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SNOMED CT Drug Model for National Extensions

version 1.0

Publication date: 2024-05-03

Web version link: http://snomed.org/ndem

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The SNOMED CT Drug Model for National Extensions describes the classes of concepts required to extend the international SNOMED CT Medicinal Product Specification, to represent a national drug dictionary in a standardized way. This drug extension concept model describes the real or actual medicinal products (sometimes referred to as 'branded products') available for use in a particular country/territory, and how they can be defined using consistent attributes. The purpose of providing a shared concept model for these drug extensions, is to enable comparison and interoperability between drug concepts in different drug dictionaries, thus enabling use cases such as the sharing of medication lists, contraindication checking, and cross-border pharmacovigillence.

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1. Introduction

Rationale for the National Drug Extension Model

The international content of SNOMED CT is, by definition, globally applicable. For example, most clinicians will agree on what constitutes a diagnosis of atrial fibrillation and how this concept should be logically defined. Therefore, wherever in the world a patient suffers from atrial fibrillation, there is a common understanding of what that is, and the SNOMED CT concept for atrial fibrillation can represent and reflect that.

But medicinal products are different. Concepts in a Medicinal Product terminology can be divided into two types:

1. 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 (whenever possible) using their international non-proprietary names (INNs) 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 (represented as a concrete value) and units (represented as a SNOMED CT concept)
    - Pharmacopoeial / internationally defined dose forms
    - Pharmacopoeial / internationally defined units of presentation (when appropriate)
2. 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

International SNOMED CT releases contain concepts of the first type, i.e., 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 requires both the first *and* the second type of representation for medicinal products to enable each country to express *their* medicinal products with *their* names, *their* definitions, and if required, additional defining attributes that fit with *their* regulation and *their* healthcare culture and practice. This national drug extension model is provided to support the authoring of drug concepts of this second type, and to enable the sharing of tools (e.g., drug authoring tools), rules (e.g., international decision support rules), and drug extension content (e.g., to support the interoperability of a patient's medication information, for cross-border dispensing with contraindication checking).

Use Cases for the National Drug Extension Model

National drug extensions have to support a variety of use cases; these can include any or all of:

- Prescribing medicines - such that medicinal products are described in *sufficient* detail that the next action in the process (either dispensing or administration) can identify the correct product to dispense/administer
- Dispensing
    - Reimbursement information
    - Supply chain management (including ordering of medicines for dispensing)
    - "Track and trace" including fraudulent medicines avoidance
- Administration
    - Closed loop medication systems
- Medication history/patient medication lists
- Linking to decision support
- Pharmacovigilance
- Secondary uses (clinical research, pharmacoepidiemiology)
- Supporting electronic data exchange for any or all of the above use cases (for both human users and for system users)

Purpose

This document specifies a drug extension concept model that can be used to represent the real or actual medicinal products (sometimes referred to as *branded products*) available for use in a particular country/territory. This model is compatible with the international core model for Medicinal Products. This compatibility means that, when classified using the appropriate tooling, the extension concepts will be correctly placed alongside other concepts in the international Medicinal Product hierarchy. This document should therefore be read together with the Medicinal Product Model Specification, which describes the classes of concepts present in the SNOMED CT international edition.

This document is a model specification, and as such, it does not describe the detailed rules and processes required to populate a national terminology. Some general principles are given, and terming suggestions are provided. However, national extensions must be mindful of their own terming requirements when authoring synonym terms to support direct implementation. In situations where additional concepts for core classes of the international model are required in the national extension (e.g. MP, MPF, and CD), the naming guidelines for the international release should be followed (particularly for the FSN).

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

Scope

The scope of this concept model (as defined) is limited to medicinal products (pharmaceutical and biological). Blood products, foods, additives, and complementary medicines (including homeopathic products) are out of scope. Vaccines are also out of scope (even though they are biological medicinal products).

National extensions will need to make decisions about the scope of their own medicinal product terminology and may require the representation of products that are beyond the international scope. In these cases, it may be necessary to author Clinical Drug concepts (and their associated MP and MPFs) within the extension (e.g., 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 include:

- 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. 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, held a valid authorisation within the extension's jurisdiction, but which no longer do. Some of these previously licensed products may continue to be available (e.g., via import)

- Medicinal products holding a valid authorisation in a **different** jurisdiction, which are (regularly) used within the extension's jurisdiction by practitioners at their own clinical discretion
- 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 are required. This may be challenging for unlicensed medicines and even for some "over the counter" medicines.

It can be helpful when considering the boundary for inclusion of products in the national extension (if the national prescribing use case is in scope), 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. The scope must also 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. 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). The implications of this, in terms of use cases for active supply of medicines, must also be considered.

This specification does not propose a model for the types of additional knowledge that may be a useful part of a national medicinal product catalogue, such as product availability or pricing. That is a matter for each jurisdiction.

Audience

This document is written primarily for those responsible for the development and maintenance of a Medicinal Product terminology (national, regional or organisational) that is managed within a SNOMED CT extension. However, it will also be of value to those who have an existing Medicinal Product terminology (national, regional or organisational) which may or may not be managed in a SNOMED CT extension, who wish to develop a mapping from concepts in their own Medicinal Product terminology to a standardized SNOMED CT representation to harness the interoperability benefits of using a common concept model defined in a clinical reference terminology.

1.1 Glossary

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

Term/Abbreviation	Definition
Active ingredient substance	The substance that provides the intended therapeutic effect of the medicinal product, described usually but not always without modifiers such as esters, salts or other non-covalent derivatives
Administrable dose form	The (pharmaceutical) dose form of a medicinal product for administration to a patient, after any necessary transformation (from the manufactured dose form) has been carried out
Basis of strength substance (BoSS)	The substance against which the strength quantity of a medicinal product is measured
Clinical Drug (CD)	A representation of a medicinal product based on the description of 1) its precise active ingredient substances only and explicitly, 2) the stated basis of strength substance(s) with strength, expressed as presentation strength with unit of presentation or as concentration strength as appropriate, and 3) with its manufactured dose form
Clinical Drug presentation (CD presentation)	A representation of a medicinal product based on the description of 1) its precise active ingredient substances only and explicitly, 2) the stated basis of strength substance(s) with strength, expressed as presentation strength with unit of presentation, and 3) with its manufactured dose form
Clinical Drug concentration (CD concentration)	A representation of a medicinal product based on description of 1) its precise active ingredient substances only and explicitly, 2) the stated basis of strength substance(s) with strength, expressed as concentration strength and 3) with its manufactured dose form

Term/Abbreviation	Definition
Combination grouper	A concept grouping together medicinal products based on both the chemical structure and behaviour (mechanism of action) of their active ingredient substance(s)
Concentration strength	A type of strength description where the amount of the basis of strength substance present per unitary amount (volume, mass) of the single clinical drug being represented
Disposition grouper	A concept grouping together medicinal products based on the behaviour (mechanism of action) of their active ingredient substance(s)
Dose form (Pharmaceutical dose form)	The physical manifestation or formulation of a medicinal product that contains the active ingredient substance(s) intended to be delivered to a patient; the pharmaceutical dose form may be a manufactured dose form or an administrable dose form
IDMP	**Identification of Medicinal Products** A suite of ISO standards concerned with the unique identification of medicinal products, primarily within the regulatory domain of use The suite includes: ISO 11615:2017 *Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated medicinal product information* ISO 11616:2017 *Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated pharmaceutical product information* ISO 11238:2018 *Health informatics -- Identification of medicinal products -- Data elements and structures for the unique identification and exchange of regulated information on substances* ISO 11239:2012 *Health informatics - Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated information on pharmaceutical dose forms, units of presentation, routes of administration and packaging* ISO 11240: 2012 *Health informatics - Identification of medicinal products -- Data elements and structures for the unique identification and exchange of units of measurement*
Intimate container	The receptacle or vessel used to contain (or bound) liquid medicinal products into countable entities
Manufactured dose form	The (pharmaceutical) dose form of a medicinal product as it is presented by the manufacturer into the supply chain, before any transformation into an administrable dose form
Medicinal Product (MP)	An abstract representation of a medicinal product based on description of active ingredient substance(s) that it contains (regardless of any modification of those active ingredient substance(s)), but not exclusively limited by those substances, in that other substances may be present
Medicinal Product only (MP only)	An abstract representation of a medicinal product based on description of only and exclusively the active ingredient substance(s) that it contains but regardless of any modification of those active ingredient substance(s)
Medicinal Product precisely (MP precisely)	An abstract representation of a medicinal product based on description of only and exclusively the precise active ingredients it contains
Medicinal Product Form (MPF)	An abstract representation of a medicinal product based on description of active ingredients it contains, but not limited by that description, and on the (generalised) intended site of use for the product
Medicinal Product Form Only (MPF only)	An abstract representation of a medicinal product based on description of only and exclusively the active ingredient(s) it contains and on the (generalised) intended site of use for the product
Real Medicinal Product (RMP)	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
Real Clinical Drug (RCD)	The representation of a medicinal product marketed by a by a single organisation (supplier) in a single jurisdiction under a single name and which contains the same set precise active ingredient substances and strengths in a single manufactured dose form

Term/Abbreviation	Definition
Packaged Clinical Drug (PCD)	An abstract 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
Real Packaged Clinical Drug (RPCD)	The representation of a medicinal product as it is supplied in a package by a by a single organisation (supplier) in a single jurisdiction under a single name for placement into the supply chain
Structural grouper	A concept grouping together medicinal products based on the chemical structure of their active ingredient substance(s)
Precise active ingredient substance	The substance that provides the therapeutic effect of the medicinal product, described using the fullest and most specific description of the substance *as it is used in the product(s) being represented. This may include* various modifiers, such as salts, esters, polymers (e.g. pegylation), and/or solvates
Presentation strength	A type of strength description where the amount of the basis of strength substance present in the unit of presentation of or in the volume (or mass) of the single clinical drug being represented
Therapeutic role grouper	A concept grouping together medicinal products based on a broad description of their use in treatment of disease
Unit of presentation	A qualitative concept that describes a countable entity in which the clinical drug is presented, or in which it is bounded

2. National Drug Extension Model

Model Overview

The diagram below shows the concept classes for the extension model with the related concept classes from the international medicinal product model. No role or grouper classes (i.e., parents of the international Medicinal Product (MP) class) 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 in the national drug extension model, the closed world view applies. 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 Supporting Attributes).

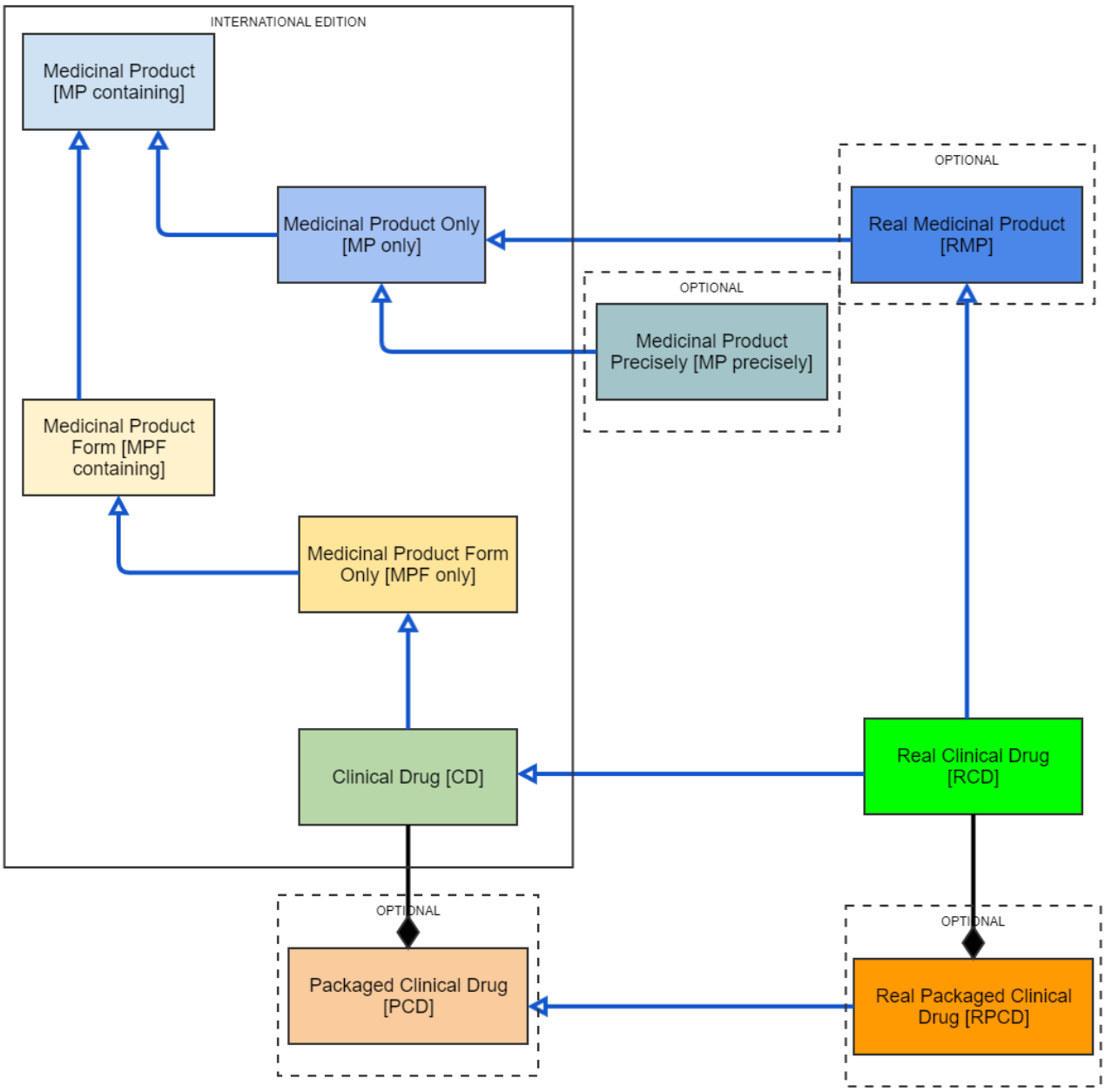

Figure 1: Diagram of the classes of the SNOMED CT national extension model for Medicinal Products

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 brighter shades.

