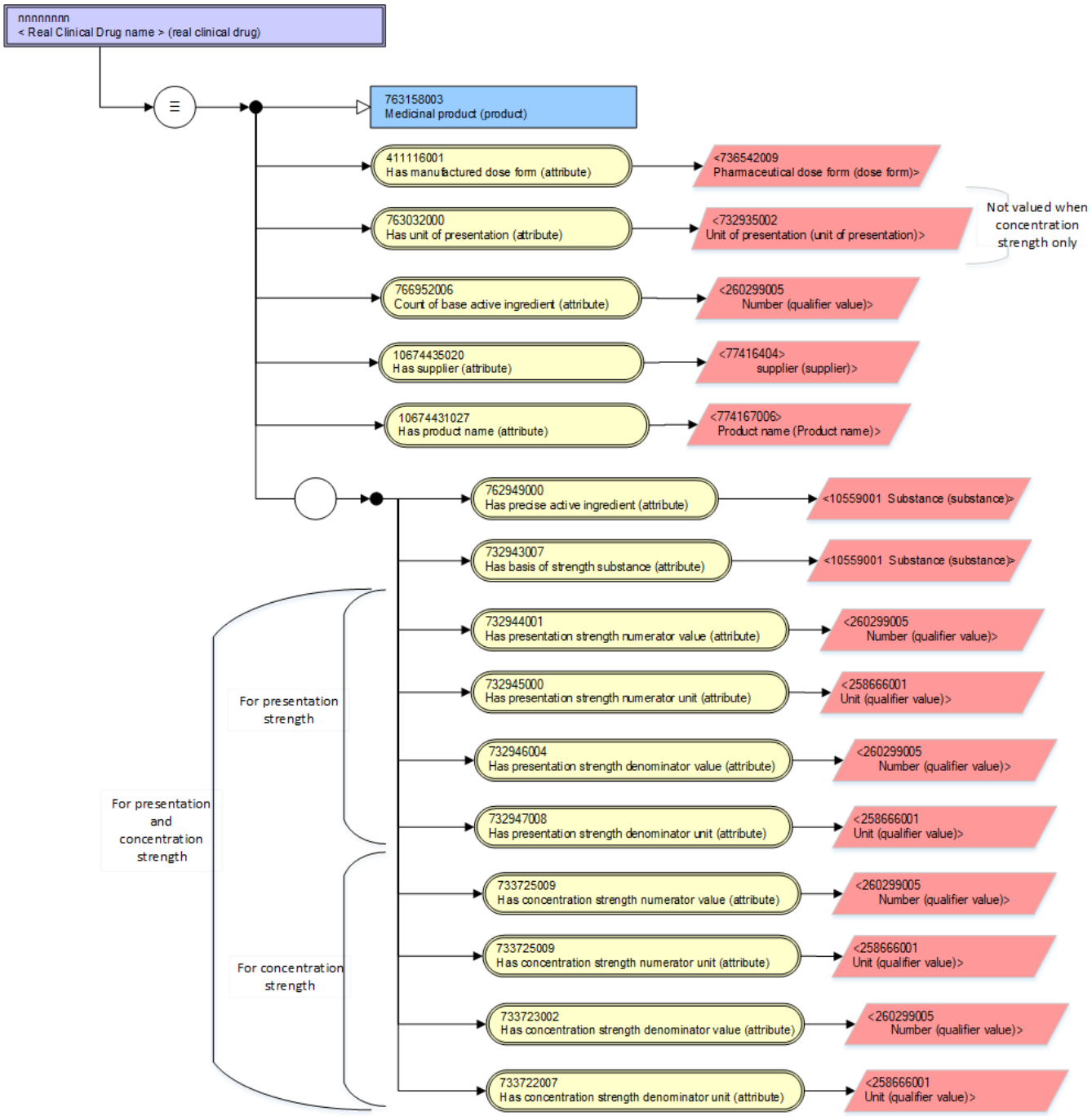


Figure 11: Template for a real clinical drug

Example (stated view):

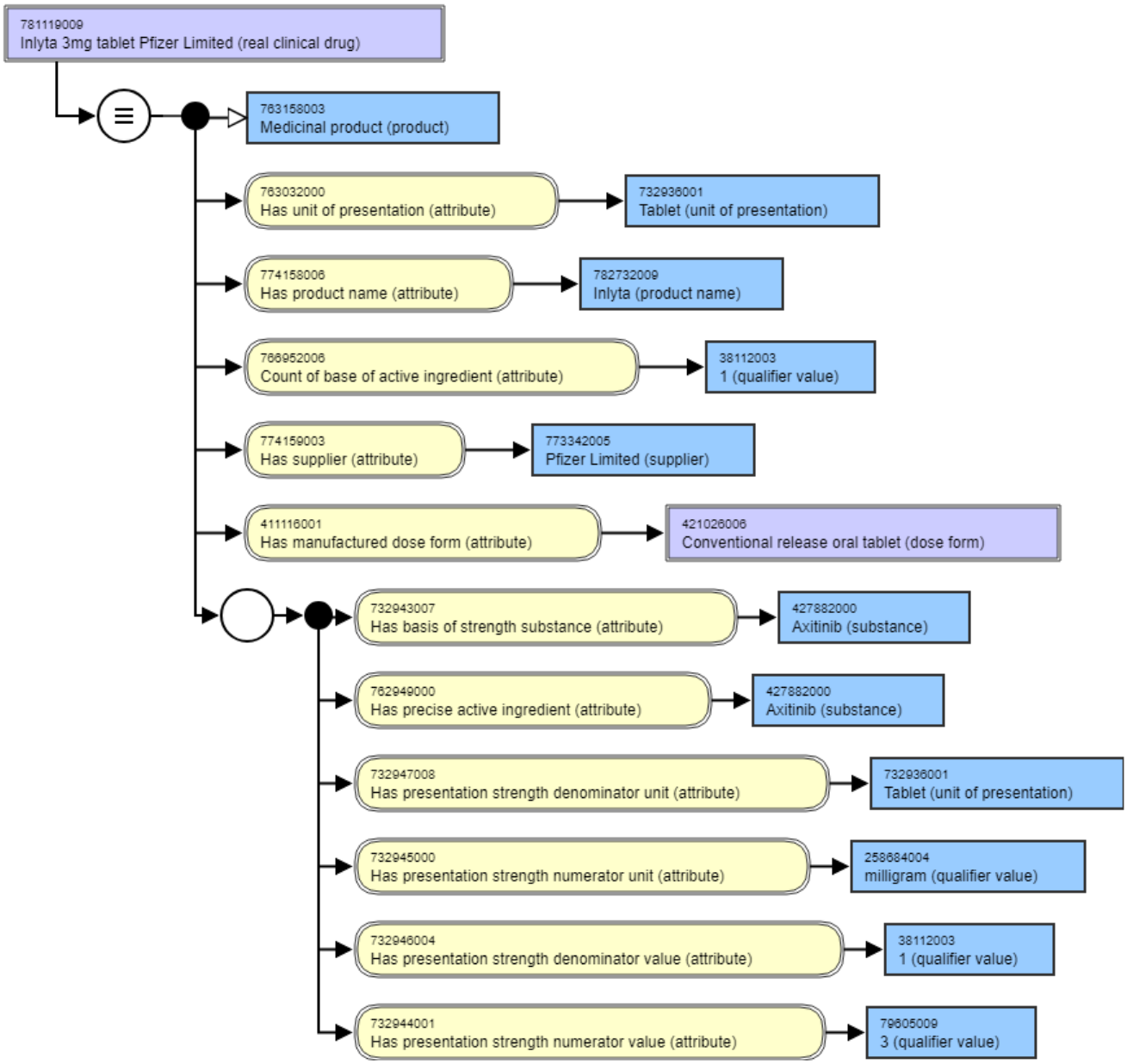


Figure 12: Example of a real clinical drug (presentation strength) - stated view

Example (inferred view):

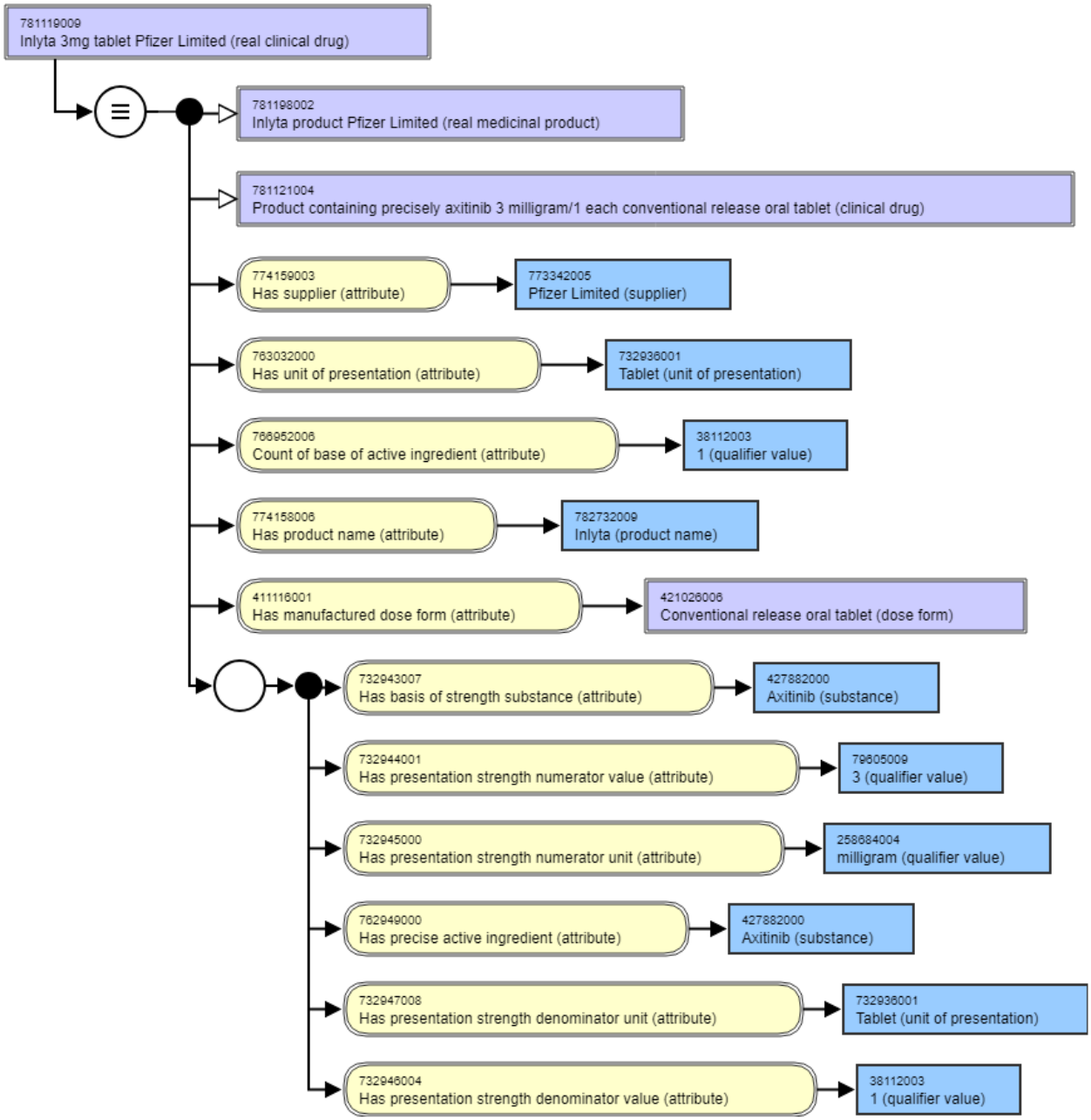


Figure 13: Example of a real clinical drug (presentation strength) - inferred view

Example (stated view):

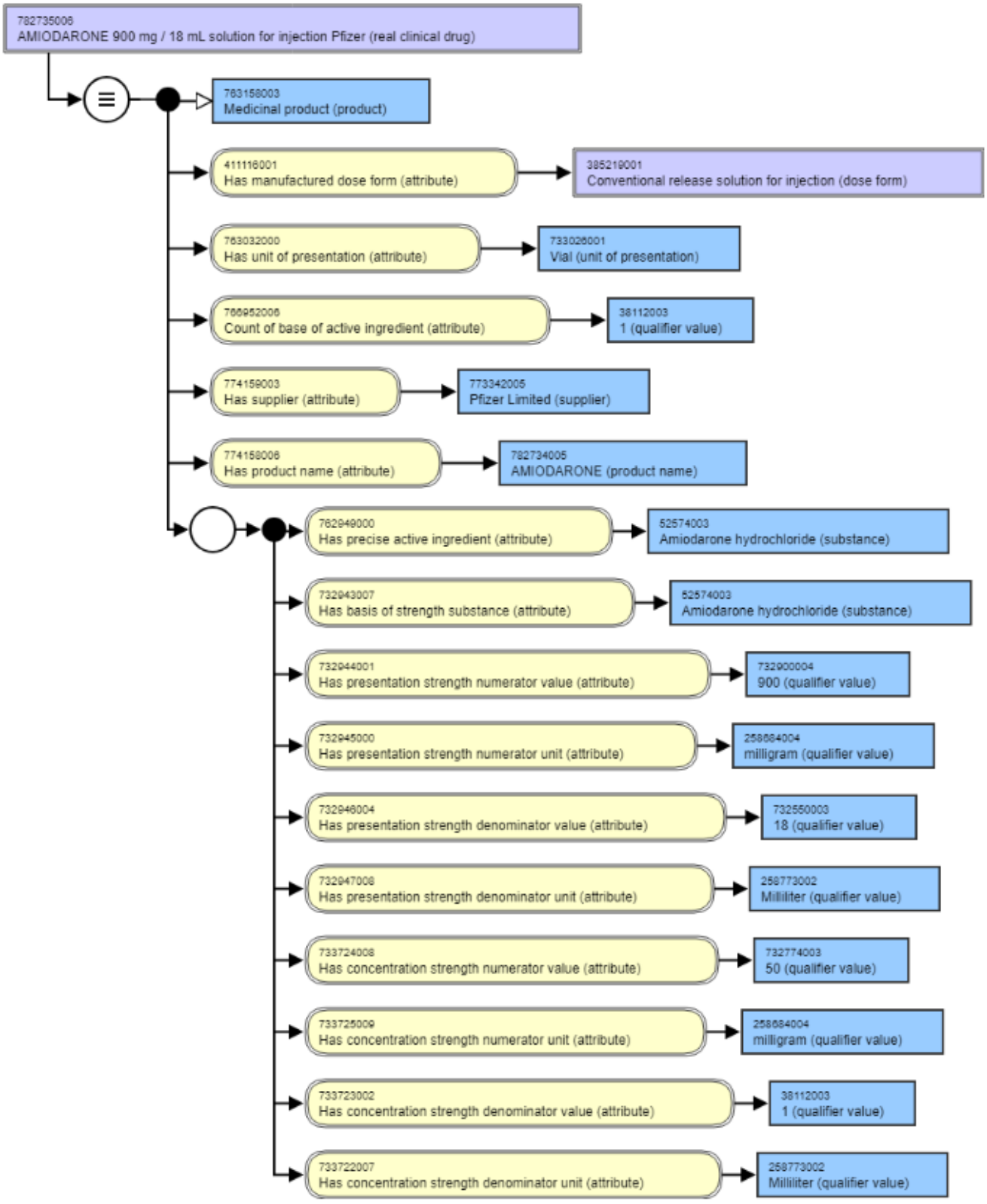


Figure 14: Example of a real clinical drug (presentation and concentration strength) - stated view