Classes of National Drug 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 Precisely is also shown, as that class may be used in a national extension model, if required. Definitions, descriptions and examples of the five concepts in these classes can be found in the SNOMED CT Medicinal Product Model Specification.

The classes of the national extension model are, with the exception of the MP Precisely and 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 optional 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; this class, like its partner in the international edition content, is at the core of the specification.

Then there are three classes in the national extension model that represent classes that are more specific than the classes of the international model in that they represent either a more specific abstraction of a medicinal product (the MP Precisely) or medicinal products as they are presented in the supply chain in packages for clinical/patient use in a particular country. Any subpackaging used inside a single package (for example, blister strips) and the aggregate packaging used in wholesaling and delivery, such as shrink-wraps and pallets, are excluded. The three additional package classes are:

- The optional Medicinal Product Precisely (MP Precisely) which is an abstract representation of a medicinal product based on description of only and exclusively the precise active ingredients it contains.
- The optional Real Packaged Clinical Drug (RPCD) which 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 one or more Real Clinical Drugs within it, in set amounts.
- The optional Packaged Clinical Drug (PCD) which 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.

All concept classes in the national extension model use the closed world view and therefore include the ingredient count attributes, because when describing the real products that are authorised for supply in a country, what is stated about them must be true, and only what is stated can be true.

No requirement has been identified to suggest that the MPF class from the international core requires a mirrored class in the national extension model.

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

Implementation Options

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, as will the real clinical drug in a national extension, 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.
- Conversely, 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 should be populated, as it acts as a grouper concept for all the packages associated with it. This grouper concept is important particularly if extensions require additional product characteristic information, such as for excipients of concern.

Similarly, some nations may require the MP Precisely concept for some classes of medicines 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 Precisely concepts can be authored in a national extension using the principles given in the international Medicinal Product Model Specification.

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.

All authored concepts should classify correctly despite the absence of some intermediary classes, provided that they have been modeled according to the SNOMED International standards, that is using the proximal primitive parent and the relevant attributes for the concept class.

Class Relationships

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. It also 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. This is reflected in the 774160008 | Contains clinical drug (attribute)| that is part of the logical definition of a Packaged Clinical Drug. 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 usual SNOMED CT generalisation relationship and partitive relationship is manageable within 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 with a direct relationship to the Clinical Drugs that they contain (as in "under" them in a hierarchical display), 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 774160008 | Contains clinical drug (attribute)| must be used to facilitate that.

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.

Relationship between International and Extension Content

The international core content of SNOMED CT will provide all the **attribute relationships** needed to define medicinal product concepts in a national extension. These will be suitably defined according to SNOMED CT Machine-Readable Concept Model (MRCM) principles and available for use in the tooling. The concepts to provide the **values** for the product name and supplier cannot be present in the International edition, as these do not have international applicability or even international uniqueness (especially for product name). This specification therefore cannot provide ranges for these attributes; the supertype concepts are available (774167006 | Product name (product name)| and 774164004 | Supplier (supplier)|) 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 edition; some additional content may require authoring in the nation's own extension. All the substance, dose form, unit of presentation, and package type concepts to value the attributes

should be available in the international content to satisfy the interoperability use cases for the medicinal product hierarchy. Strengths can be described accurately using the appropriate integer or decimal, following editorial rules.

All concepts in the classes of the national extension model should be modelled using the proximal primitive parent modeling pattern and be fully defined wherever possible, using the attribute relationships and values from the international content for the substance, dose form and unit of presentation 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.

Please note in the following diagrams, the terming pattern for the Fully Specified Name and other descriptions is not finalised, and more than one terming pattern has been used in the diagrams in this specification. General terming guidance for all concepts in this specification will be issued in the future, acknowledging that different countries and different languages will need to adapt to their local needs.

2.1 Real Medicinal Product (RMP)

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.

Use Cases

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/guideline management may have a use case for this class (for example, to change presentation or strength within a product family)
- Pharmacovigilance (abstract representation of a manufactured medicinal product)

Discussion

The real medicinal product class is a grouper concept for products containing the same set of active ingredient substance(s) and marketed under the same name by the same supplier.

Single ingredient substance branded products

The RMP "Zocor (product)" shown in a taxonomic view in Figure 2 below presents products marketed by Organon Pharma UK Limited under a single name (Zocor) and containing only simvastatin as the active ingredient substance and shows the RCD concepts associated with it:

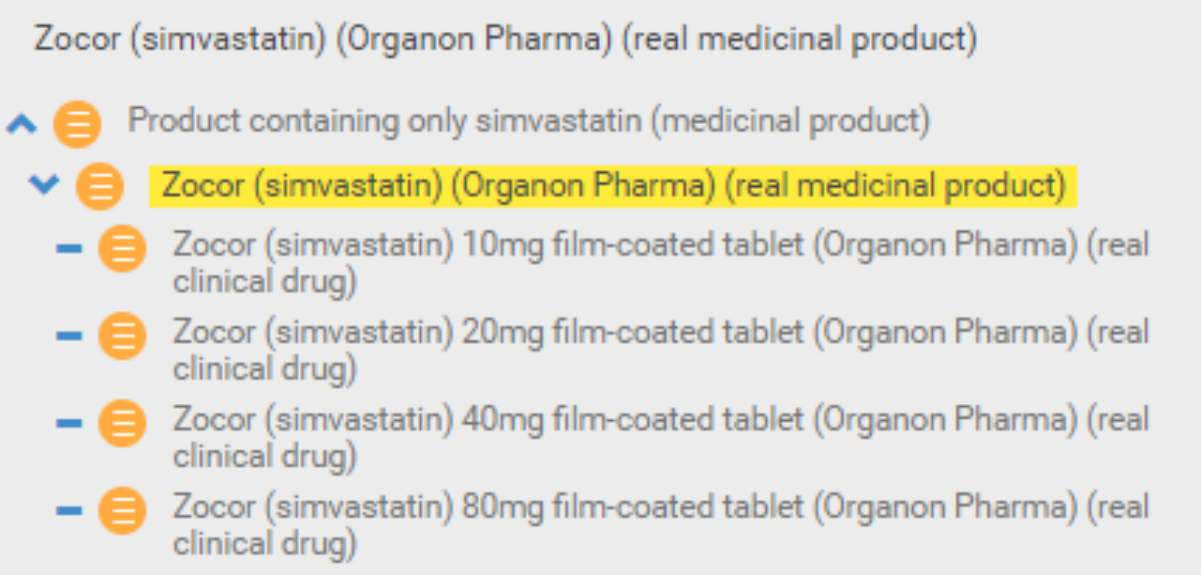

Figure 2: Diagram showing a branded single ingredient substance real medicinal product and its supporting real clinical drug concepts (Note: not all possible real clinical drug concepts are shown.)

Single ingredient generic products

For those products without a unique (i.e., invented) product name, where the product uses the international non-proprietary name of the active substance as its product name (i.e., so called *generic* products), extensions may choose not to populate the Real Medicinal Product class, as shown below, with each RCD being associated directly with the CD in the International content:

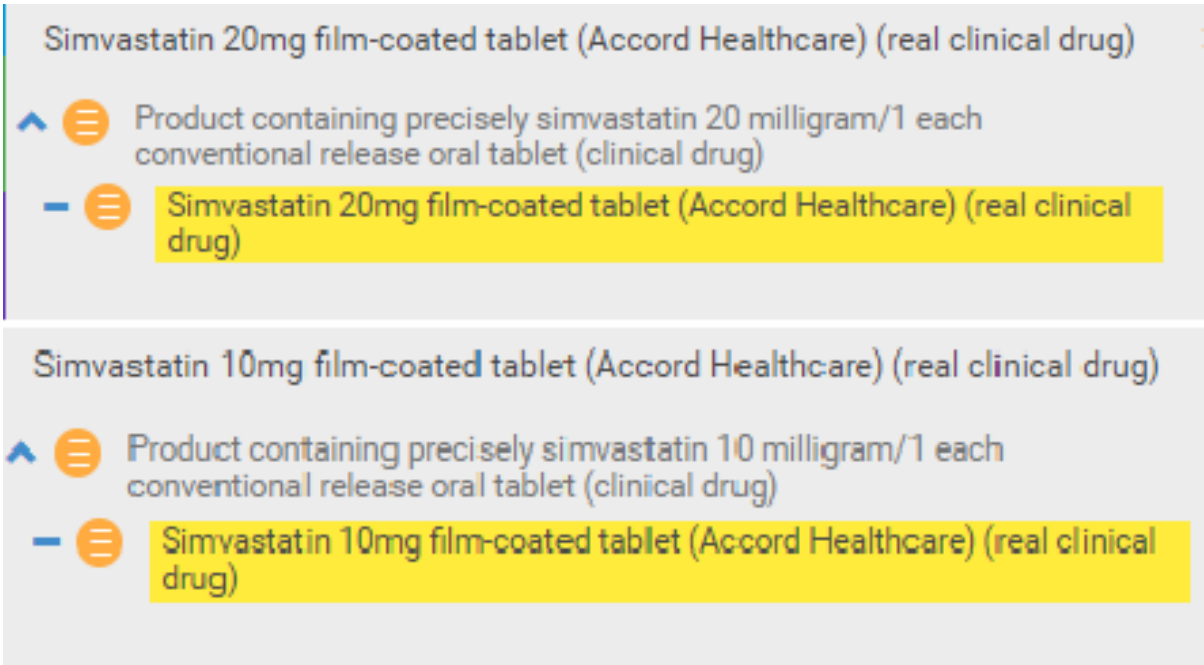

Figure 3: Example of real clinical drug "generic" products where a real medicinal product concept has not be authored

Alternatively, for products without a unique (i.e. invented) product name (*generic* products) a national extension may choose to populate the Real Medicinal Product using the generic name AND supplier, since this gives a unique RMP concept, as shown below:

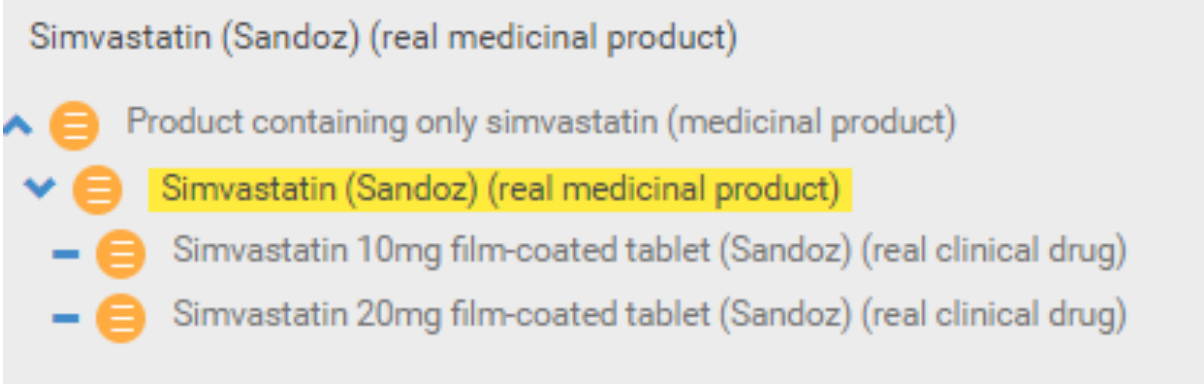

Figure 4: Example of real clinical drug "generic" products where a real medicinal product concept has been authored using product and manufacturer name

Note that here the product name attribute is valued as "simvastatin", which in text looks similar to both the substance concept 387584000 | Simvastatin (substance) | and to the two medicinal product concepts 96304005 | Product containing simvastatin (medicinal product) | and 777537002 | Product containing only simvastatin (medicinal product) |. But it is a different concept and has its own semantic tag of "product name"; it is therefore a different concept (unit of thought): Simvastatin (product name).

Multi-Ingredient substance branded products

One of the fundamentals of a Real Medicinal Product is that it represents a single set of active ingredient substances, reflecting its associated MP only class that also represents a single set of active ingredient substances, without dose form or strength information.