Example (inferred view):

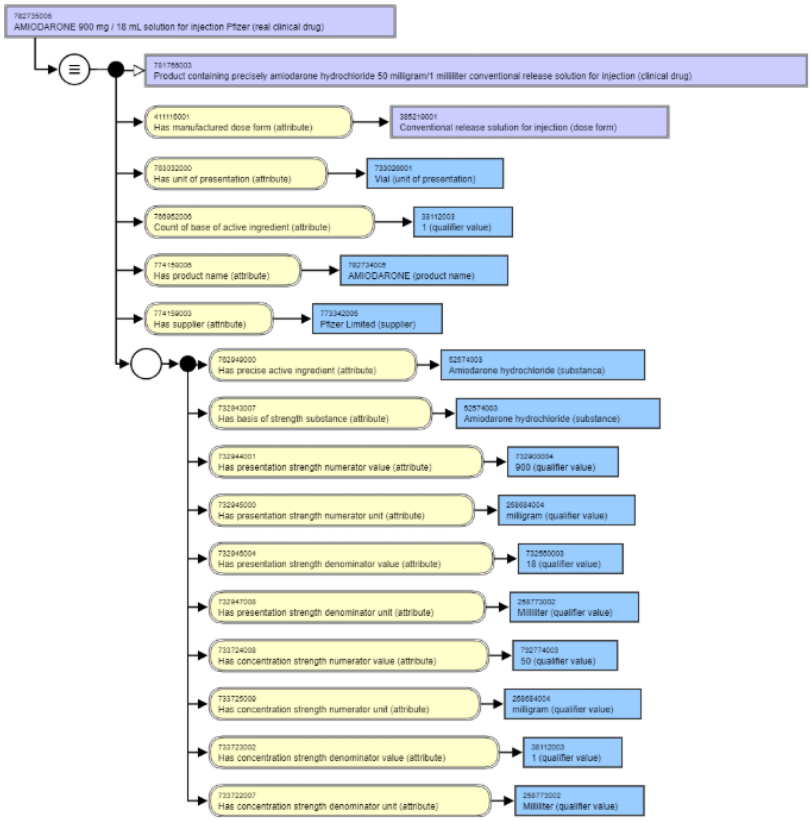


Figure 15: Example of a real clinical drug (presentation and concentration strength) - inferred view

7.3 Optional additional information

Some or all of the following items of information may be used to describe the Real Clinical Drug concept in a national extension. The attribute concepts and values to populate these, if this data is to be held in a structured form, would need to be authored into the extension using reference sets.

- Name parts (in addition to the product name and manufacturer/supplier organisation, which are definitional attributes):
  - A description of the strength of the product, which may be mathematical (e.g. "50mg" or may be descriptive (e.g. "low strength" or "adult strength")
  - A description of the dose form as it appears in the name, when this is a non-standard, invented or trademarked dose form (e.g. "caplet")
  - A description of the formulation (e.g. "with preservative" or "gluten free") and/or flavour information (e.g. "strawberry flavour") or, for influenza vaccines, which are currently out of scope, this may also the year/season of applicability
  - A description of the indication for the product (e.g. "Shingles treatment")
  - A description of the intended population for the product (e.g. "for children")
  - A description of the unit of presentation as it appears in the name, when this is a non-standard, invented or trademarked unit of presentation (e.g. "Nebule®"))
- Excipient substances playing some or all of the following roles:
  - Flavours
  - Colours
  - Preservatives
  - Stabilisers
- License information
  - License holding organisation
  - License identification ("authorisation number")
  - Licensing class and/or legal status of supply
- Usage information (prescribability within a particular jurisdictional context) including legal status and licensed indications
- In jurisdictions where repackaging and/or "parallel importing" are authorised, a national extension may wish to consider having a relationship between the repackaged or parallel imported Real Clinical Drug and the Real Clinical Drug supplied by the original manufacturer, if that is present within the jurisdiction too.

7.4 Use cases supported by Real Clinical Drug

The following use cases are supported by the Real Clinical Drug concept class:

- Supporting medication process activities: prescribing, dispensing, administration and medication statements
    - In prescribing and in medication statements, especially in situations where the patient should always use a particular Manufactured Product, for reasons of bioavailability (such as a lithium product) or use of administration system (such as an insulin pen)
    - In dispensing and administration, to identify exactly which product was provided/used
- Reimbursement: national or local systems may set pricing or eligibility against particular manufactured products, regardless of how they are supplied (i.e. with no reference to pack size)
- Allergy checking of specific excipients (if described)
- Pharmacovigilance

7.5 IDMP Compatibility

For most authorised medicinal products, this class is roughly equivalent to the core Medicinal Product class, with its MPID identification in ISO 11615 of IDMP. However, the Medicinal Product class in IDMP explicitly includes combination (kit) products within it whereas this model describes combination products as packaged products only (see below). Implementation considerations may require combination products to be available to users alongside clinical drug and real clinical drug concepts; mechanisms such as the use of reference sets can support this requirement.

8. Packaged Clinical Drug (PCD)

Definition: A representation of a medicinal product as it is supplied in a package for placement into the supply chain, based on description of and quantity of the clinical drug(s) contained within that package. As an abstract class, the Packaged Clinical Drug is placed on the left hand side of the overall model, relating directly to the Clinical Drug class in the international core by means of a composition relationship, but its population is the responsibility of national extensions since the amount of content needed to support this internationally would be overwhelming and unmanageable in maintenance and verification.

This definition supports the description of kit or combination products (medicinal products that are composed of more than one Clinical Drug - such as a package containing fluconazole oral capsules and clotrimazole cream for treatment of vaginal thrush) as Packaged Clinical Drugs, and therefore the pack size information for each Clinical Drug that is a component in the package is grouped together. Further detail on the description of combination products (multi-component or kit products) is given in Section 11 below.

Packs of medicinal products must be represented using the closed world view; they contain ***only*** the clinical drug content stated. To correctly describe that and to ensure that pack concepts classify correctly, so that packs that contain more than one (type of) clinical drug (i.e. combination packs) do not classify as children of packs that contain only one type of clinical drug, it is necessary to use a count attribute as a proxy for the closed world view. This mirrors the use of the count attribute for active ingredient in the MP only, MPF only and CD concepts in the main medicinal product hierarchy. By using a "count" attribute in the definition of Clinical Drug and Package concepts, when concreted domains are implemented in the SNOMED CT overall concept model, the count information will be machine processable; similarly if/when a more expressive description logic becomes available to properly represent the closed world view, then all the count attributes can be removed consistently.

The national extension model does not represent intermediate layers of packaging; it represents only the outer package used in the supply chain. Describing "sub-packs" (e.g. tablets within blister sleeves, which are then within a container such as a box) is complex for a description logic based model. In most nations, sub-packs are re primarily used for supply chain management and reimbursement purposes, and possibly rounding of dispense amounts so that sub packs are not split. Many medicinal product terminologies do not represent sub-packs. ISO 11615, the Medicinal Product part of the IDMP suite of standards, has a full sub-pack mode, but the sub-packs themselves are not identified concepts and so are not available for mapping etc.; however the GS1 implementation of ISO TS 16791 does include identification of sub packs. The basic model described here does not deal with sub-packs; a concept model for sub-packs will not be undertaken until there are requests with confirmed clinical use cases. See also Appendix 2.

Figure 16: Diagram the Packaged Clinical Drug class and its composition relationship to Clinical Drug, with an example

Existing national terminology equivalents:

- UK's NHS dm+d this is the Virtual Medicinal Product Pack (VMPP) class
- The AMT/NZULM it is the Medicinal Product Pack
- In Ireland, this is in effect those packaged products on the Representative Pricing list
- The generic pack (GPCK) class in RxNorm

8.1 Attributes of Packaged Clinical Drug

The following is described for Packaged Clinical Drugs that contain one Clinical Drug only, that is they are NOT combination (multi-component or kit) products. See Section 11 below for Combination Products.

The Packaged Clinical Drug class is related to the Clinical Drug class by a composition relationship relationship, and therefore the attribute "contains clinical drug" is used to make the association between the Packaged Clinical Drug and the Clinical Drugs it contains.

Representation of packaged medicinal products should use Clinical Drugs that have presentation strength (either only or in addition to concentration strength) whenever possible in order to be able to accurately describe the number of presentation units present in the package. The exception will be for continuous products such as semi-solid dose forms of creams, gels etc. where strength pattern 3a is used (see international Editorial Guidelines). In all cases the pack size and pack size unit should relate to the denominator unit of the strength.

Semantic tag	(packaged clinical drug)
Definition status	900000000000073002|Sufficiently defined concept definition status (core metadata concept)
Relationship group	One relationship group containing one instance of each of the following attributes is required for each clinical drug that the packaged clinical drug is composed of.
Attribute: **Contains clinical drug**	• Range: 763158003 |Medicinal product (product)| - descendants only (see Note 1 below) • Cardinality: 1..1 The attribute value should represent the clinical drug that is contained in the packaged product
Attribute: **Count of clinical drug type**	• Range: 260299005|Number (qualifier value) - descendants only • Cardinality: 1..1 This attribute value should represent the count of distinct Clinical Drugs present in the pack
Attribute: **Has pack size**	• Range: 260299005|Number (qualifier value) - descendants only • Cardinality: 1..1 (per relationship group) The attribute value should represent the amount or quantity of clinical drug present in the package (see 10.3 below)

Attribute: **Has pack size unit**	• Range: 258666001|Unit (qualifier value) - descendants only • Cardinality: 1..1 (per relationship group) The attribute value should represent the units for the amount or quantity of clinical drug present in the package (see 10.3 below)

Note 1: It is currently not possible to explicitly specify an expression to describe the range of Clinical Drugs to populate this attribute, since (for example) a range cannot currently recognise a set of concepts with a particular semantic tag - in this case "(clinical drug)". This may be possible in the future; alternatively the range expression might be expressed as: "all products with a dose form, precise ingredient substance and basis of strength substance". For the interim, the range is specified as the descendants of the root medicinal product concept: 763158003 |Medicinal product (product)|.

Note 2: More specific range expressions such as "One of EITHER 732935002 | Unit of presentation (unit of presentation) - descendants only OR 258680008 | Unit of mass (qualifier value) - descendants only OR 258769000 | Unit of volume (qualifier value) - descendants only" are currently not supported, nor are rules based on the strength patterns that (for example) assert "if the clinical drug has a unit of presentation of 'tablet' then the Has_pack_size_unit will be valued as 'tablet"). Therefore, the Has_pack_size_unit should be explicitly valued.