The RMP "Inegy (product)" shown in a taxonomic view in Figure 2 below presents products marketed by Organon Pharma UK Limited under a single name (Inegy) and containing only simvastatin AND ezetimibe as the active ingredient substances, and showing the RCD concepts associated with it:

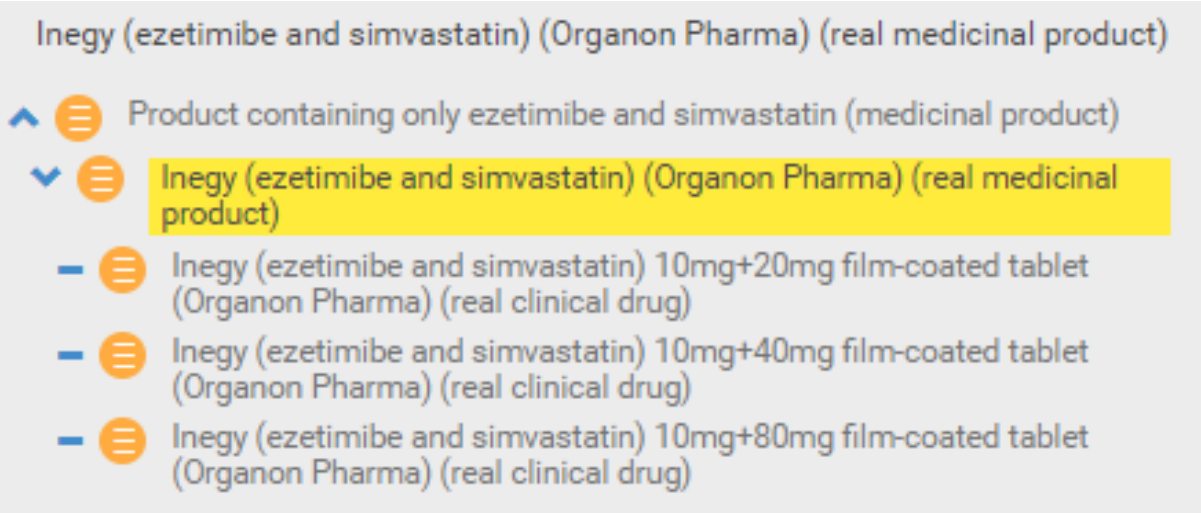

Figure 5: Diagram showing a branded multi-ingredient substance real medicinal product and its supporting real clinical drug concepts (note, not all possible real clinical drug concepts are shown)

Not all authorised 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 due to differences in their active ingredient substances.

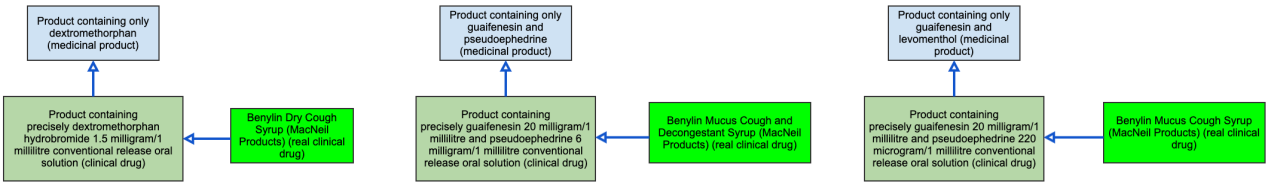

Figure 6: Example of branded real clinical drug products sharing the same product name but not relating to a Real Medicinal Product due to differences in their set of active ingredient substances

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:

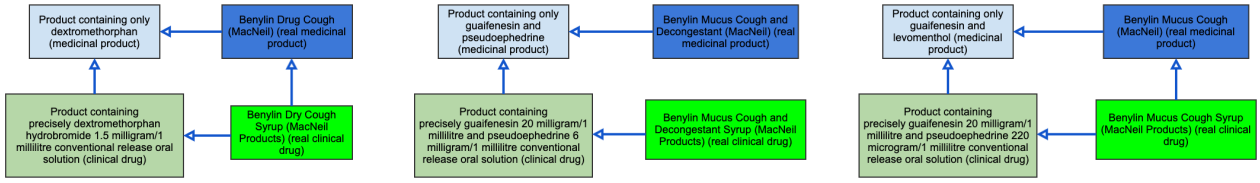

Figure 7: Example of branded real clinical drug products relating to appropriate real medicinal products by authoring of specific product name concepts

Existing national terminology equivalents for real medicinal product:

- Trade family in NHS dm+d
- Trade Product (TP) in AMT/NZULM
- Brand Name (BN) in RxNorm (possibly)

Attributes

The following attributes apply to Real Medicinal Product (RMP) concepts in a national extension. The RMP class has two attributes inherited from the Medicinal Product (only) class in the international content and two additional attributes.

Semantic tag	(real medicinal product)
Definition status	900000000000073002 |Sufficiently defined concept definition status|
Attribute 1142139005 | Count of base of active ingredient|	**Range** • INT (Integer) **Cardinality** • 1..1 **Notes**

	• This attribute provides the number of base active ingredient substances present in the medicinal product
Attribute 774159003 |Has supplier|	**Range** • < 774164004 |Supplier (supplier)| ▪ 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 **Notes** • 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 below).
Attribute 774158006 |Has product name|	**Range** • < 774167006 |Product name (product name)| ▪ 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 **Notes** • 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 below).
Role Group **Attribute** 127489000 |Has active ingredient|	**Range** • < 105590001 |Substance| ▪ Excluding concepts representing structural groupers, dispositions, or combined substances **Cardinality** • 1..* **Notes** • There is no technical limit on the number of |Has active ingredient|attributes that may be added to a concept; a practical limit may be imposed by national extensions. In order to classify correctly to the international content, this attribute value should represent the base ingredient substance, not a modification, unless explicitly identified as an exception and requiring an association to MP precisely concept. This attribute describes the set of active ingredient substances that the concept minimally contains. A set of active ingredient substances may well have only one member.

Note: The cardinalities given in the above table are for concepts in the RMP class. These cardinalities may be stricter than those in the MRCM, which typically apply across a broader range of concepts.

Example Diagrams

Stated template view:

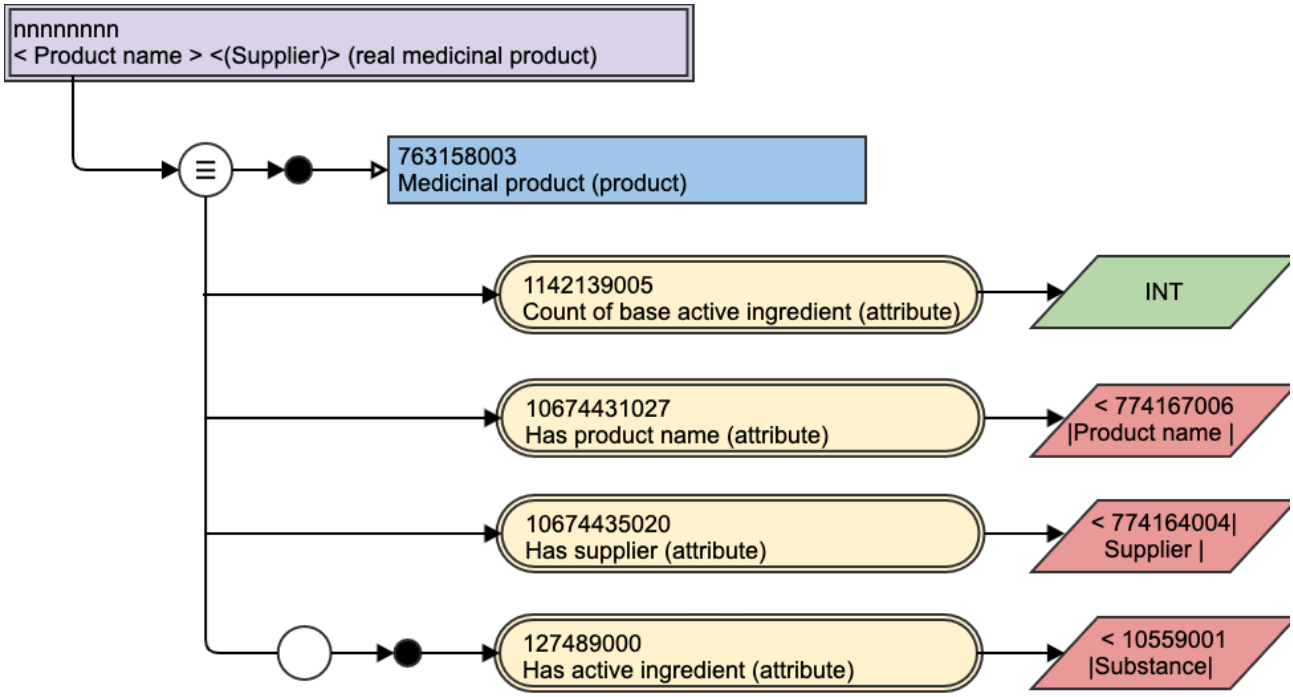

Figure 8: Real Medicinal Product (RMP) stated template view

Example: single active ingredient substance branded product (Zocor): state view followed by the inferred view

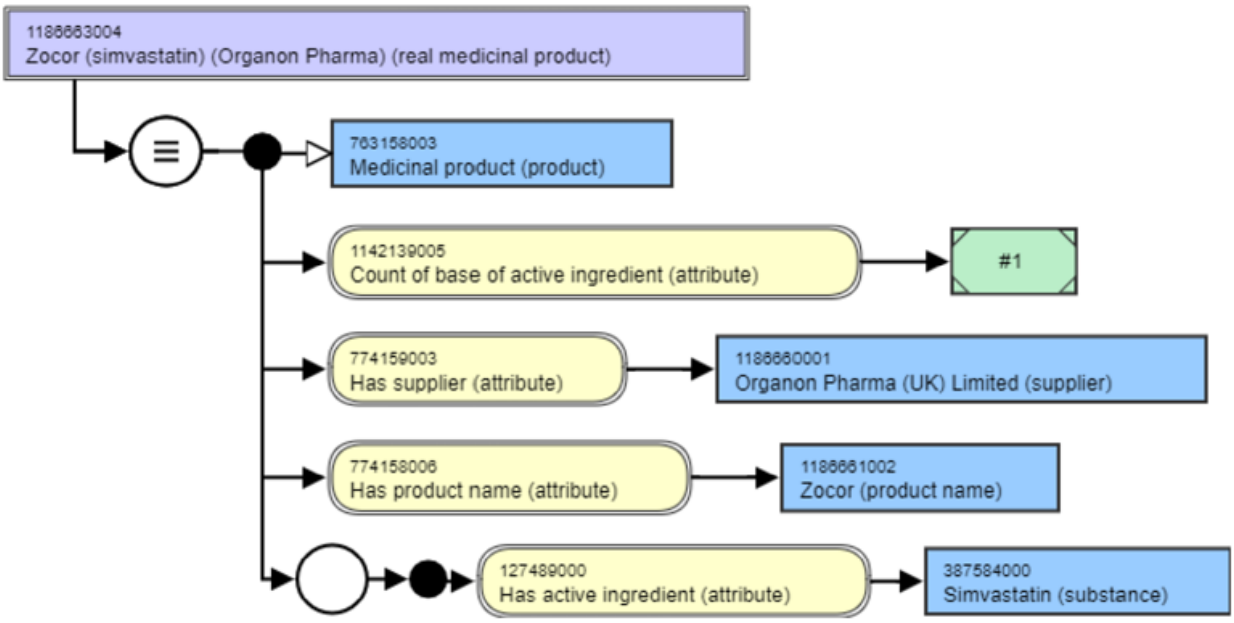

Figure 9: Single active ingredient substance real medicinal product example stated view

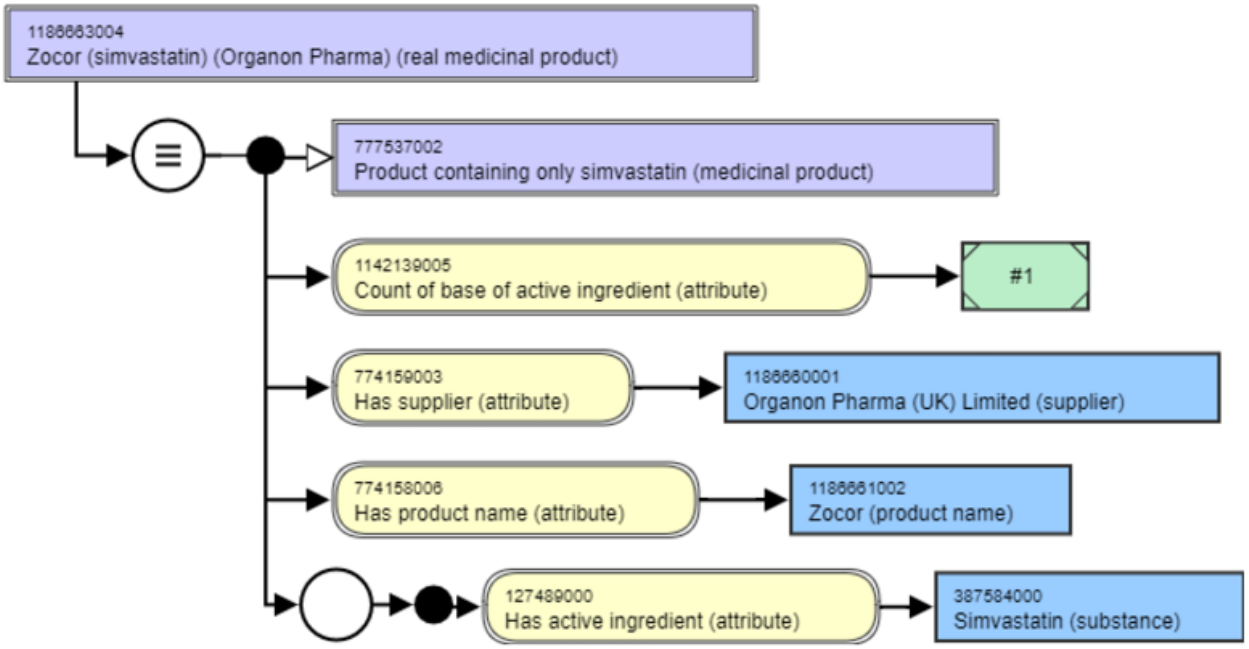

Figure 10: Single active ingredient substance real medicinal product example inferred view

Example: multiple active ingredient substance branded product (Inegy): stated view followed by the inferred view