8.2 Examples

Stated template view:

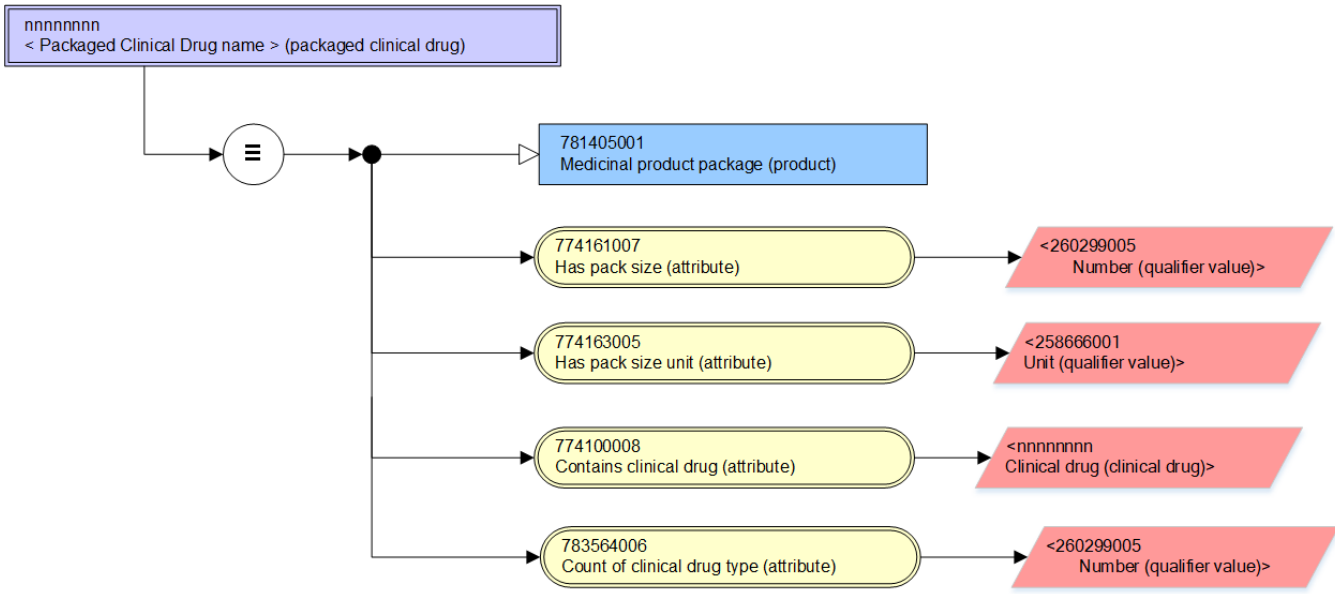


Figure 17: Template for Packaged Clinical Drug

Example (stated view):

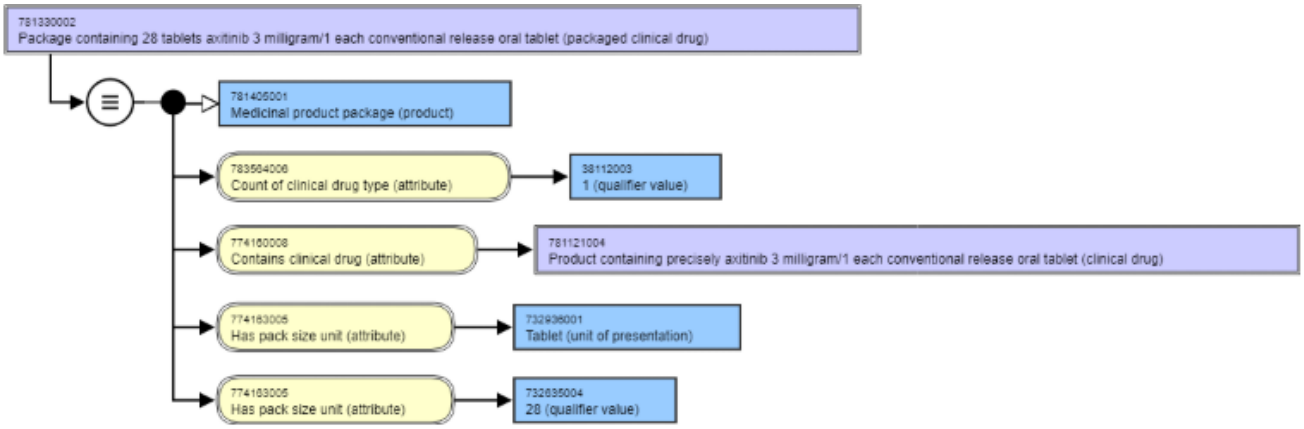


Figure 18: Example of a packaged clinical drug - stated view

Example (inferred view):

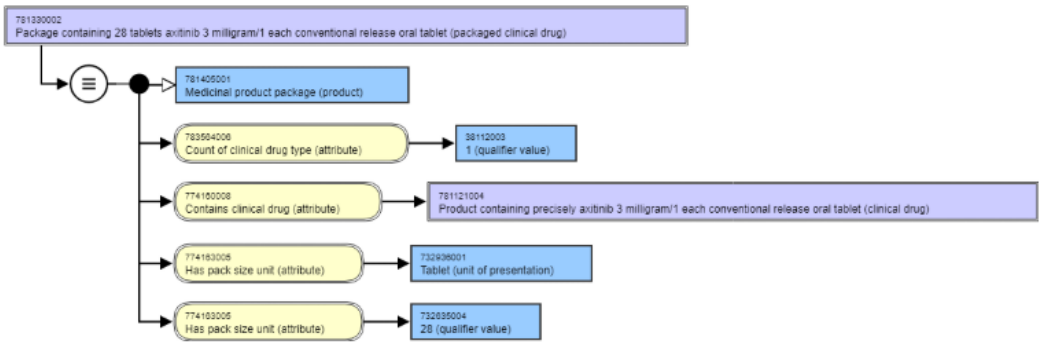


Figure 19: Example of a packaged clinical drug - inferred view

8.3 Optional additional information

The following information may be additionally used to describe the Packaged Clinical Drug concept in a national extension. The attribute concepts and values to populate these if this data is to be held in a structured form, may be available in the international release in the future, particularly for those concepts such as package/container types that have international applicability and which can be sourced and maintained reliably.

- Package/container type (e.g. bottle, box, jar, tube) - see 10.6
- Administration device supplied in the package (e.g. medicine spoon, vaginal applicator, applicator brush for cutaneous liquid products)

8.4 Use cases supported by Packaged Clinical Drug

The following use cases are supported by the Packaged Clinical Drug concept class:

- Reimbursement: national or local systems may set pricing or eligibility against an abstract representation of real packaged products (e.g. for interchangeability and substitution)
- As a linking class from the international core to the Packaged Product class for any national extension that did not require a Real Clinical Drug class (i.e. if all products are authorised in their packaged form)
- To support description of combination packaged products, if the quantity of each component in the combination packaged product is required

8.5 IDMP Compatibility

There is no representation of a class similar to the Packaged Clinical Drug concept class; the primary use case for this class beyond support for generic representation of combination products is reimbursement, which is out of scope of IDMP. Combination products in their entirety are only represented in IDMP in their authorised form; there is no PhP type representation for them.

9. Real Packaged Clinical Drug (RPCD)

Definition: A representation of a medicinal product as it is supplied in a package by a by a single organisation (manufacturer or supplier) in a single jurisdiction under a single name (which may be a trade or brand name) for placement into the supply chain. It is a subtype of and real world equivalent to the Packaged Clinical Drug (PCD) class described above.

Since this class represents real products as authorised in a jurisdiction, description of additional information, such as excipient substances (flavours, preservatives, sweeteners etc.) or details about the product name parts or product authorisation information can be attached to Real Packaged Clinical Drug concepts, should a national extension wish to do this. For further details, see section 7.3 above.

As described above in the PCD section, this national extension model does not represent intermediate layers of packaging; it represents only the outer package used in the supply chain.

National extensions that require the Real Packaged Clinical Drug class should define their RPCD concepts using Clinical Drug concepts from the international release or national extension as available.

Existing national terminology equivalents:

- Actual Medicinal Product Pack (AMPP) in NHS dm+d and Belgian SAM
- Trade Product Pack (TPP) in in AMT/NZ ULM

- Semantic Branded Drug Pack (BPCK) in RxNorm
- the "Product" class in the Dutch Z-Index

9.1 Attributes of Real Packaged Clinical Drug

The following is described for Real Packaged Clinical Drugs that contain one Clinical Drug only, that is they are NOT combination (multi-component or kit) products. See Section 11 below for Combination Products.

The Real Packaged Clinical Drug class is related to the Real Clinical Drug class by a composition relationship relationship, and therefore the attribute "contains real clinical drug" is used to make the association between the Real Packaged Clinical Drug and the Real Clinical Drugs it contains.

Representation of packaged medicinal products should use presentation strength whenever possible. The exception will be for continuous products such as semi-solid dose forms of creams, gels etc. where strength pattern 3a is used (see international Editorial Guidelines). In all cases the pack size and pack size unit should relate to the denominator unit of the strength.

Semantic tag	(real packaged clinical drug)
Definition status	900000000000073002|Sufficiently defined concept definition status (core metadata concept) Note: This can only be the case if extensions author concepts to represent product names and manufacturer/supplier organisations
Attribute: **Has product name**	• Range: Extensions must author product name concepts within their extension using the root of 774167006| Product name (product name)| from the Qualifier hierarchy Cardinality: 1..1 The attribute value should represent the (authorised) product name; this may (or may not) be a trademarked name, and is often referred to as the "brand name" (see section 10.1 below)
Attribute: **Has supplier**	• Range: Extensions must author concepts to value supplier organisation information within their extension using the root of 774164004| Supplier (supplier)| from the Qualifier hierarchy • Cardinality: 1..1 The attribute value should represent the holder of the marketing authorisation or authorisation for supply; this may or may not be the organisation responsible for the actual manufacture of the product (see section 10.2 below)
Attribute: **Contains clinical drug**	• 763158003 |Medicinal product (product)| - descendants only (see Note 1 above in the PCD section) • Cardinality: 1..1 The attribute value should represent the clinical drug that is contained in the packaged product - either a CD or an RCD
Attribute: **Count of clinical drug type**	• Range: 260299005|Number (qualifier value) - descendants only • Cardinality: 1..1 This attribute value should represent the count of distinct Clinical Drugs present in the pack
Attribute: **Has pack size**	• Range: 260299005|Number (qualifier value) - descendants only • Cardinality: 1..1 (per relationship group) The attribute value should represent the amount or quantity of clinical drug present in the package (see section 10.3 below)
Attribute: **Has pack size unit**	• Range: 767524001 | Unit of measure (qualifier value) - descendants only (see Note 2 above in the PCD section) • Cardinality: 1..1 (per relationship group) The attribute value should represent the units for the amount or quantity of clinical drug present in the package (see 10.3 below)

9.2 Examples

Stated template view:

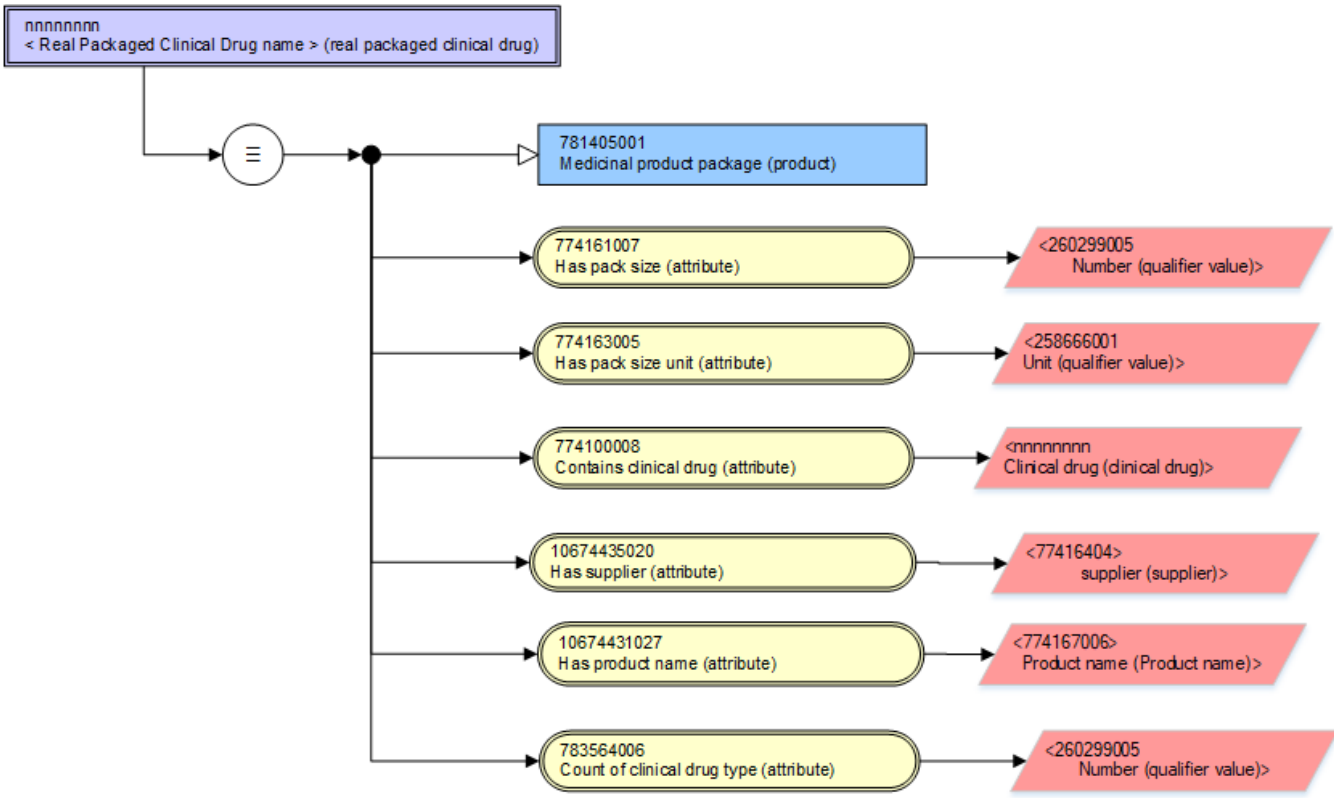


Figure 20: Template for a real packaged clinical drug

Example (stated view):

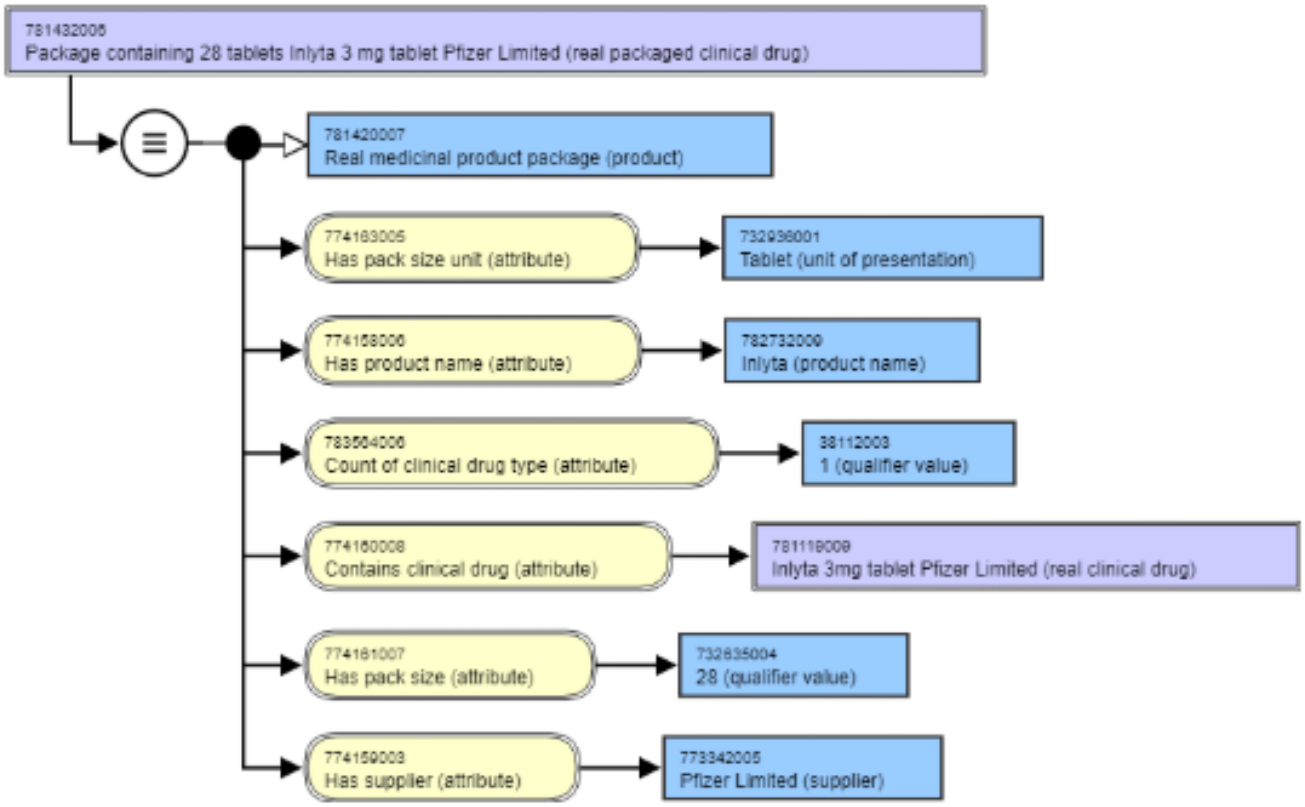


Figure 21: Example of a real packaged clinical drug - stated view

Example (inferred view):

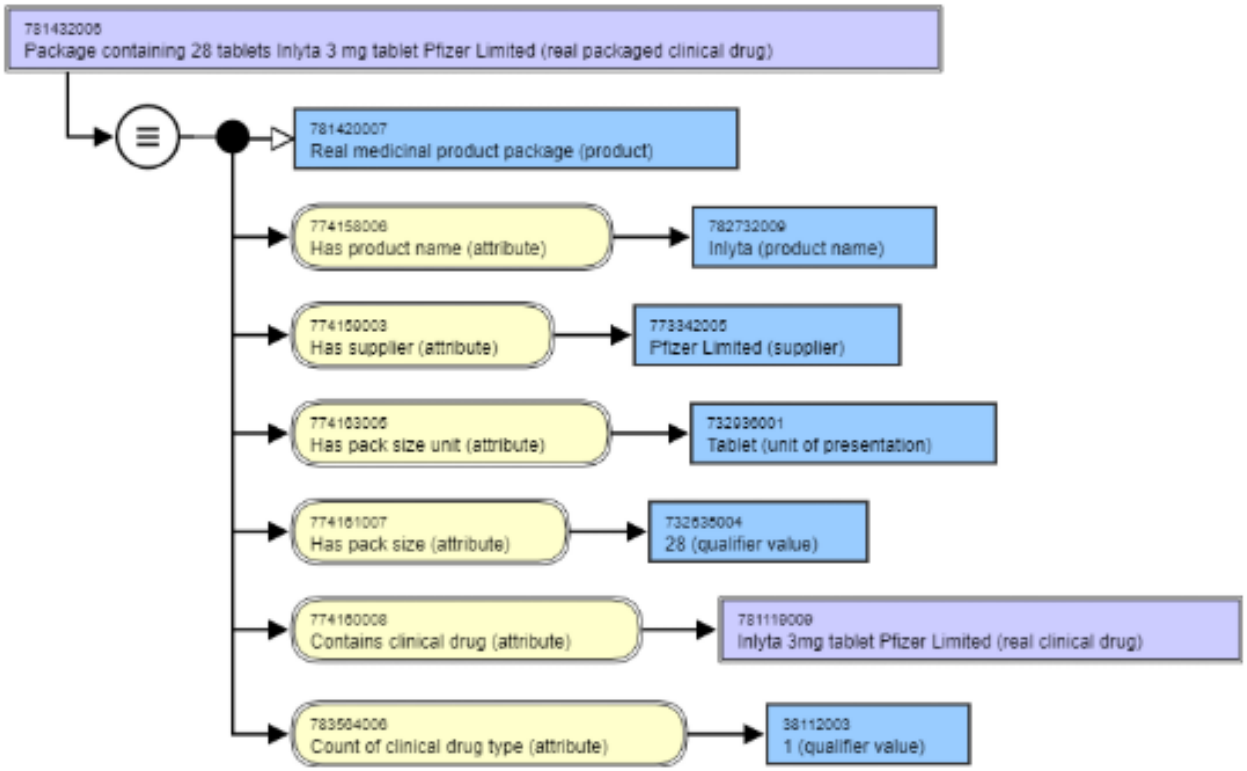


Figure 22: Example of a real packaged clinical drug - inferred view

9.3 Optional additional information

The following information may be additionally used to describe the Real Packaged Clinical Drug concept in a national extension. With the exception of container information, the attribute concepts and values to populate these, if this data is to be held in a structured form, would need to be authored into the extension using reference sets.

- Package/container type (e.g. bottle, box, jar, tube) (see 10.6 below); some use cases may also require information about sterile wrapping of some medicinal product packaging
- License information - for those jurisdictions that license at a package level rather than at the Real Clinical Drug level
    - License holding organisation
    - License identification ("authorisation number")
    - Licensing class and/or legal status of supply
- Usage information (prescribability within a particular jurisdictional context) including legal status and licensed indications
- Reimbursement information
- Administration device supplied in the package (e.g. medicine spoon, vaginal applicator, applicator brush for cutaneous liquid products)

9.4 Use cases supported by Real Packaged Clinical Drug

The following use cases are supported by the Real Packaged Clinical Drug concept class:

- The 1:1 "join" between the regulatory representation of medicinal products and the clinical representation of them (see below in IDMP Compatibility)
- The 1:1 "join" between the clinical representation of medicinal products and their representation in the supply chain and particularly for support of AIDC – automatic data capture identification. See also Section 12 - Cross maps
- Describing medication process activities: prescribing, dispensing, administration and medication statements; of these, dispensing and administration will use this concept when it is available to clearly state which actual packaged product (or content from it) was used/supplied to the patient (with batch/lot and expiry information if required, either manually or by AIDC)
- Compliance monitoring, using pack size information
- Anti-counterfeiting: in support of initiatives such as the Falsified Medicines Directive (see amended Directive 2001/83/EC) which will use AIDC and which will require scanning of medicines at the point of supply (to the patient)
- Reimbursement: national or local systems may set pricing or eligibility against actual packaged products

- Pharmacovigilance – especially for product defects and labelling issues

9.5 IDMP Compatibility

This concept as defined is equivalent to the Packaged Medicinal Product of ISO 11615, which in that standard is identified by a PCID. As the representation of the "real world product" authorised for sale and/or supply that exists for all jurisdictions and which is marketed into the supply chain for use, it is the concept that should form the 1:1 join between representation in the regulatory domain (IDMP) and representation in the clinical domain (SNOMED CT and national medicinal product terminologies), even if some national medicinal product terminologies choose not to represent it, but only an abstraction of it (i.e. the Real Clinical Drug class of concepts).

10. Supporting Attributes

10.1 Has product name

Definition: The (authorised) product name for the medicinal product as designated by the license holder (supplier); this may (or may not) be a trademarked name, and is often referred to as the "brand name".

It is not essential that the product name be an invented or brand name - it can be a generic name if extensions choose to follow the pattern shown in Figure 4 above. The product name concepts are authored to value the definitional attribute for the real products in the national extension as required by the use cases for that extension. This means that for those extensions that wish to author a hierarchy of product name concepts, they can choose to value the has product name attribute differently for the different levels in the model.

For example:

Figure 23: Diagram of examples of a product name hierarchy

In a product name hierarchy, the parent product name concept should be authored to reflect the unique set of active ingredient substances for the Real Medicinal Product (see the brand family example in Figure 6 above) and associated Real Clinical Drug and Real Packaged Clinical Drug concepts. It should therefore not include any reference to dose form (e.g. "LA" or "Retard") or to strength (e.g. "Double Strength" of "for Children") or any other information such as indication (e.g. "Shingles Treatment"). Child product name concepts can be authored to include additional information as provided in the authorised name for Real Clinical Drugs and/or Real Packaged Clinical Drugs.

Product name concepts must be authored in each national extension since the same product name can represent products containing different active ingredients in different jurisdictions, and therefore the product name has a different meaning in different jurisdictions.

The "has product name" attribute is available from the Concept model attribute hierarchy; values for the "has product name" attribute should be authored in the national extension, using the root of 774167006 | Product name (product name) | from the Qualifier hierarchy.

10.2 Has supplier

Definition: the (name of the) organisation that holds the authorisation for marketing or supply of the medicinal product.

Medicinal products, like other complex products, are rarely "manufactured" by one single organisation; the substances in a product, including active ingredient substance may be sourced from a range of specialist manufacturers and then assembled into the manufactured dose form by another organisation. The assembling organisation may be a contract manufacturer holding a manufacturing license and working for a variety of clients. In ISO 11615:2017 the "manufacturer" of a medicinal product is defined as the "organisation that holds the authorisation for the manufacturing process", and it notes that "establishment is a synonym of manufacturer"; establishment is a term that is often used in the USA. In national terminologies for clinical use however, the term "manufacturer" usually refers to the organisation whose name and details are associated with the public facing information about the product. This is the organisation responsible for providing the clinical information to support the product use (both for patients and healthcare professionals) and is also responsible for the quality and safety of the product, including for managing all adverse event information relating or possibly relating to the product in use. Some healthcare cultures allow agreements whereby an organisation may obtain supplies of a medicinal product and then to re-package or re-label that medicinal product and place it into the supply chain, either within a single jurisdiction, or across a group of jurisdictions. In this case, the organisation is acting as a supplier, and their name and details are likely to be present on the packaging, either exclusively or in addition to the primary organisation. In these cases, the responsibility for the product information and the product quality and safety is shared in various ways depending on the agreement and jurisdictional regulations.

Nations/affiliates will need to decide the principles under which they will populate the manufacturer/supplier attribute, based on their own regulations and context of practice. The simplest rule is to use the company who holds the authorisation to market the medicinal product, but, as described above, there can be complexities.

Issues to consider are:

- whether re-packaging or re-labelling is allowed by regulation and whether this is internal to the jurisdiction (as in the USA) or external to the jurisdiction (sometimes known as "parallel importing" or sale of "grey products") or whether both are allowed, and how the authorisations for these are managed and therefore which organisation (the licensed re-packager or the marketing authorisation holder) to designate as the manufacturer/supplier
- the role of the manufacturer/supplier information and the use case(s) to be supported, which may include
    - contact for queries from clinicians and/patients
    - pharmacovigilance and product safety
- whether the national medicines terminology will include medicines not authorised in their jurisdiction, and if so, how they wish to provide manufacturer/supplier information for these
    - for medicinal products licensed outside the jurisdiction, reference to the manufacturer is still likely to be appropriate
    - for compounded specials, to reference a generic "specials manufacturer" concept is possible since most of these will hold an authorisation to undertake specials manufacture

Manufacturer/supplier organisations, by virtue of being corporate bodies and legal entities, are unique to a given nation and must have their representation authored within the national extension.

Due to the nature of the domain where either individual products or whole product sets, with their brand name and authorisation, can be sold from one organisation to another it may be that even within one jurisdiction a single product name will be associated with more than one supplier. In situations where individual Real Clinical Drugs (or Real Packaged Clinical Drugs, for those products authorised at that level) that share the same product name , but have different supplier organisations, two Real Medicinal Products will exist, as shown in the example below:

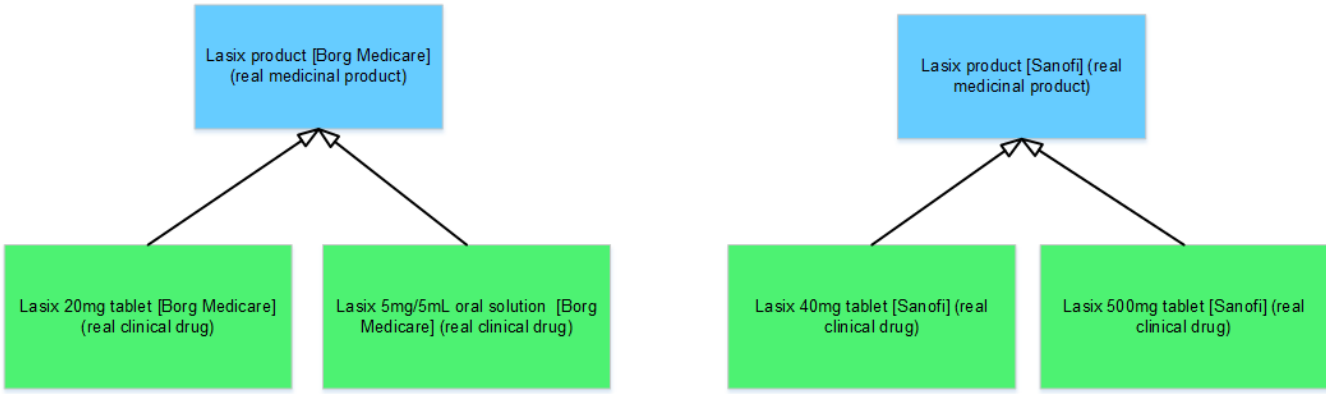


Figure 24: Diagram to show RCDs sharing a single product name associated with different RMPs due to having different suppliers

The has supplier attribute will be available from the Concept model attribute hierarchy; values for the Has Supplier attribute will be authored in the national extension, using the root of 77416004 | Supplier (supplier)| from the Qualifier hierarchy.