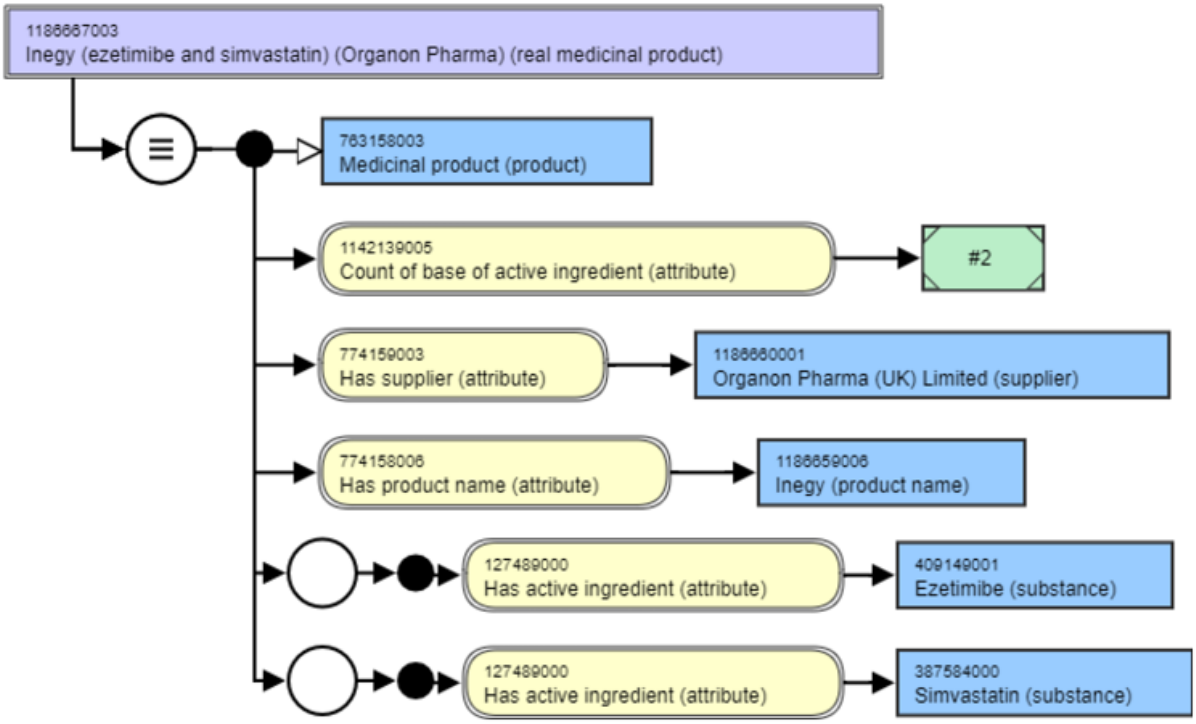

Figure 11: Multiple active ingredient substance real medicinal product example stated view

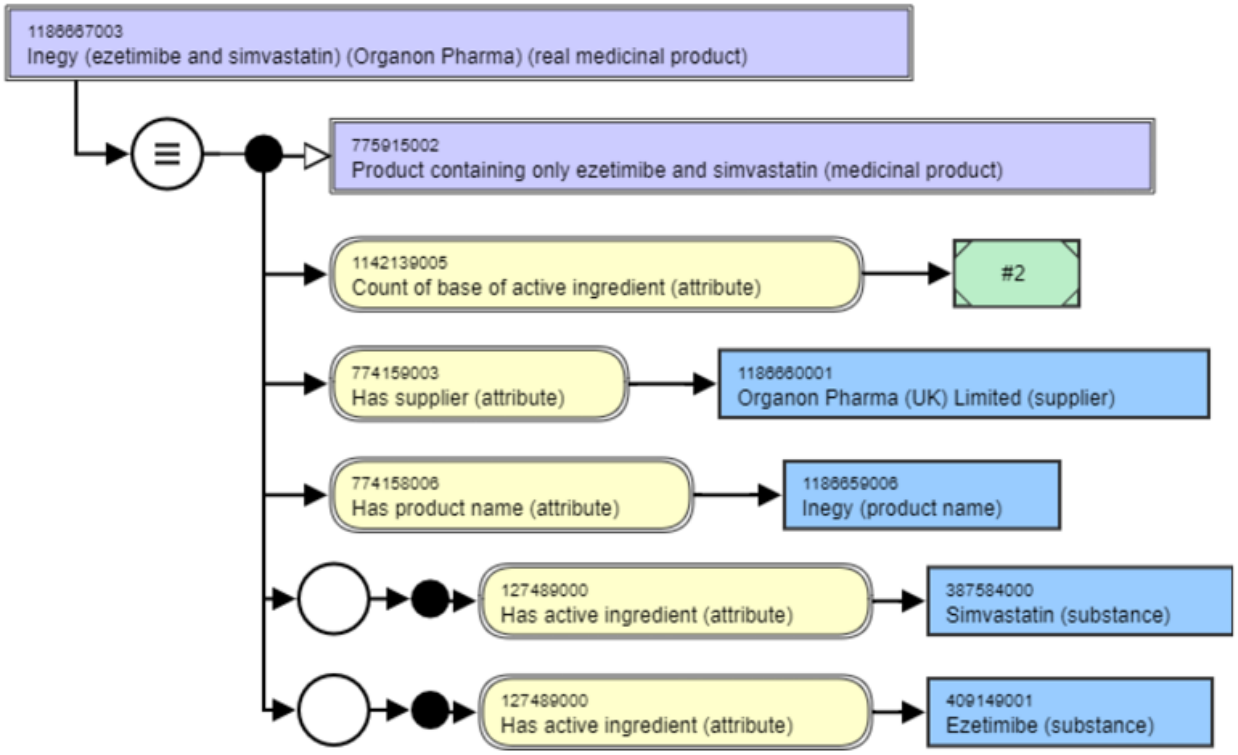

Figure 12: Multiple active ingredient substance real medicinal product example inferred view

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.

2.2 Medicinal Product Precisely (MP precisely)

Definition

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

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

Use cases

The use case for the MP (precisely) concept is primarily to provide a more exact and explicit medicinal product concept for use in those scenarios where different modifications of the base active ingredient have clinical significance, usually because of different potency and different dosing schedules. There are several groups of products where this is the case; for example: corticosteroids, various anti-epileptic medications (e.g., phenytoin and valproic acid), and insulins. The MP (precisely) class can be deployed in national extensions for those use cases that need it, such as prescribing scenarios (so called "abstract" or "non-product-based" prescribing where no

product and no dose form are specified by the prescriber) and in medication history and in medication profiles, and in decision support, in protocols and treatment guidelines. However, all the use cases described for MP (only) could use MP (precisely) as necessary when more exact and explicit representation is required.

Discussion

A Medicinal Product (MP precisely) concept may be created in national extensions when use case(s) require this and for those national extensions where products exist, such that the active ingredient count attribute for the MP precisely has a different value from the active ingredient count of the parent Medicinal Product (MP only) concept.

Attributes

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

In national extensions, using the MP precisely concept related to CD concepts in the international edition which do not have multiple ingredient counts may give classification results that are not as initially expected; in this case, it may be necessary to override the international definition of some concepts in the subhierarchy in the national extension (e.g., if a CD containing one of the precise ingredient substances has only one count attribute in the international but requires two or three count attributes in the national in order to get correct classification into an MP precisely concept).

Semantic tag		(medicinal product)
Definition status		• 900000000000073002 |Sufficiently defined concept definition status|
Role Group	**Attribute** 762949000 |Has precise active ingredient|	**Range** • < 105590001 |Substance| ▪ Excluding concepts representing structural groupers, dispositions, or combined substances **Cardinality** • 1..* **Notes** • This is the set of precise active ingredient substances that the medicinal product contains. A set of precise active ingredient substances may have only one member.
Attribute 1142139005 |Count of base of active ingredient|		**Range** • Integer **Cardinality** • 1..1 **Notes** • This attribute provides the number of base active ingredient substances present in the medicinal product.
Attribute 1142141006 |Count of base and modification pair|		**Range**

	• Integer **Cardinality** • 0..1 **Notes** • This attribute provides the number of base active ingredient substances present in the medicinal product. • This attribute should only be present and valued for multi-ingredient product concepts where two or more active ingredients share the same base active ingredient (i.e., parent ingredient substance) and for single ingredient product concepts where the active substance is an ingredient in multi-ingredient products. As discussed above, and as described in the MRCM rules, the additional ingredient count attributes must be applied iteratively.
Attribute 1142140007 |Count of active ingredient|	**Range** • Integer **Cardinality** • 0..1 **Notes** • This attribute provides the number of active ingredients present in the medicinal product. • This attribute should only be present and valued for multi-ingredient concepts where two or more active ingredients share the same base active ingredient (i.e., parent ingredient substance) and where one is a further modification of the other (for example, a multi-ingredient product containing both dexamethasone phosphate and dexamethasone sodium phosphate, where the dexamethasone phosphate is a modification of dexamethasone (base) and dexamethasone sodium phosphate is a further modification of the dexamethasone phosphate), and for single ingredient product concepts where the active substance is an ingredient in multi-ingredient products. As discussed above, and as described in the MRCM rules, the additional ingredient count attributes must be applied iteratively.

Example diagrams

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

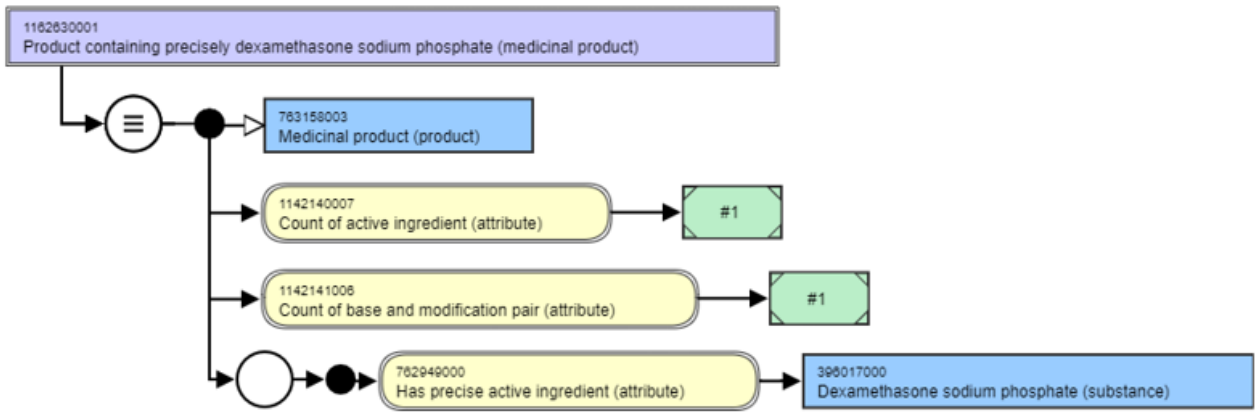

Figure 13: Single Ingredient Medicinal Product (precisely) example stated view

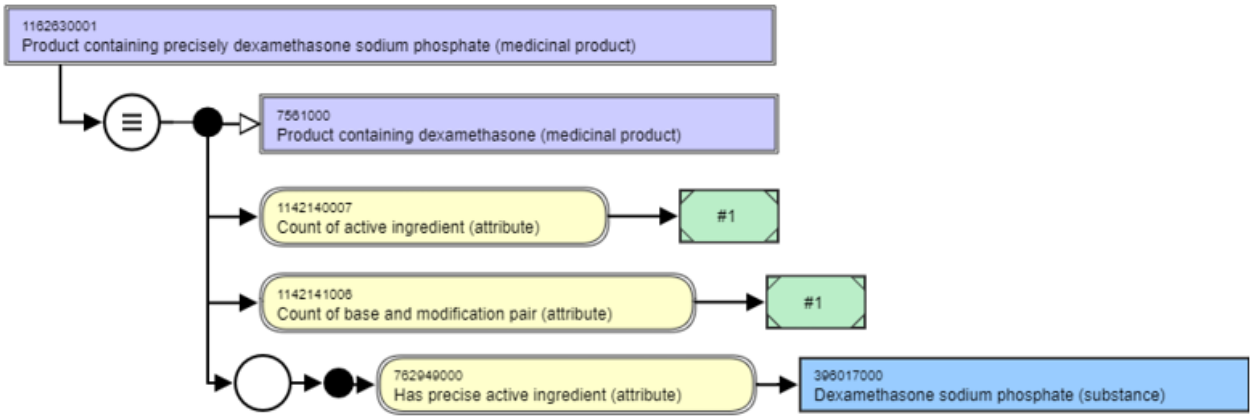

Figure 14: Single Ingredient Medicinal Product (precisely) example inferred view

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

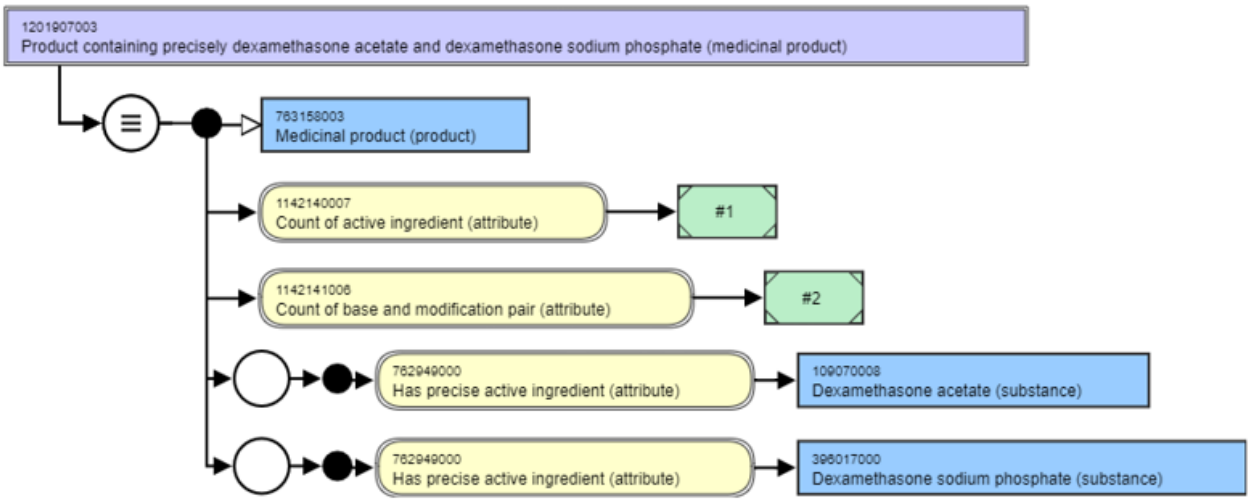

Figure 15: Medicinal Product (precisely) example stated view - multi-ingredient concept