10.3 Contains clinical drug

Definition: The Clinical Drug contained in the packaged product.

The contains 'clinical drug attribute' can be valued with either a Clinical Drug from the international release or from the national extension (for example, if a liquid presentation has presentation strength Clinical Drugs in the national extension) .

For Combination (Packaged Medicinal) Products, there will be one Clinical Drug for each of the components in the packaged product that is placed into the supply chain. When a non-therapeutically active component such as a diluent is provided in a packaged medicinal product placed into the supply chain, extensions may choose whether to describe the diluent as a separate Clinical Drug or whether to manage the inclusion of the diluent in the product name only (see below in section 11).

10.4 Has pack size and has pack size unit

Definition: The amount or quantity of clinical drug present in the package. For clinical drugs described with a unit of presentation, the pack size reflects the number of units of presentation present in the package, and the pack size unit relates to the unit of presentation; for clinical drugs with a continuous presentation, this is the amount of the clinical drug present in the package with pack size units of either weight or volume.

The following table describes some patterns and gives examples:

Product type	CD strength type	Unit of presentation	Pack size	Pack size unit
Discrete dose forms: tablets, capsules, pessaries, suppositories etc.	presentation strength	basic dose form	number of units of presentation present in package	same as unit of presentation
Bendroflumethiazide 5mg conventional release oral tablet 28 pack		*tablet*	*28*	*tablet(s)*
Discrete dose forms: sachets, ampoules, vials containing powders, granules etc	presentation strength	"intimate container"	number of units of presentation present in package	same as unit of presentation
Cefotaxime 2g (per vial) powder for solution for injection 10 vial pack		*vial*	*10*	*vial(s)*
Metered dose forms: pressurised inhalers, cutaneous sprays, nasal sprays etc. with a metered dose valve	presentation strength	actuation	number of units of presentation present in package	same as unit of presentation
Beclometasone dipropionate 100 mcg per actuation pressurised inhalation 200 actuation inhaler		*actuation*	*200*	*actuation(s)*
Liquid dose forms: parenteral liquids, unit dose nebuliser solutions etc. in an "intimate container"	presentation strength (with concentration strength)	"intimate container"	number of units of presentation present in package	same as unit of presentation
Metoclopramine hydrochloride 100 mg per 20 mL solution for injection ampoule 5 ampoule pack		*ampoule*	*5*	*ampoule(s)*
Liquid products described using concentration strength but which have a unit of presentation	concentration strength	"intimate container"	number of units of presentation present in package	same as unit of presentation
Insulin human soluble 100 unit per mL solution for injection 5 cartridges		*cartridge*	*5*	*cartridge(s)*
Continuous preparation No unit of presentatation exists	concentration strength	NA	Quantity of product in package	unit of measure for quantity (volume or weight)
Hydrocortisone 10mg/1g cutaneous cream 30g tube		*NA*	*30*	*grammes*

Note for those liquid products described using concentration strength, the size of the intimate container is not described (a 1.5mL cartridge or a 3 mL cartridge). For liquid products presented in an intimate container described using a concentration strength, the volume of clinical drug present in the intimate container may need to be described separately. This could be achieved using "unit of presentation volume" and "unit of presentation volume units" attributes and values if this were required.

10.5 Count of Clinical Drug Type

Packs of medicinal products must be represented using the closed world view; they contain ***only*** the clinical drug type(s) content stated. In order to ensure that pack concepts classify correctly, so that packs that contain more than one (type of) clinical drug (i.e. combination packs) do not classify as children of packs that contain only one type of clinical drug, a "count of clinical drug type" attribute is used.

Standard packs containing a single clinical drug type have a count of "one" for the "count of clinical drug type attribute".

Combination packs have the appropriate count (always greater than one) for the number of clinical drug types present in the combination pack. If one of the components of a combination pack is a therapeutically inactive diluent, national extensions can choose whether to include this in the "count of clinical drug" and therefore whether the pack containing the diluent will classify as a sibling or as a child of any pack not containing a diluent. See also section 11 below.

10.6 (Outer) Container

Description of the container that forms the outer package (the box, bottle, tube or jar) is not considered to be a definitional attribute for the Packaged Clinical Drug or Real Packaged Clinical Drug classes; no use cases have been presented to date to require this as a definitional attribute. However, national extensions may have a use for the information, possibly even with dimensions, to support robotic dispensing and supply chain use cases, using reference sets and/or additional axiom functionality.

Currently there are no plans to maintain container concepts that could be used to value a "has outer container" attribute in the international release, but such concepts may exist in the future. EDQM (the European Directorate for the Quality of Medicines and HealthCare) maintains a set of Packaging concepts, including both Container terms and Closure Terms.

11. Combination (Real) Packaged Medicinal Products

Definition: A representation of a medicinal product supplied in a package by a single organisation (manufacturer or supplier) in a single jurisdiction under a single name (which may be a trade or brand name) for placement into the supply chain that contains within the package more than one clinical drug (type).

A combination packaged product may also be called a "component product" or a "multi-component package" as the product itself is a package that contains more than one type of component element (clinical drug) within it; it may also be known as or a "kit". Occasionally a combination packaged product is may be known as a "compound product" but term risks being confused with products that are extemporaneously compounded by a pharmacist from a formula provided by the prescriber for an individual patient (sometimes also known as "magistral products").

Examples of combination packaged products include:

- a package containing clotrimazole cutaneous cream and one or more clotrimazole vaginal tablets for treatment of vaginal candidiasis
- a package containing combinations of ethinyl estradiol and levonorgestrel tablets in different strengths and which may also include inert tablets for oral contraception (note that in this example, the components are themselves multi-ingredient items)
- a package containing amoxicillin, clarithromycin and lansoprazole for treatment of Helicobacter infection
- a package containing a budesonide dispersible tablet and the vehicle to disperse it in, to make a rectal solution for treatment of colitis
- a package containing rasburicase 1.5 mg powder for solution for injection and the diluent solution

The model specification and its relationship pattern for national extensions recommended that combination products in their entirety should be represented only as packaged products (real packaged clinical drugs and, if required as packaged clinical drugs), with their individual components represented as clinical drugs. For practical implementation of a national terminology, mechanisms such as reference sets may be used to group combination packaged medicinal products with other classes of medicinal product (such as clinical drugs) to aid users in finding and selecting these products.

The following diagram gives an example of how the packaged medicinal product classes should be used to describe combination medicinal products:

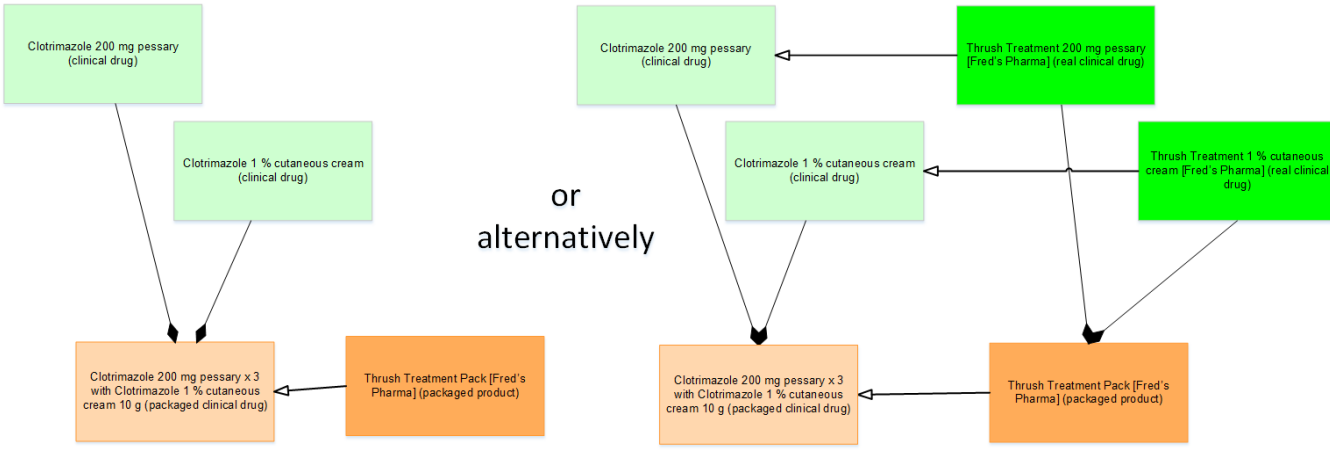


Figure 25: Diagram of options for a national extension describing combination real packaged clinical drugs

In some representations of combination medicinal products, and particularly in ISO 11615 in IDMP, a "combined dose form" concept is used in the name of the combination product (for example "pessary and cream"). Although useful as a concept to describe the dose form of a combination medicinal product using a single attribute and value, a combination dose form concept does not easily support knowing which component has which dose form. The model used here, whereby each clinical drug is described with its appropriate dose form and they are brought together into the packaged product containing the components, does not require the use of combination dose form concepts. If national extensions have a use case for describing combination medicinal products with a combined dose form, this could be supported in the same way as other optional descriptive information.

For those combination products that contain a diluent as an additional item in the package, national extensions may decide not to explicitly describe the diluent as a component, but merely to describe its presence in the text of the fully specified name for the real packaged medicinal product; alternatively the national extension may author a "diluent" Clinical Drug concept and use that as one of the components of the combination product. If the constitution of the diluent is known (e.g. water for injections, 0.9% sodium chloride solution for injection), the clinical drug for the diluent can be explicitly described. Dual chamber products containing the two components (where one is the diluent) in a single unit of presentation can be described as combination products if required.

11.1 Attributes of Combination (Real) Packaged Medicinal Products

Attributes of Combination Packaged Medicinal Products

The Packaged Clinical Drug class is related to the Clinical Drug class by a composition relationship relationship, and therefore the attribute "contains clinical drug" is used to make the association between the Packaged Clinical Drug and the Clinical Drugs it contains.

Representation of packaged medicinal products should use Clinical Drugs that have presentation strength (either only or in addition to concentration strength) whenever possible in order to be able to accurately describe the number of presentation units present in the package. The exception will be for continuous products such as semi-solid dose forms of creams, gels etc. where strength pattern 3a is used (see international Editorial Guidelines). In all cases the pack size and pack size unit should relate to the denominator unit of the strength.

Semantic tag	(packaged clinical drug)
Definition status	900000000000073002|Sufficiently defined concept definition status (core metadata concept)
Relationship group	One relationship group containing one instance of each of the following attributes is required for each clinical drug that the packaged clinical drug is composed of.
Attribute: **Contains clinical drug**	• Range: 763158003 |Medicinal product (product)| - descendants only (see Note 1 below) • Cardinality: 1..1 The attribute value should represent the clinical drug that is contained in the packaged product
Attribute: **Count of clinical drug type**	• Range: 260299005|Number (qualifier value) - descendants only • Cardinality: 1..1 This attribute value should represent the count of distinct Clinical Drugs present in the pack
Attribute: **Has pack size**	• Range: 260299005|Number (qualifier value) - descendants only • Cardinality: 1..1 (per relationship group) The attribute value should represent the amount or quantity of clinical drug present in the package (see 10.3 below)
Attribute: **Has pack size unit**	• Range: 258666001|Unit (qualifier value) - descendants only • Cardinality: 1..1 (per relationship group) The attribute value should represent the units for the amount or quantity of clinical drug present in the package (see 10.3 below)

Attributes of Combination Real Packaged Medicinal Products

Semantic tag	(packaged clinical drug)
Definition status	900000000000073002|Sufficiently defined concept definition status (core metadata concept)
Attribute: **Has product name**	• Range: Extensions must author product name concepts within their extension using the root of 774167006| Product name (product name)| from the Qualifier hierarchy Cardinality: 1..1 The attribute value should represent the (authorised) product name; this may (or may not) be a trademarked name, and is often referred to as the "brand name" (see section 10.1 below)
Attribute: **Has supplier**	• Range: Extensions must author concepts to value supplier organisation information within their extension using the root of 774164004| Supplier (supplier)| from the Qualifier hierarchy • Cardinality: 1..1 The attribute value should represent the holder of the marketing authorisation or authorisation for supply; this may or may not be the organisation responsible for the actual manufacture of the product (see section 10.2 below)
Relationship group	One relationship group containing one instance of each of the following attributes is required for each clinical drug that the packaged clinical drug is composed of.
Attribute: **Contains clinical drug**	• Range: 763158003 |Medicinal product (product)| - descendants only (see Note 1 below) • Cardinality: 1..1 The attribute value should represent the clinical drug that is contained in the packaged product

Attribute: **Count of clinical drug type**	• Range: 260299005|Number (qualifier value) - descendants only • Cardinality: 1..1 This attribute value should represent the count of distinct Clinical Drugs present in the pack
Attribute: **Has pack size**	• Range: 260299005|Number (qualifier value) - descendants only • Cardinality: 1..1 (per relationship group) The attribute value should represent the amount or quantity of clinical drug present in the package (see 10.3 below)
Attribute: **Has pack size unit**	• Range: 258666001|Unit (qualifier value) - descendants only • Cardinality: 1..1 (per relationship group) The attribute value should represent the units for the amount or quantity of clinical drug present in the package (see 10.3 below)

11.2 Examples

Example Combination Packaged Clinical Drug (stated view):

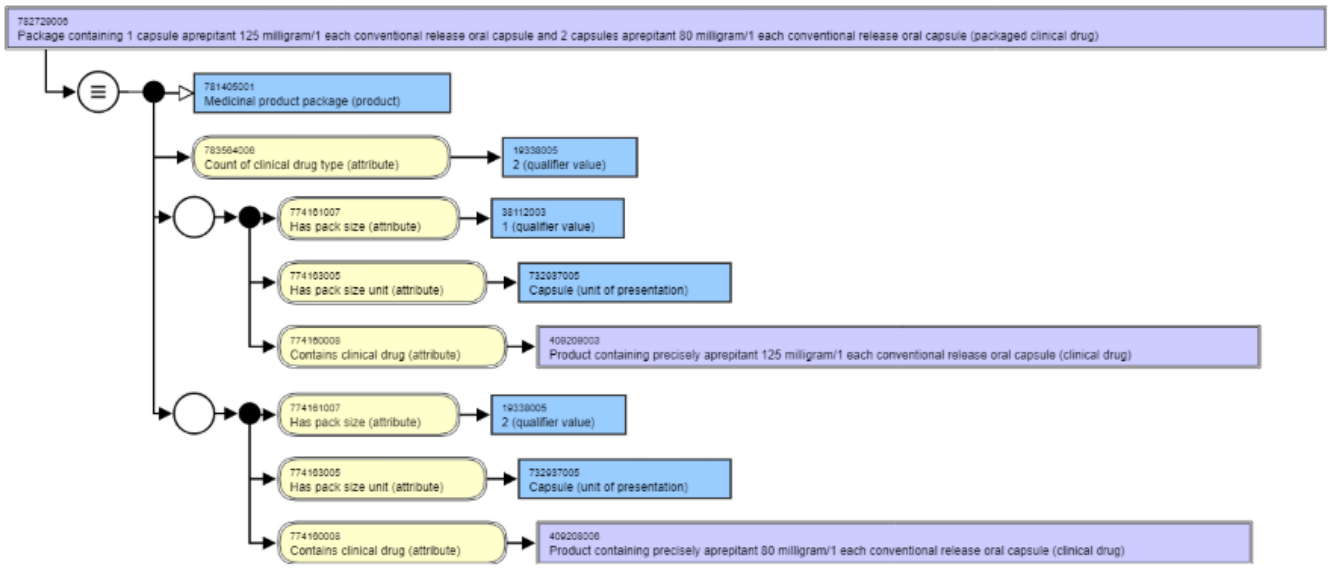


Figure 26: Example of a combination packaged clinical drug - stated view

Example Combination Packaged Clinical Drug (inferred view):

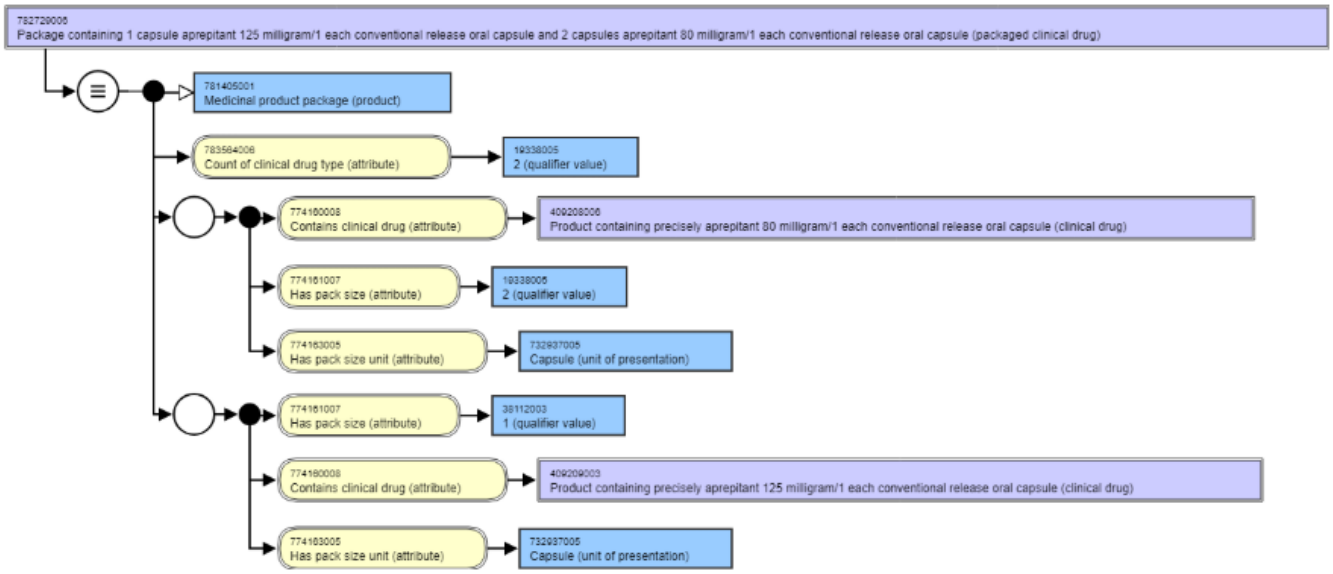


Figure 27: Example of a combination packaged clinical drug - inferred view

Example Combination Real Packaged Clinical Drug (stated view):

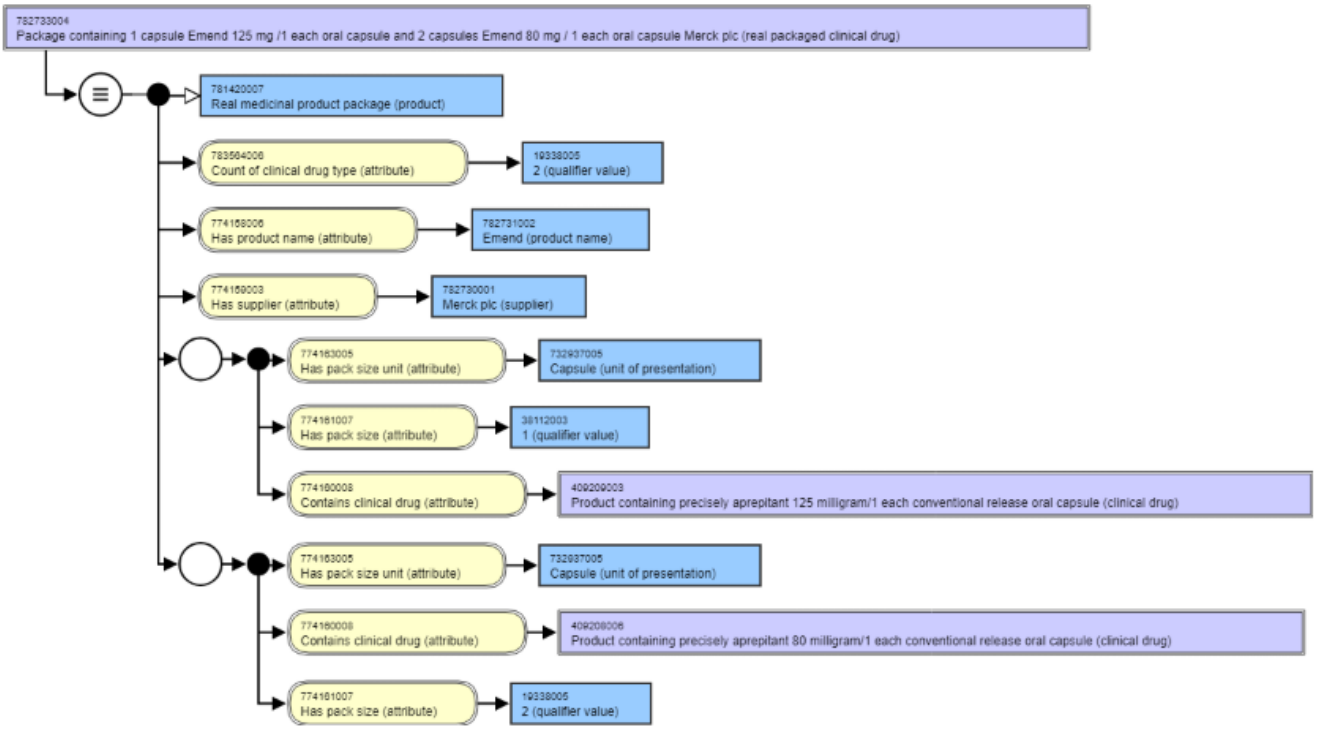


Figure 28: Example of a combination real packaged clinical drug - stated view

Example Combination Real Packaged Clinical Drug (inferred view):

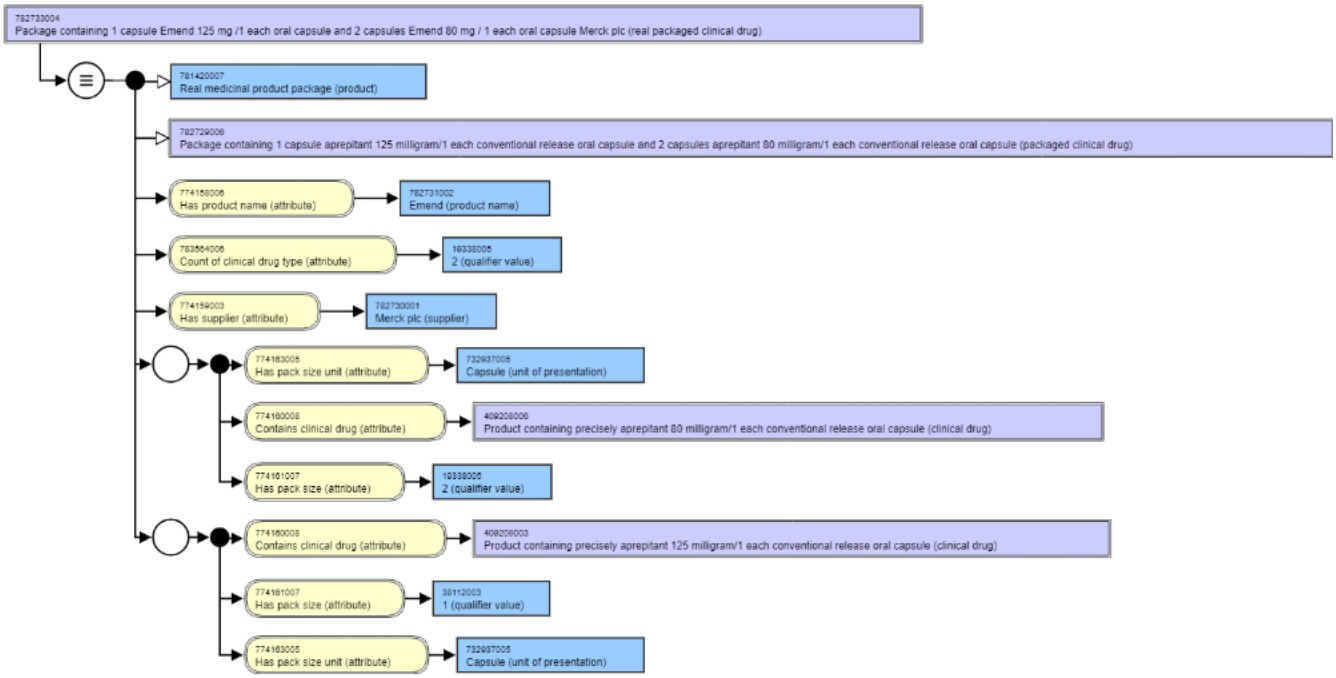


Figure 29: Example of a combination real packaged clinical drug - inferred view

11.3 Use cases for Combination (Real) Packaged Medicinal Products

As for the Real Packaged Medicinal Product, the following use cases are supported by the Combination Real Packaged Clinical Drug concept type:

- The 1:1 "join" between the regulatory representation of combination medicinal products and the clinical representation of them (see below in IDMP Compatibility)
- The 1:1 "join" between the clinical representation of combination medicinal products and their representation in the supply chain and particularly for support of AIDC – automatic data capture identification. See also Section 12 - Cross maps
- Describing medication process activities: prescribing, dispensing, administration and medication statements; of these, dispensing and administration will use this concept when it is available to clearly state which actual packaged product (or content from it) was used/supplied to the patient (with batch/lot and expiry information if required, either manually or by AIDC), although administration records may wish to identify which of the particular component clinical drugs were administered at any particular point in time administration event
- Compliance monitoring, using pack size information
- Anti-counterfeiting: in support of initiatives such as the Falsified Medicines Directive (see amended Directive 2001/83/EC) which will use AIDC and which will require scanning of medicines at the point of supply (to the patient)
- Reimbursement: national or local systems may set pricing or eligibility against actual packaged products; some jurisdictions have different reimbursement arrangements for Combination Real Packaged Clinical Drug products
- Pharmacovigilance – especially for product defects and labelling issues

11.4 IDMP Compatibility

Since the ISO 11615 standard treats all Packaged Medicinal Products in the same manner, whether they are standard products or combination products, because the associations between the manufactured item(s) present in the package are described using recursive relationships, the Combination Real Packaged Medicinal Product is equivalent to a Packaged Medicinal Product identified by a PCID. As with the Real Packaged Medicinal Product. the Combination Real Packaged Medicinal Product is a representation of the "real world product" authorised for sale and/or supply that exists for all jurisdictions and which is marketed into the supply chain for use, it is a concept that should form the 1:1 join between representation in the regulatory domain (IDMP) and representation in the clinical domain (SNOMED CT and national medicinal product terminologies), even if some national medicinal product terminologies choose not to represent it.

12. Cross Maps

12.1 ATC - WHO Anatomic Therapeutic Chemical Classification System

The WHO's ATC system is a five level classification of medicinal products whose primary purpose is to support pharmacoepidemiological study in order to improve the quality of medicines use. The ATC systems provides an international classification of medicinal products based on their active substance(s) and their main therapeutic use(s). See https://www.whocc.no/atc_ddd_methodology/purpose_of_the_atc_ddd_system/ for further information. National extension terminologies may wish to map their concepts to the ATC system using a cross map reference set. To support pharmacoepidemiological use cases, the mapping should be *from* concepts in the national terminology *to* the ATC classification. A mapping policy should support the generation of the cross map reference set. Maps may exist at MP, MPF, CD or PCD levels, depending on requirements. Note that for some ATC codes, mapping from MP concepts may not be possible as products with different intended sites of administration are classified separately in ATC (e.g. oral steroid products are classified in H02 whereas cutaneous steroid products are classified in D07).