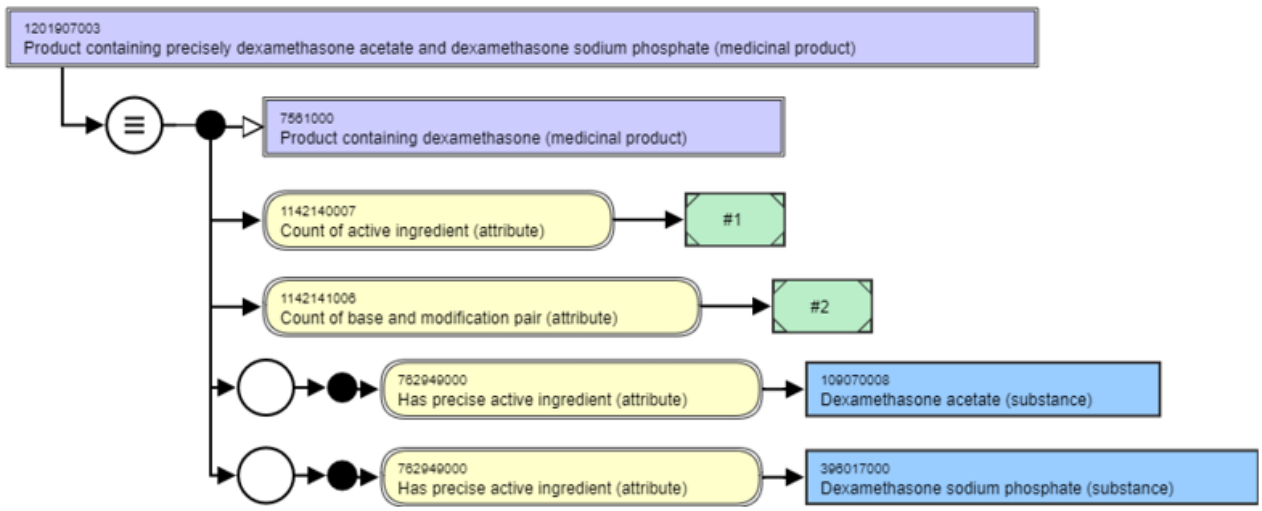

Figure 16: Medicinal Product (precisely) example inferred view - multi-ingredient concept

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

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

For further details, see the Ingredient Count attributes in the International Model specification.

2.3 Clinical Drug (CD) with Concentration and Presentation Strengths

Discussion

Clinical drug concepts in the international edition are authored ***either*** using presentation strength (for discrete dose forms) ***or*** using concentration strength (for liquid dose forms and patches, etc.) as appropriate for different types of product (see Appendix A of the International Medicinal Product Model specification). Concentration strength in SNOMED CT is where the description of the strength of a clinical drug has been normalised such that the denominator value is "one" and the denominator unit is a unit of mass (e.g., grams) or volume (e.g., millilitres). Presentation strength is a description of the strength of the clinical drug as it is present in its unit of presentation (vial, ampoule, sachet). In national extensions, the concentration strength clinical drug may be sufficient, or there may be a requirement to represent some, usually liquid dose form product clinical drugs, using **both** concentration and presentation strength either for the abstract clinical drug, or for the real clinical drug, or for both. This is shown in the diagram below:

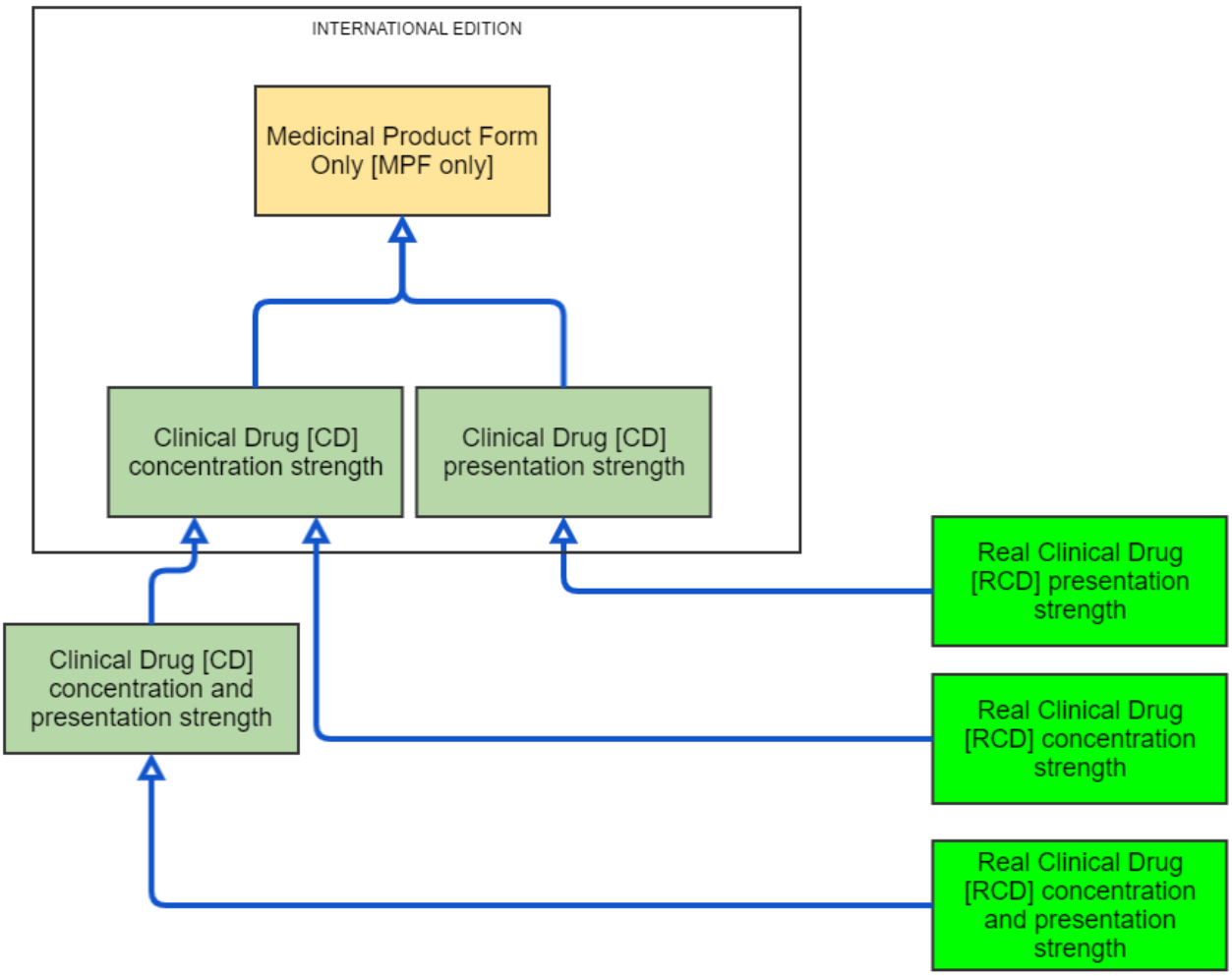

Figure 17: Diagram of relationships and optionality for presentation strength and concentration strength Clinical Drug and Real Clinical Drug

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 some products such as insulins and large volume parenteral fluid replacement products and bulk use vials, etc.); other agencies have been or are using this pattern for some products (e.g., pre-filled syringes) and may change for others as IDMP takes effect. Some national terminologies are working to normalise the patterns of strength representation particularly for safety considerations; others are dealing with the mixed economy that exists "as is". This specification provides support for the different patterns for both clinical drugs and real clinical drugs whilst maintaining the requirement that concepts will classify correctly within the system.

This modeling pattern is advised for use with usually liquid products that are placed inside a unit of presentation such as an ampoule, vial, cartridge or pre-filled syringe, which itself is then put inside a package, usually but not always with other identical units, for placement into the supply chain. For these products, the presentation strength is itself often clinically relevant, and therefore, although the fully specified name pattern (as currently described) uses the concentration strength, a synonym (which could be the preferred term for a national extension) could use the presentation strength description; for example: "enoxaparin sodium 120 milligram/0.8 millilitre conventional release solution for injection in pre-filled syringe".

As the unit of presentation is the "countable entity" of the clinical drug, this modeling pattern is not advised for continuous semi-solids (creams, ointments, etc.) or continuous liquids (oral solutions, suspensions) where there is no "countable entity". The unit of presentation should not be confused with the package for continuous semi-

solids and liquids that is placed into the supply chain (tubes, bottles, etc.). The package should be described using the (R)PCD structure which describes the package size but not currently the package type. For example: chloramphenicol 5 milligram/1 milliliter conventional release eye drops are supplied in a 10mL bottle; the clinically relevant information is the "10mL" volume, which is the package size.

Use cases

This is the pattern for a national extension to author a presentation strength representation of a clinical drug that is described using concentration strength in the international edition. This can be used for:

- liquid parenteral products presented in units of presentation, such as ampoules, vials, pre-filled syringes, cartridges, or bags/bottles
- liquid oral products presented in a sachet or other unit dose unit of presentation
- liquid pulmonary products presented in a unit dose presentation unit of presentation

In addition to the usual attributes for a concentration strength clinical drug, the unit of presentation size and unit of presentation unit attributes are used. The concept will then classify correctly as a child of the existing concentration strength clinical drug. This does mean that the exact presentation strength must be authored manually as an additional description and that the exact presentation strength is not provided in the logical definition (other than via calculation), but this pattern has been found to be the most efficient method for authoring such concepts, especially when there are multiple active ingredient substances. The alternative was to author both concentration strength and presentation strength in two role groups, which, whilst it does also give the correct classification, is very labour intensive.

Attributes

The following attributes apply to Clinical Drug (CD) concepts in a national extension, which require both concentration and presentation strength.

Semantic tag	**(clinical drug)**
Definition status	• 900000000000073002 |Sufficiently defined concept definition status|
Attribute 411116001 |Has manufactured dose form|	**Range** • < 736542009 |Pharmaceutical dose form| **Cardinality** • 1..1 **Notes** • This attribute describes a grouping dose form concept for the medicinal product, where the grouping is the intended site for administration of the dose form of the product.
Attribute 1142139005 |Count of base of active ingredient|	**Range** • INT (integer) **Cardinality** • 1..1 **Note** • This attribute provides the number of base active ingredient substances present in the medicinal product.
Attribute 763032000 |Has unit of presentation|	**Range** • < 732935002 |Unit of presentation| **Cardinality**

		• 0..1 **Notes** • This is the unit of presentation that the liquid product is presented in (vial, ampoule, sachet, pre-filled syringe, etc.).
Attribute **Attribute** 1148793005 |Unit of presentation size quantity|		**Range** • DEC (decimal) **Cardinality** (within role group) • 1..1 **Notes** • This is the volume of liquid that the unit of presentation contains.
Attribute **Attribute** 320091000221107 |Unit of presentation size unit|		**Range** • < 767524001 |Unit of measure (qualifier value)| **Cardinality** (within role group) • 1..1 **Notes** • This is the unit of measure for the volume of liquid that the unit of presentation contains (usually millilitres)
Role Group [1..*] One role group is required for each precise active ingredient	**Attribute** 762949000 |Has precise active ingredient|	**Range** • < 105590001 |Substance| **Cardinality** (within role group) • 1..1 **Notes** • This is a precise active ingredient substance that the concept contains. • In each role group, only one precise active ingredient substance is stated.
	Attribute 732943007 |Has basis of strength substance|	**Range** • < 105590001 |Substance| **Cardinality** (within role group) • 1..1 **Notes** • This is the basis of strength substance that the concept uses. • In each role group, only one precise active ingredient substance is stated. • The basis of strength substance is always stated explicitly, even when it is the same as the precise active ingredient substance.
	Attribute 1142138002 |Has concentration strength numerator value|	**Range** • DEC (decimal) **Cardinality** (within role group) • 1..1

	Attribute 733725009 |Has concentration strength numerator unit|	**Range** • < 767524001 |Unit of measure (qualifier value)| **Cardinality** (within role group) • 1..1
	Attribute 1142137007 |Has concentration strength denominator value|	**Range** • DEC (decimal) **Cardinality** (within role group) • 1..1
	Attribute 733722007 |Has concentration strength denominator unit|	**Range** • < 767524001 |Unit of measure (qualifier value)| **Cardinality** (within role group) • 1..1

Note: The cardinalities given in the above table are for concepts in the CD class with concentration and presentation strength. These cardinalities may be stricter than those in the MRCM, which typically apply across a broader range of concepts.

Also note that the unit of presentation, the unit of presentation size quantity, and the unit of presentation size unit are not role grouped together, as there should only ever be 0..1 of each present for any one clinical drug concept.