12.2 GTIN (Global Trade Item Numbers)

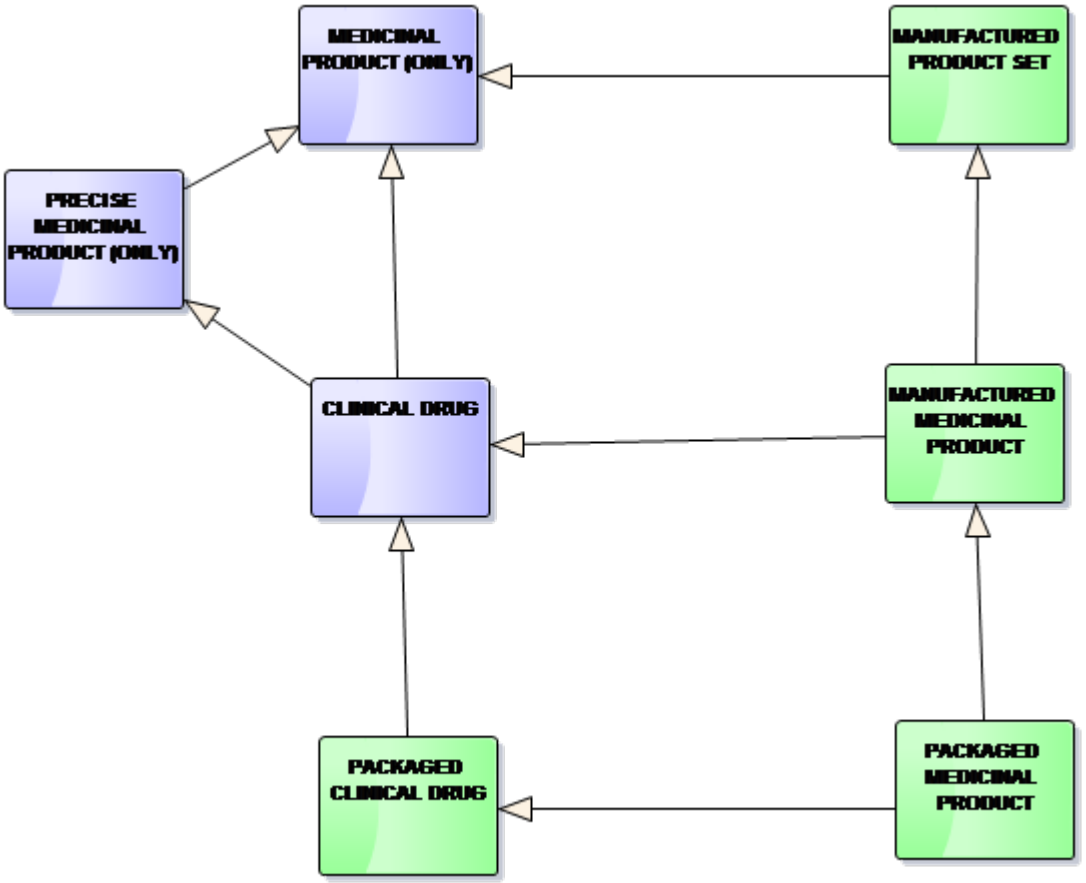
GS1's Global Trade Item Numbers (GTINs) are the codes used by an organisation to uniquely identify all of the items it places into the supply chain. Product GTINs can be implemented in AIDC systems (automatic identification and data capture systems) through the use of bar codes or radio frequency identification (RFID). Medicinal products will usually have GTINs assigned at the Real Packaged Clinical Drug level, although other levels of identification may be present and are described in ISO TS 16791:2014 Health informatics — Requirements for international machine-readable coding of medicinal product package identifiers. GTINs and AIDC systems for medicinal products may be used in a variety of healthcare applications involving medicinal products, including support for "right patient, right medicine" administration systems, robotic and unit dose dispensing systems and supply chain verification/anti-counterfeiting measures. National extension terminologies may wish to map their concepts to their national set of medicinal product GTINs; further information on mapping of GTINs to SNOMED CT, including principles and use cases, can be found at https://www.snomed.org/about/partnerships/gs1.

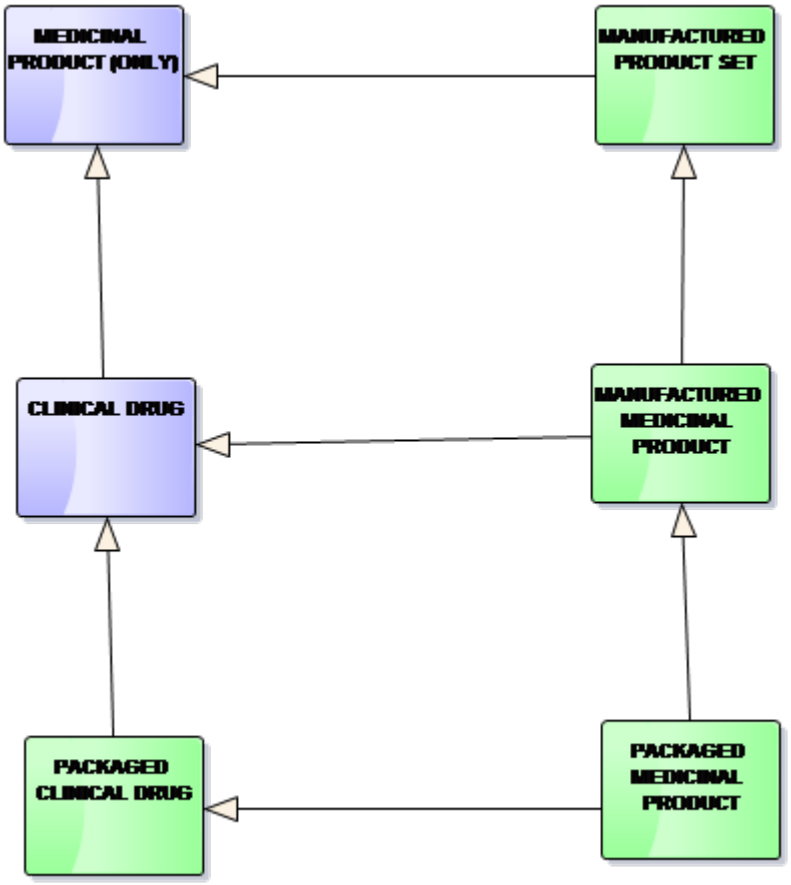
Supranational/Regional Extensions

The SNOMED CT structure supports the development of supranational extensions (for example to support a region with co-operative regulation of medications, such as the European Union). In the Medicinal Product hierarchy, this could support a region having a "shared module" that might include (for example) the Packaged Clinical Drug class, since this might contain information that is common to most or all of the jurisdictions in the region and therefore it is of value to hold this more centrally in a module between the international core and the national extension. Similarly, a regional module may hold a subset of the Clinical Drug and Medicinal Product concepts that are applicable within that region, to aid implementation within that region. However, it is essential that implementations understand that some of the value of the international core is to provide support for international use cases such as the International Patient Summary, and therefore providing access to information from the core about medicinal products beyond their own jurisdiction is important.

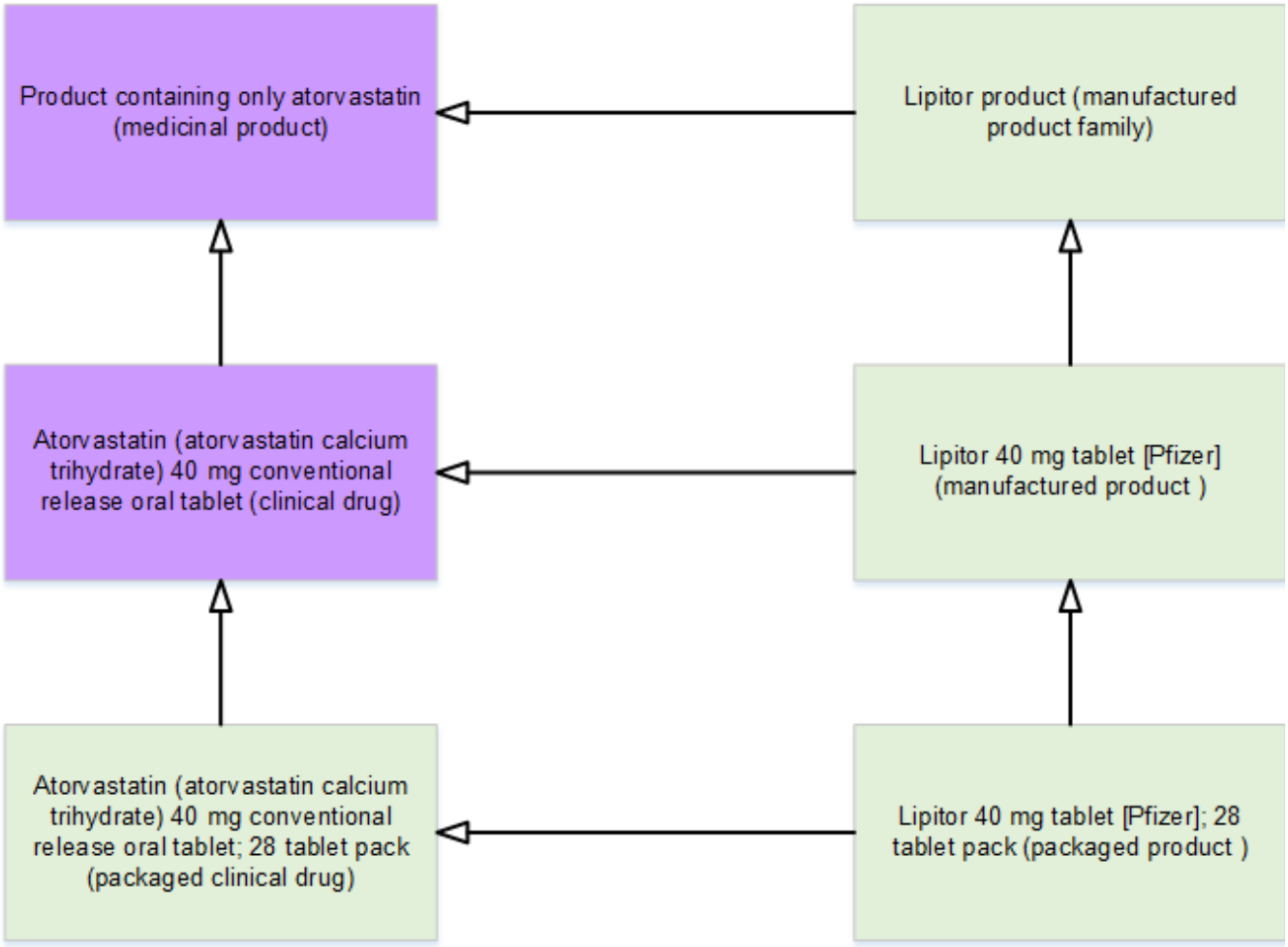
Appendix 1 - Alternative general modelling considered but not adopted

Option A: Standard generalisation/specialisation

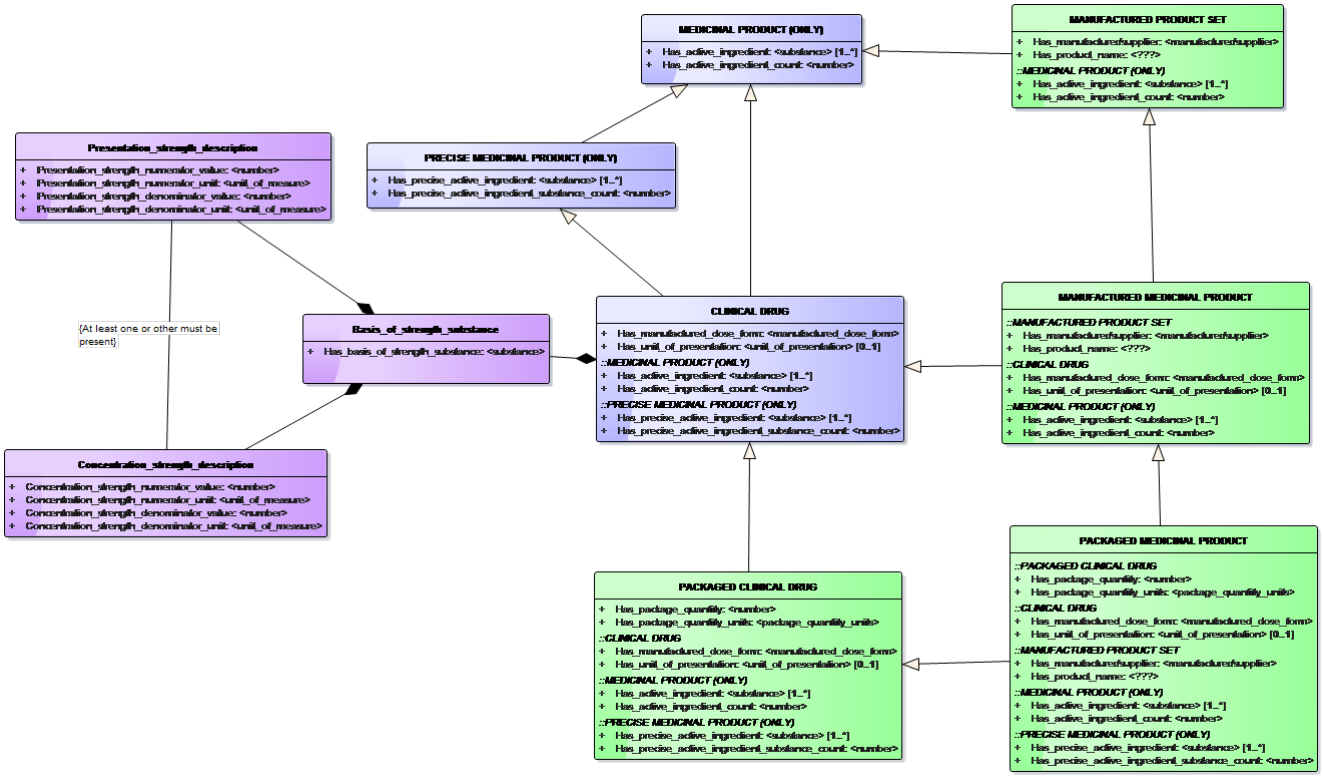




Two sub-options are shown, to accommodate the discussion of Medicinal Product (only) using precise ingredient substance as its basis. An example of this, with only the product name given is below:



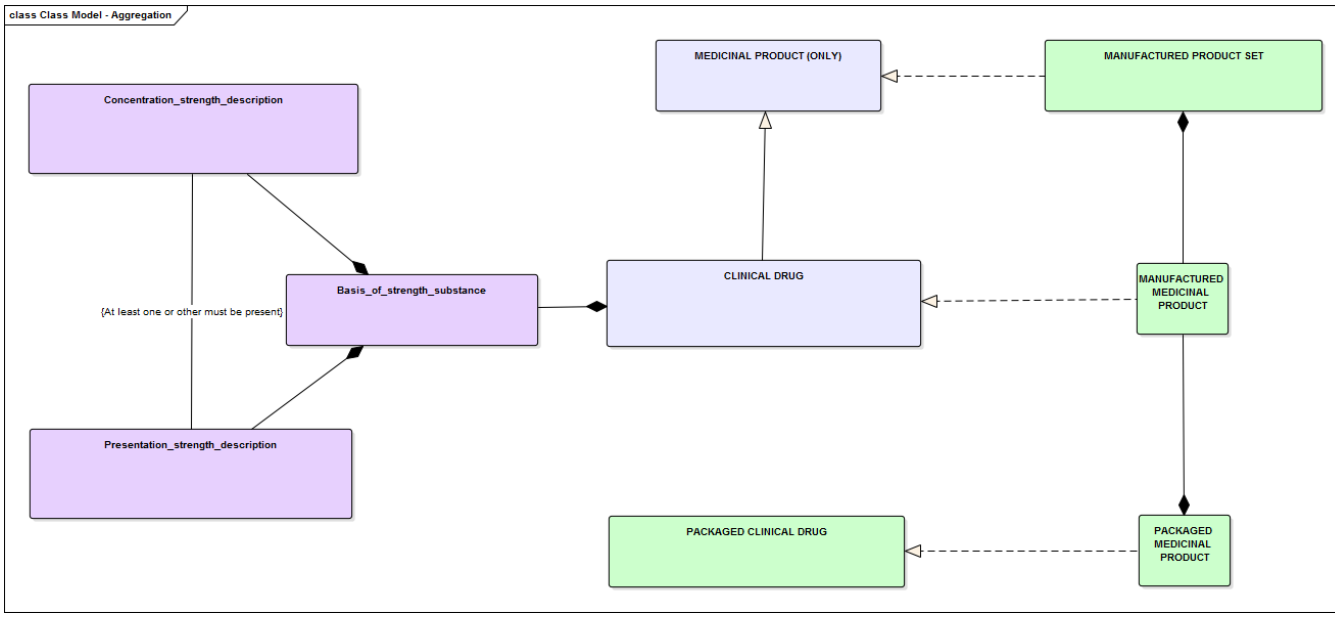
In this option, all the relationships used in the model are generalisations; this means that information (attributes and aggregations) from the parent will flow to the child concept as in normal inheritance. This is demonstrated in the diagram below for the attributes; UML diagramming does not clearly show the flow of aggregation information - in this case the Basis_of_strength_substance information which will flow to all child classes (Packaged Clinical Drug, Manufactured Medicinal Product and Packaged Medicinal Product).



Discussion

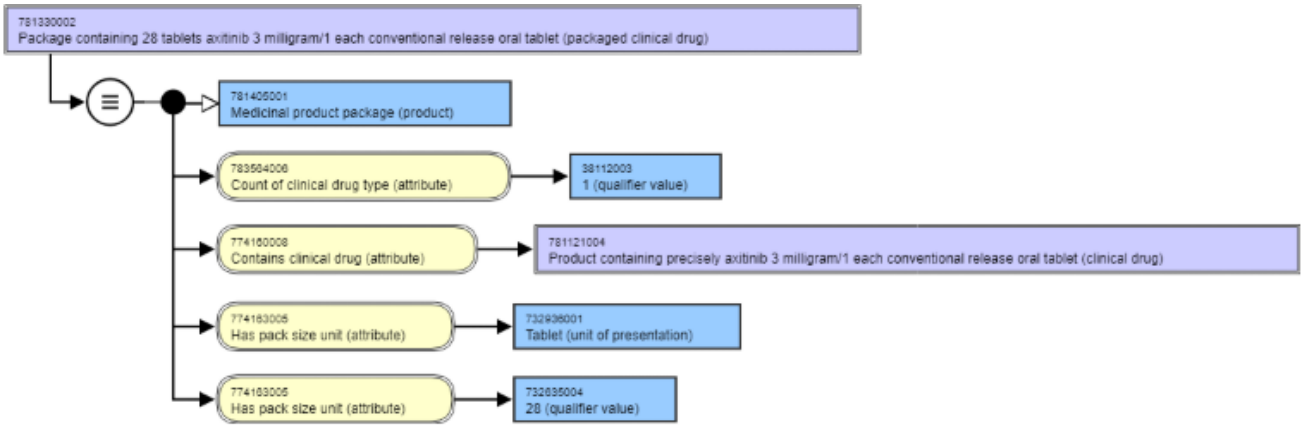
The advantage of using the generalisation/specialisation relationship for all relationships between classes in the extension is that it is the standard pattern for SNOMED CT and as such is (probably) the simplest to implement. It allows information to flow from the parent to the child, which can be of great benefit for decision support use cases.
The semantic says a Manufactured Medicinal Product represents what exists and the Clinical Drug is a universal (or generalised) representation of it. However the disadvantage is that a Packaged Medicinal Product is not truly a subtype of a Manufactured Medicinal Product; it is the thing that makes the Manufactured Medicinal Product available in the supply chain and as such the Packaged Medicinal Product is *composed* of Manufactured Medicinal Product; therefore the generalisation/specialisation relationship here is not strictly semantically correct. This pattern also does not give good support for Packaged Medicinal Products that contain multiple Clinical Drugs within it.

Option B: Alternative relational semantics



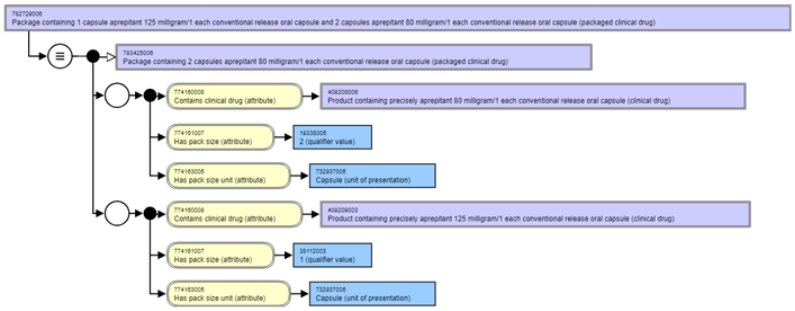
In this representation, the relationship between the classes that represent real world things available in the jurisdiction and their more generic, virtual or universal representation in the core is shown as a *realisation*, whereby the real world things are a realisation of the universal abstract representation. In UML, a realisation relationship is a cross between the standard generalisation relationship and a dependency relationship and is shown by the hybrid symbolism of both. The dependency relationship indicates that a change in the independent thing (effectively the parent) will have an effect on the dependent thing. Whilst realisation relationships are most often used in interfaces and collaborations, they can be useful in class models, as here. Because of its association with generalisation, a realisation relationship can allow information to flow in the same way that a generalisation does.

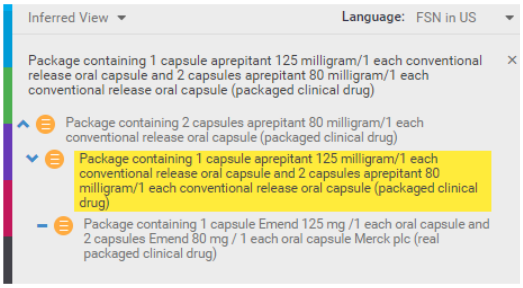
The relationship between the different classes that represent real world things is shown by a composition relationship; a Packaged Medicinal Product is composed of Manufactured Medicinal Products, and a Manufactured Product Set if composed of Manufactured Medicinal Products. The composition relationship is a specialised aggregation (partitive) relationship, introducing the time dependency (the associated classes live and die together); therefore a Manufactured Medicinal Product can only exist if there is a Packaged Medicinal Product to support it. A Manufactured Product Set is an abstract composition of Manufactured Medicinal Products and not all Manufactured Medicinal Products will become part of a Manufactured Product Set.



Appendix 2 Model Representations for Packaged Products

The open world view of the DL is giving us “incorrect subsumption” for combination pack concepts if modelled with just the component relationship on its own:





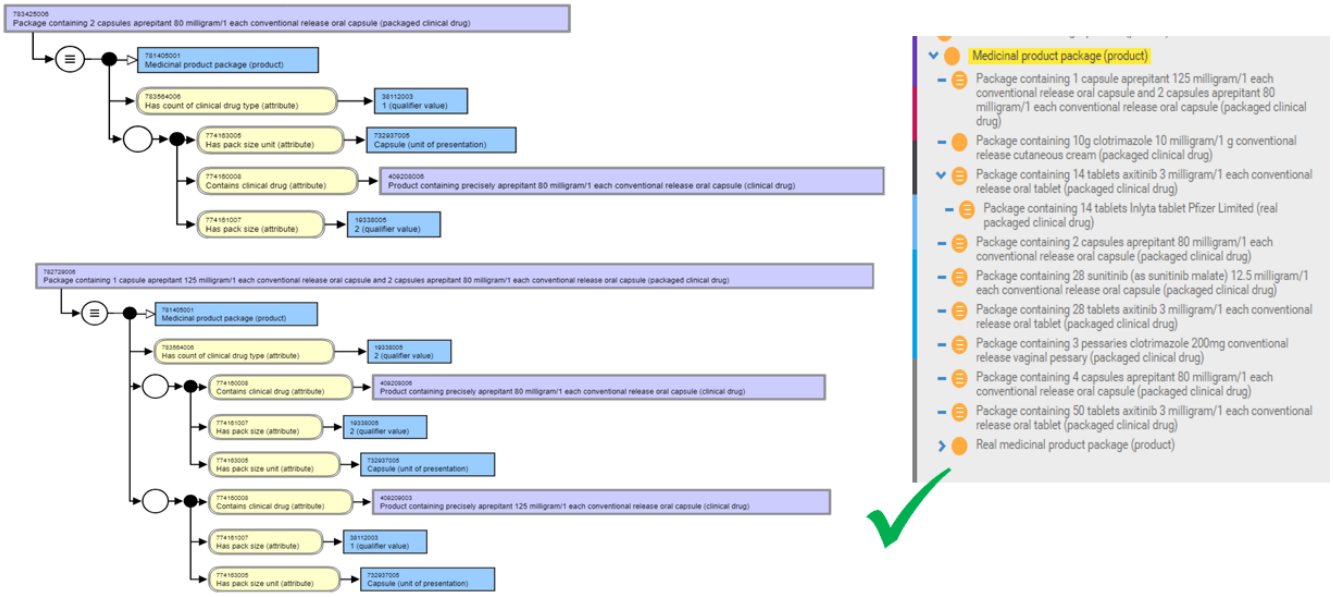
Main considerations:

- Describe packs accurately in a national extension
- Without incorrect subsumption
- To have “simple packs” and “combination packs” as sibling concepts
- To support national prescribing/dispensing/administration and medication statements and profiles
- Have to necessary set of concepts for mapping
    - to IDMP concepts (particularly PCIDs)
    - to national authorisation concepts (e.g. NDCs, Product Licences etc.)
    - to GS1 identifiers
    - to national/local reimbursement information

Options:

- Give combination packs a different proximal primitive parent? e.g. “combination pack” rather than medicinal product pack
    - Not ideal; a three component pack would subsume under a two component pack if two of the components were identical; this might seem to be a rare occurrence, but if nations described “product + diluent” as a combination pack, it might not be as rare as we think
- Have an attribute for all pack concepts that distinguishes between simple packs and combination packs?
    - Has pack type: simple pack; 2 component combination pack; 3 component combination pack
- Have a “count” concept (like for Clinical Drugs)?
    - Acts as a proxy for the closed world view

Modelling suggestion	Positives	Negatives
Different proximal primitive parent		Creates “split” hierarchy so does not give sibling pack concepts Would need one PPP for each “type” of combination pack
Pack type attribute for all packs (just attribute on combination packs will not work in the DL)	Simple (ish) especially if templated Gives sibling pack concepts	Would need one value for each “type” of combination pack
Count attribute	Will be machine processable when concrete domains are implemented Gives sibling pack concepts Can be extended to count of subpacks if a full subpack model were required If a more expressive DL becomes available to represent the closed world view, all the count attributes can be removed and replaced consistently	Like the CD count – so not totally intuitive - but less complex than the CD count



Attribute name:

“Count of clinical drug type”

- Is the count of distinct CDs present in the pack
- Could also be extended if a different count type is need for a full subpack model in the future
- The count is a definitional attribute and will always be present for all packs

Sub-packs

- Sub-packs are primarily used for supply chain management and reimbursement (in some nations)
- Many terminologies do not have sub-packs
- IDMP has a full sub-pack model, but the classes are not “identified” so concepts are not be available for mapping etc.
- Because of the complexity issues, describing sub-packs in a concept model will not be undertaken until there are requests with confirmed use cases

Subpacks