For clinical drugs that have two or more active ingredient substances that are modifications of the same base substance, **and where** MP precisely concepts are required in the national extension, and for single ingredient product concepts where the active substance is an ingredient in these multiple modification multi-ingredient products, the following extra ingredient count attribute will be required in order to support correct relationships generated by the MRCM:

Attribute 1142141006 |Count of base and modification pair|	**Range** • INT (integer) **Cardinality** • 1..1

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

Attribute 1142140007 |Count of active ingredient|	**Range** • INT (integer) **Cardinality** • 1..1

Example Diagrams

Some examples of clinical drug concepts, with concentration strength and presentation strength in a national drug extension, are shown below.

Stated template view:

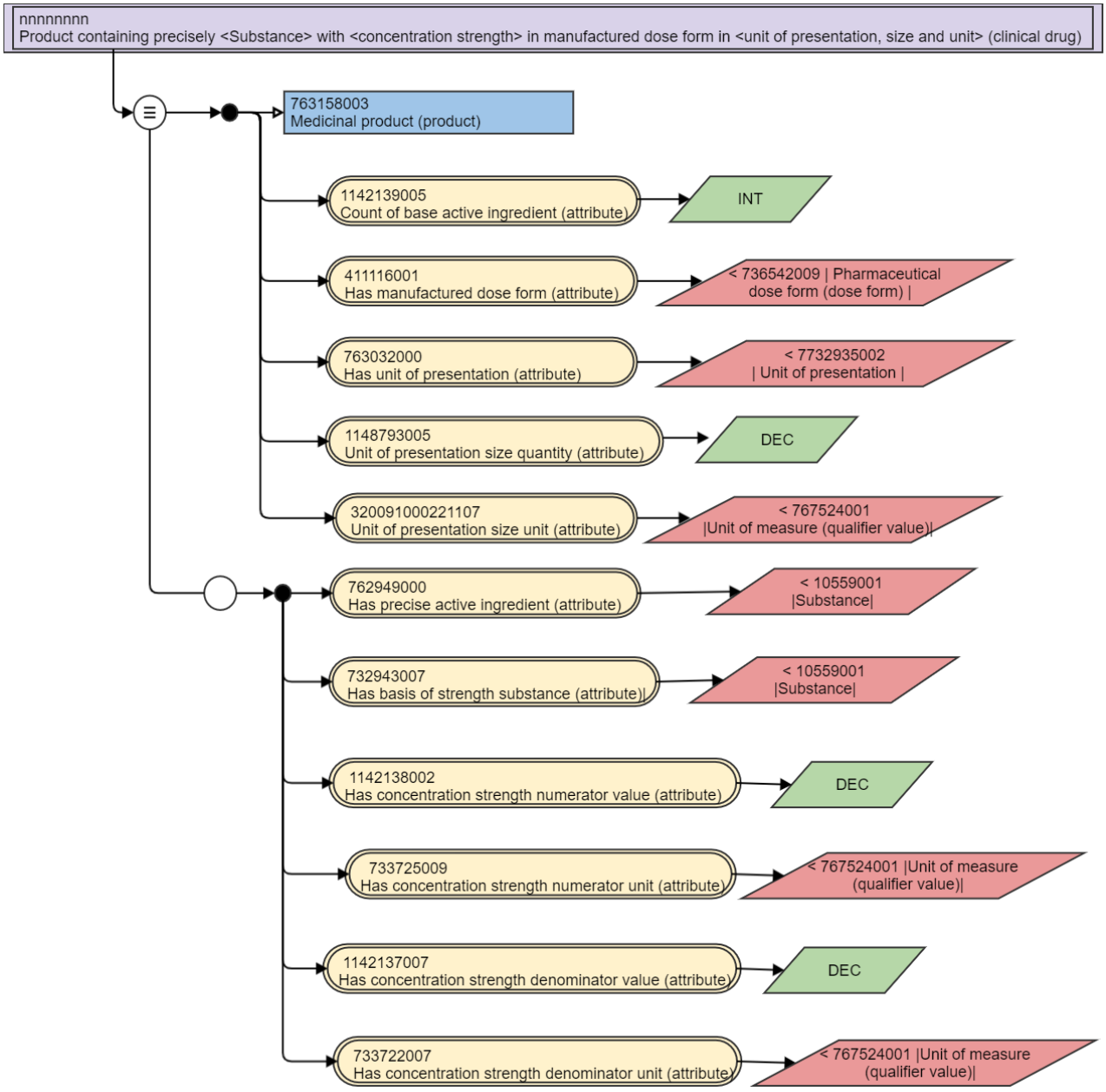

Figure 18: Clinical drug (CD) concentration and presentation strength for a national extension stated template view

Example: single active ingredient substance clinical drug with concentration and presentation strength for a national extension

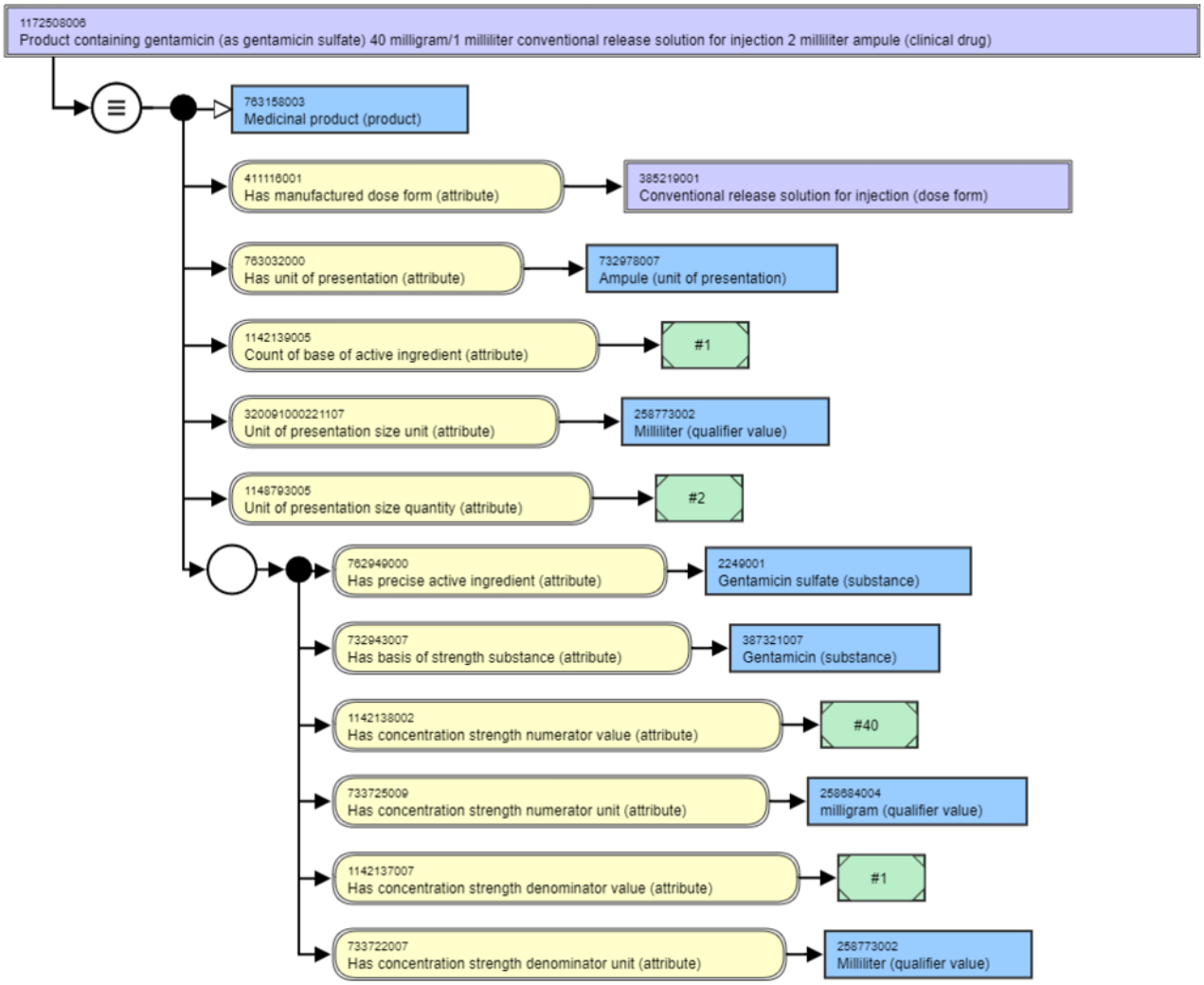

Figure 19: Clinical drug (CD) concentration and presentation strength for a national extension stated view

Figure 20: Clinical drug (CD) concentration and presentation strength for a national extension inferred view

Figure 20 shows how the concentration and presentation strength clinical drug authored in the national extension will classify as a child of the concentration strength CD in the international edition.

2.4 Real Clinical Drug (RCD)

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 or a generic/non-proprietary 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) class in the international edition of SNOMED CT.

Use Cases

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/administered
- 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

Discussion

The real clinical drug represents the product as most (but not all) regulatory authorities grant the marketing authorisation, with the individual packaged products that are marketed into the supply chain in any jurisdiction included *within* that authorisation. A small number of regulatory authorities license each package of a medicinal product separately which is represented by the real packaged clinical drug (see below). Real medicinal products must be represented using the closed world view; they contain ***only*** the content as stated in the logical definition. 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 the section on Optional Additional Information below.

The real clinical drug is the marketed (therefore "real") instantiation in any one country of the abstract clinical drug in the international edition, and as such, real clinical drugs classify as child concepts of the clinical drug as well as a child concepts of the real medicinal product, if one has been authored. This concept class is, like the clinical drug in the international edition, at the core of the way medicinal products are described and as such, should always be used in a national extension.

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

Attributes

The real clinical drug class inherits from the clinical drug class in the international edition, and the product name and supplier 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. A liquid product being described using a presentation strength in a national extension should follow the pattern used for "concentration and presentation strength clinical drugs in the national extension" in this specification.

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: 411116001 |Has manufactured dose form|	**Range:** • < 736542009 |Pharmaceutical dose form (dose form)| **Cardinality:**

	• 1..1 **Notes:** • 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: 42139005 |Count of base of active ingredient|	**Range:** • INT (Integer) **Cardinality:** • 1..1 **Notes:** • This attribute provides the number of base active ingredient substances present in the real medicinal product
Attribute: 763032000 |Has unit of presentation|	**Range** • < 732935002 |Unit of presentation| **Cardinality** • 0..1 **Notes** • This is the discrete countable entity that the real clinical drug is presented in; it should be valued for all concepts where presentation strength is used and for those real clinical drugs where both concentration strength and presentation strength is required.
Attribute **Attribute:** 1148793005 |Unit of presentation size quantity|	**Range** • DEC (decimal) **Cardinality** (within role group) • 0..1 **Notes** • This is the volume of liquid that the unit of presentation contains. This attribute should be valued for real clinical drugs where both concentration strength and presentation strength is required.
Attribute Attribute: 320091000221107 |Unit of presentation size unit|	**Range** • < 767524001 |Unit of measure (qualifier value)| **Cardinality** (within role group) • 0..1 **Notes** • This is the unit of measure for the volume of liquid that the unit of presentation contains (usually millilitres). This attribute should be valued for real clinical drugs where both concentration strength and presentation strength is required.
Attribute Attribute: 774158006 |Has product name|	**Range** • < 774167006 |Product name (product name)|

		▪ 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 **Notes** • 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*.
Attribute: Attribute: 774159003 |Has supplier|		**Range** • < 774164004 |Supplier (supplier)| ▪ 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 **Notes** • 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.
*** Role group - for presentation strength** [1..*] One role group is required for each precise active ingredient	**Attribute:** 762949000 | Has precise active ingredient|	**Range** • < 105590001 |Substance| **Cardinality** (within role group) • 1..1 **Notes** • This is a precise active ingredient substance that the concept contains. • In each role group, only one precise active ingredient substance is stated.
	Attribute: 732943007 | Has basis of strength substance|	**Range** • < 105590001 |Substance| **Cardinality** (within role group) • 1..1 **Notes** • This is the basis of strength substance that the concept uses. • In each role group, only one precise active ingredient substance is stated. • The basis of strength substance is always stated explicitly, even when it is the same as the precise active ingredient substance.
	Attribute: 1142135004 | Has presentation strength numerator value|	**Range** • DEC (decimal) **Cardinality** (within role group)

		• 1..1 **Notes:** • This is the amount of basis of strength substance present in one unit of presentation.
	Attribute: 732945000 |Has presentation strength numerator unit|	**Range** • < 767524001 |Unit of measure (qualifier value)| **Cardinality** (within role group) • 1..1 **Notes** This is the unit of measure for the amount of basis of strength substance present in one unit of presentation.
	Attribute: 1142136003 |Has presentation strength denominator value|	**Range** • DEC (decimal) **Cardinality** (within role group) • 1..1 **Notes** • This should be "one" since the strength numerator refers to amount of basis of strength substance present in **one** unit of presentation.
	Attribute: 732947008 |Has presentation strength denominator unit|	**Range** • < 767524001 |Unit of measure (qualifier value)| **Cardinality (within role group)** • 1..1 **Notes** • This should be the unit of presentation (< 732935002 |Unit of presentation|) also valued above. All units of presentation are subtypes of 767524001 |Unit of measure (qualifier value)|.
*** Role group - for concentration strength** [1..*] One role group is required for each precise active ingredient	**Attribute:** 762949000 |Has precise active ingredient|	**Range** • < 105590001 |Substance| **Cardinality** (within role group) • 1..1 **Notes** • This is a precise active ingredient substance that the concept contains. • In each role group, only one precise active ingredient substance is stated.
	Attribute: 732943007 |Has basis of strength substance|	**Range** • < 105590001 |Substance| **Cardinality** (within role group) • 1..1 **Notes** • This is the basis of strength substance that the concept uses.

		• In each role group, only one precise active ingredient substance is stated. • The basis of strength substance is always stated explicitly, even when it is the same as the precise active ingredient substance.
	Attribute: 1142138002 |Has concentration strength numerator value|	**Range** • DEC (decimal) **Cardinality** (within role group) • 1..1 **Notes:** • This is the amount of basis of strength substance present in one "denominator unit".
	Attribute: 733725009 |Has concentration strength numerator unit|	**Range** • < 767524001 |Unit of measure (qualifier value)| **Cardinality** (within role group) • 1..1 **Notes** This is the unit of measure for the amount of basis of strength substance present in one "denominator unit".
	Attribute: 1142137007 |Has concentration strength denominator value|	**Range** • DEC (decimal) **Cardinality** (within role group) • 1..1 **Notes** • This should be "one" since the strength numerator refers to amount of basis of strength substance present in **one** "denominator unit".
	Attribute: 733722007 |Has concentration strength denominator unit|	**Range** • < 767524001 |Unit of measure (qualifier value)| **Cardinality** (within role group) • 1..1 **Notes** • This is the unit of the "one" denominator unit that the strength numerator refers to (usually an SI unit of mass or volume).

For real clinical drugs that have two or more active ingredient substances that are modifications of the same base substance **and where** MP precisely concepts are required in the national extension, and for single ingredient product concepts where the active substance is an ingredient in these multiple modification multi-ingredient products, the following extra ingredient count attribute is required in order to support correct relationships generated by the MRCM:

Attribute: 1142141006 |Count of base and modification pair|	**Range** • INT (integer) **Cardinality** • 1..1

For concepts that have two or more active ingredient substances that are modifications of the same base active ingredient substance (i.e. parent ingredient substance) **and** where one is a further modification of the other (for

example, a multi-ingredient product containing both dexamethasone phosphate and dexamethasone sodium phosphate, where the dexamethasone phosphate is a modification of dexamethasone (base) and dexamethasone sodium phosphate is a further modification of the dexamethasone phosphate) **and where** MP precisely concepts are required in the national extension, and for single ingredient product concepts where the active substance is an ingredient in these multiple modification multi-ingredient products, the following extra ingredient count attribute will be required in order to support correct relationships generated by the MRCM:

Attribute: 1142140007 |Count of active ingredient|	**Range** • INT (integer) **Cardinality** • 1..1

Note: The cardinalities given in the above table are for concepts in the RCD class. These cardinalities may be stricter than those in the MRCM, which typically apply across a broader range of concepts.

Example Diagrams

Some examples of real clinical drug concepts are shown below.

Stated template view:

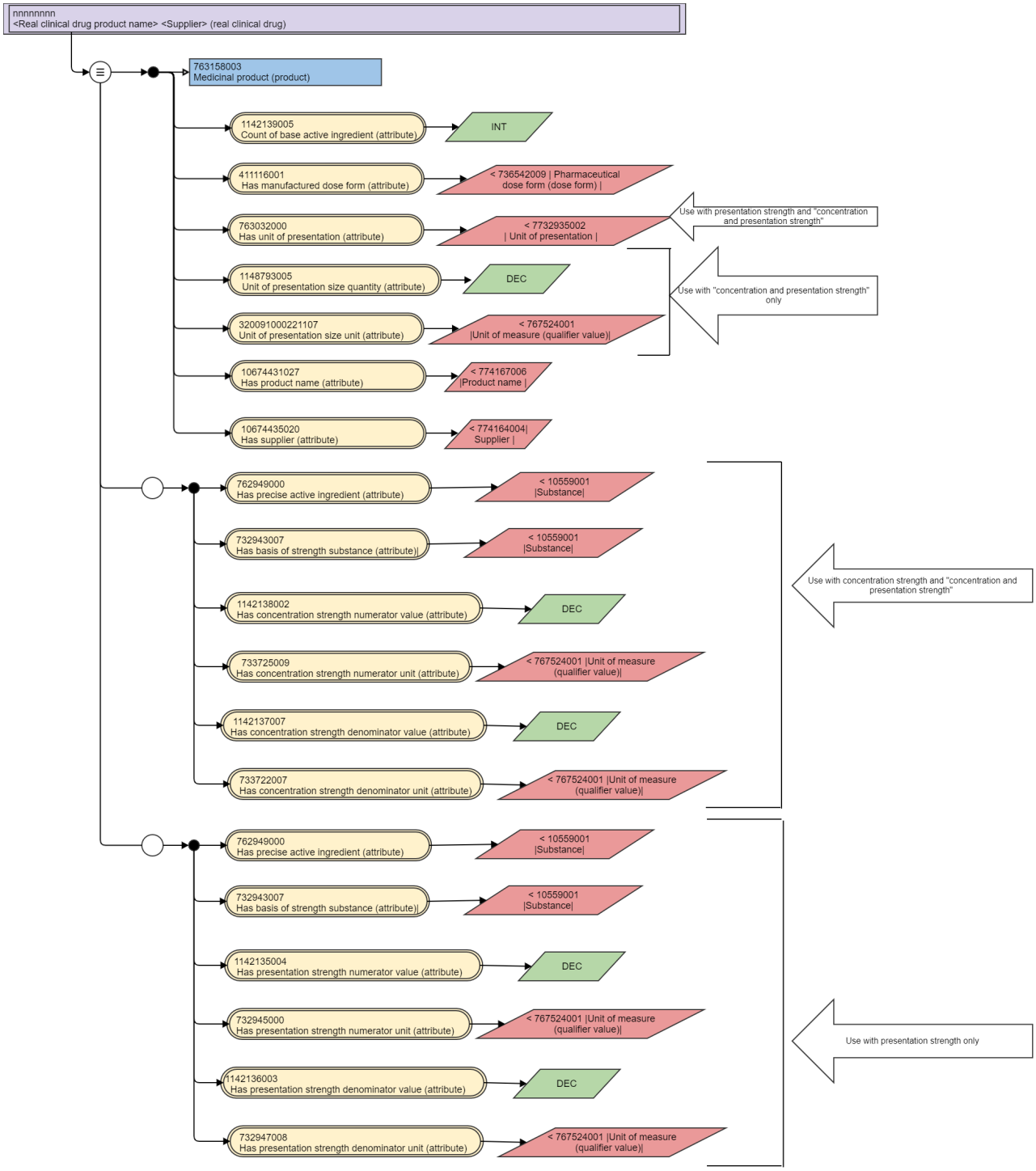

Figure 21: Template for a real clinical drug

Example: single active ingredient substance branded product (Zocor) (presentation strength): stated view followed by the inferred view

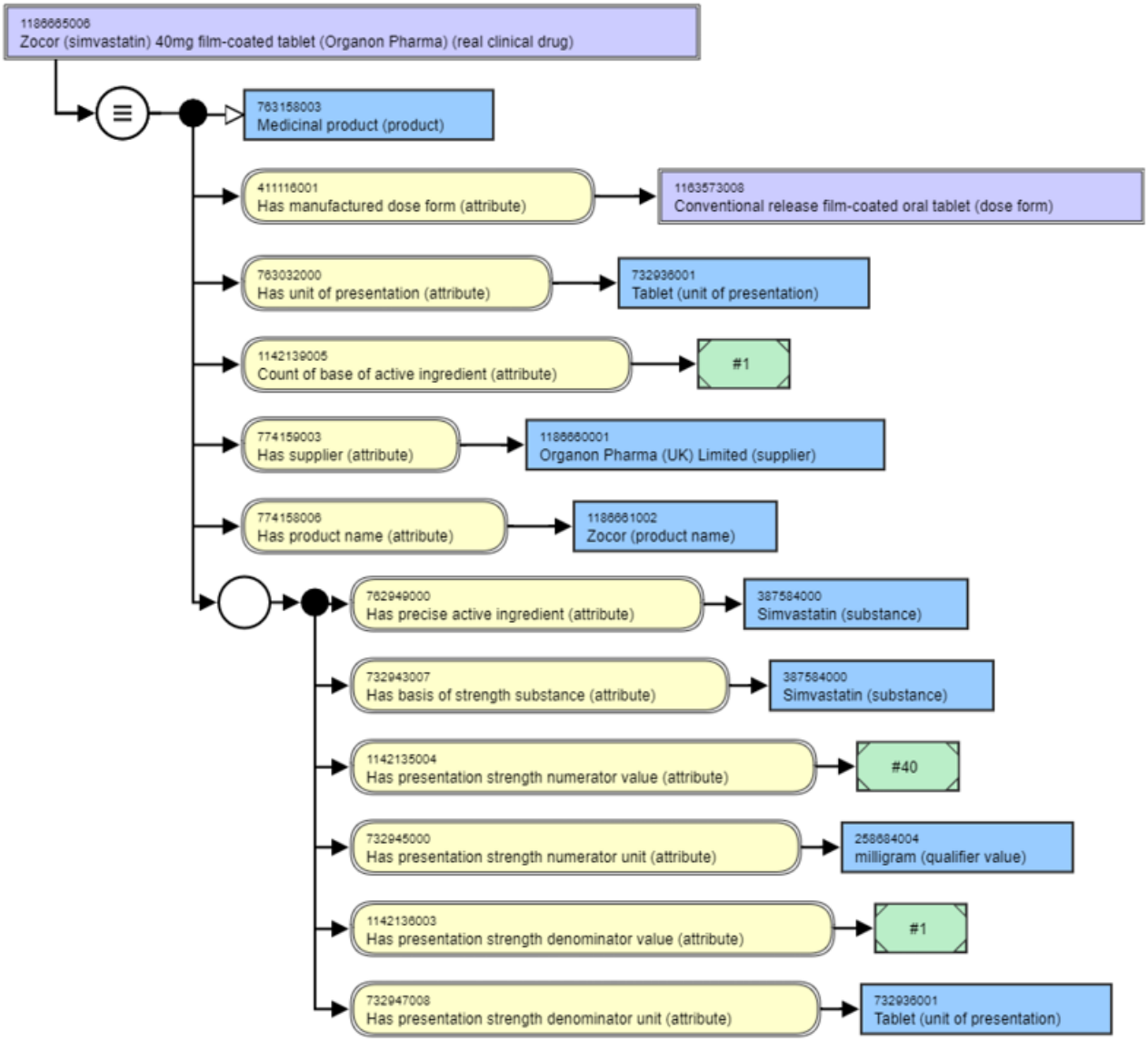

Figure 22: Single active ingredient substance (presentation strength) real clinical drug example - stated view

Figure 23: Single active ingredient substance (presentation strength) real clinical drug example - inferred view

Example: multiple active ingredient substance (presentation strength) branded product (Inegy): stated view followed by the inferred view

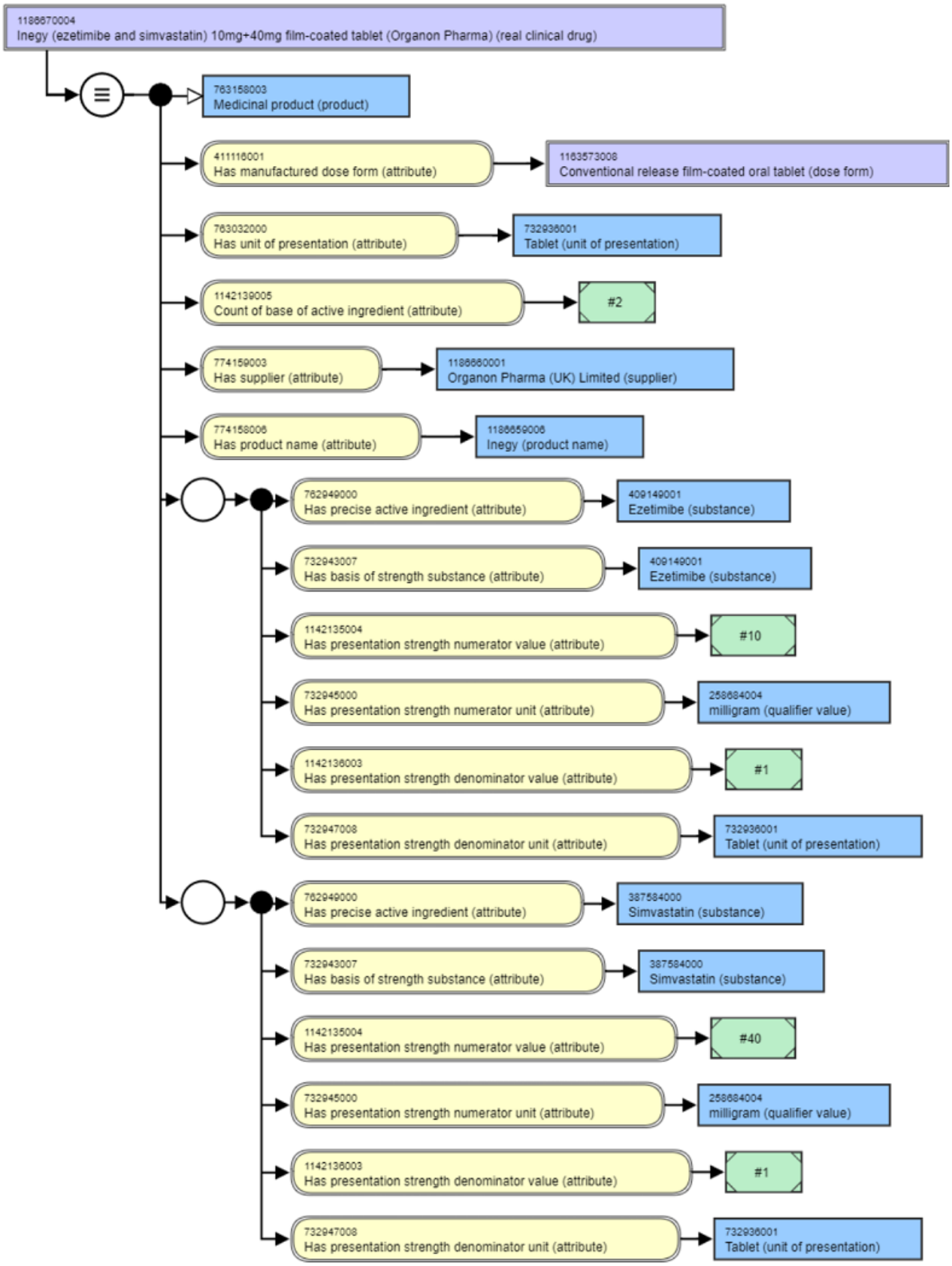

Figure 24: Multiple active ingredient substance (presentation strength) real clinical drug example - stated view

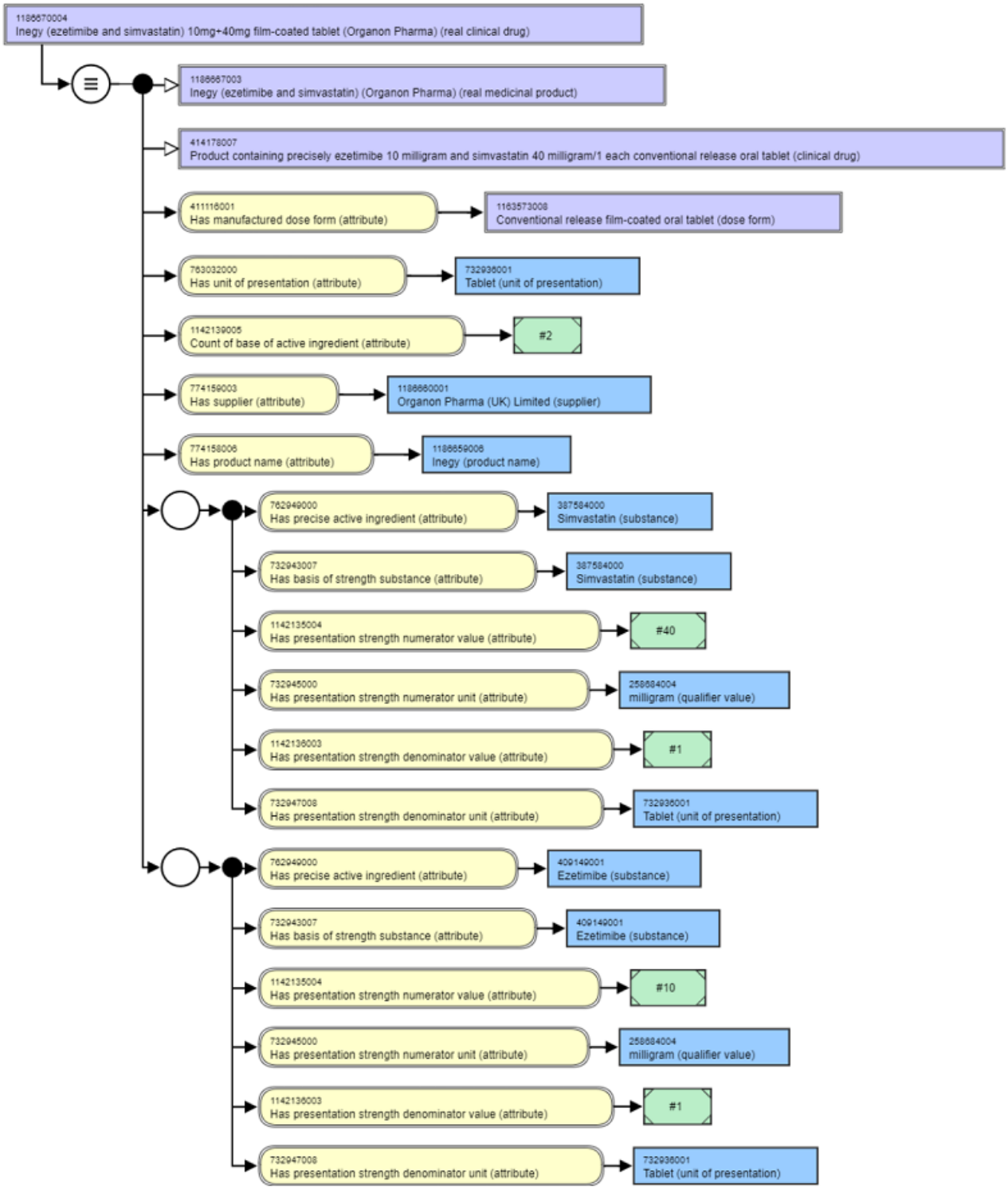

Figure 25: Multiple active ingredient substance (presentation strength) real clinical drug example - inferred view

Example: single active ingredient substance branded product (Canesten) (concentration strength): stated view followed by the inferred view

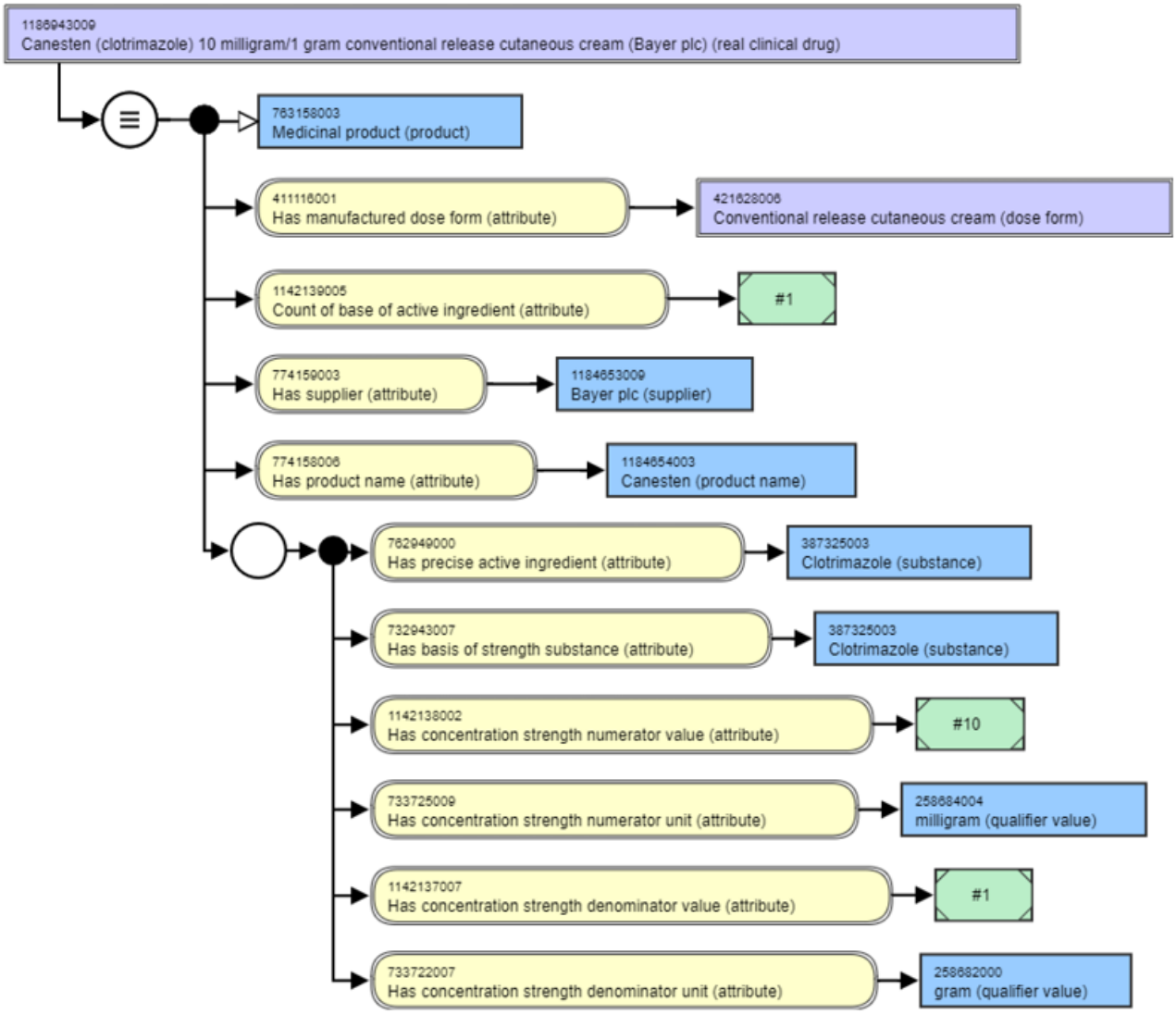

Figure 26: Single active ingredient substance (concentration strength) real clinical drug example - stated view

Figure 27: Single active ingredient substance (concentration strength) real clinical drug example - inferred view

Example: single active ingredient substance product (Gentamicin ampule (Hospira)) (concentration and presentation strength) with equivalent clinical drug: stated view followed by the inferred view

In this example, a concentration and presentation strength clinical drug has been authored in the national extension, and therefore, the real clinical drug classifies under this concept.

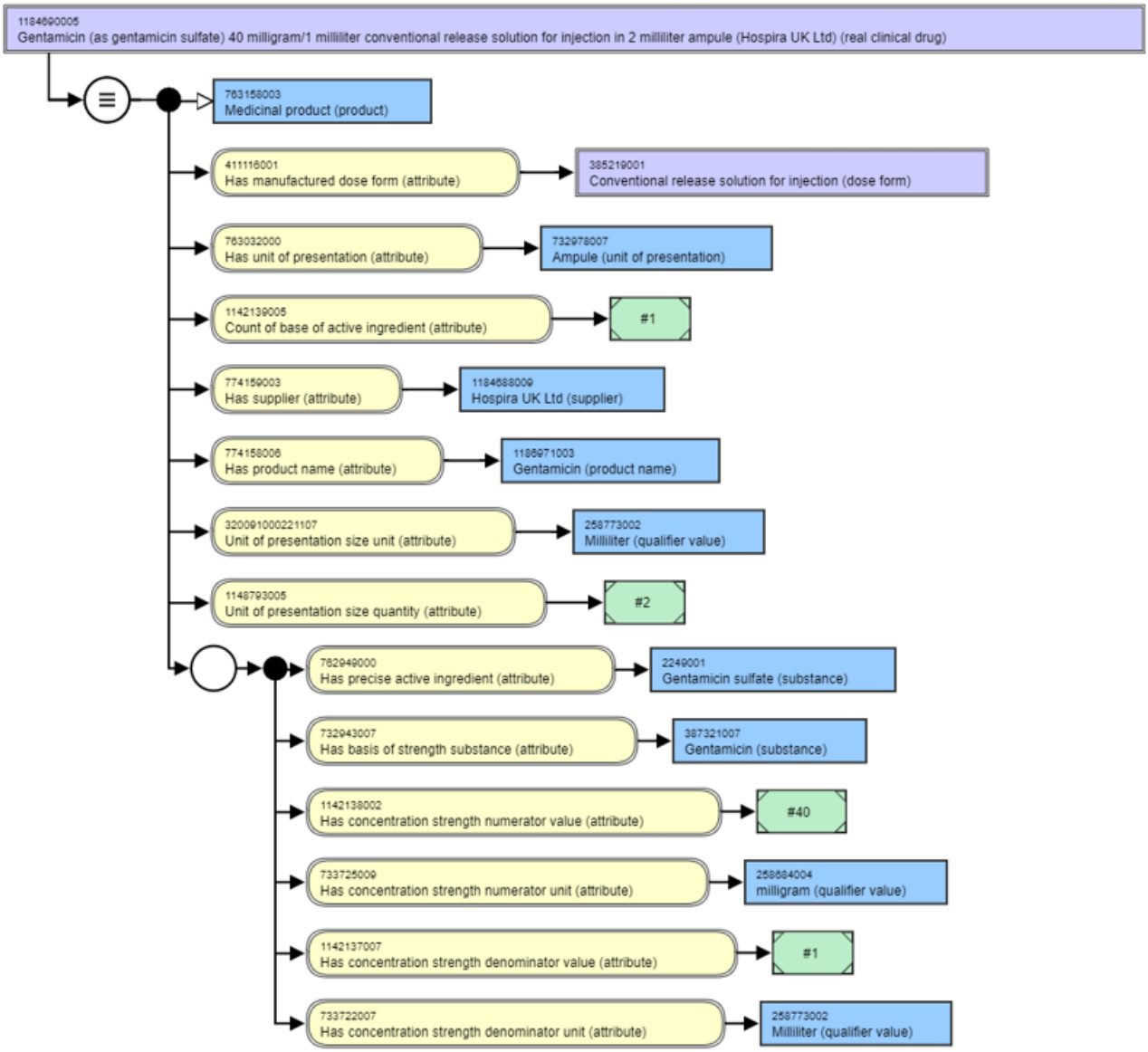

Figure 28: Single active ingredient substance (concentration and presentation strength) <u>with</u> equivalent clinical drug - real clinical drug example - stated view

Figure 29: Single active ingredient substance (concentration and presentation strength) <u>with</u> equivalent clinical drug - real clinical drug example - inferred view

Example: single active ingredient substance product (Gentamicin vial (Hospira)) (concentration and presentation strength) <u>without</u> equivalent clinical drug: stated view followed by the inferred view

In this example, a concentration and presentation strength clinical drug has been NOT authored in the national extension, and therefore, the real clinical drug classifies under the concentration strength concept in the international edition.

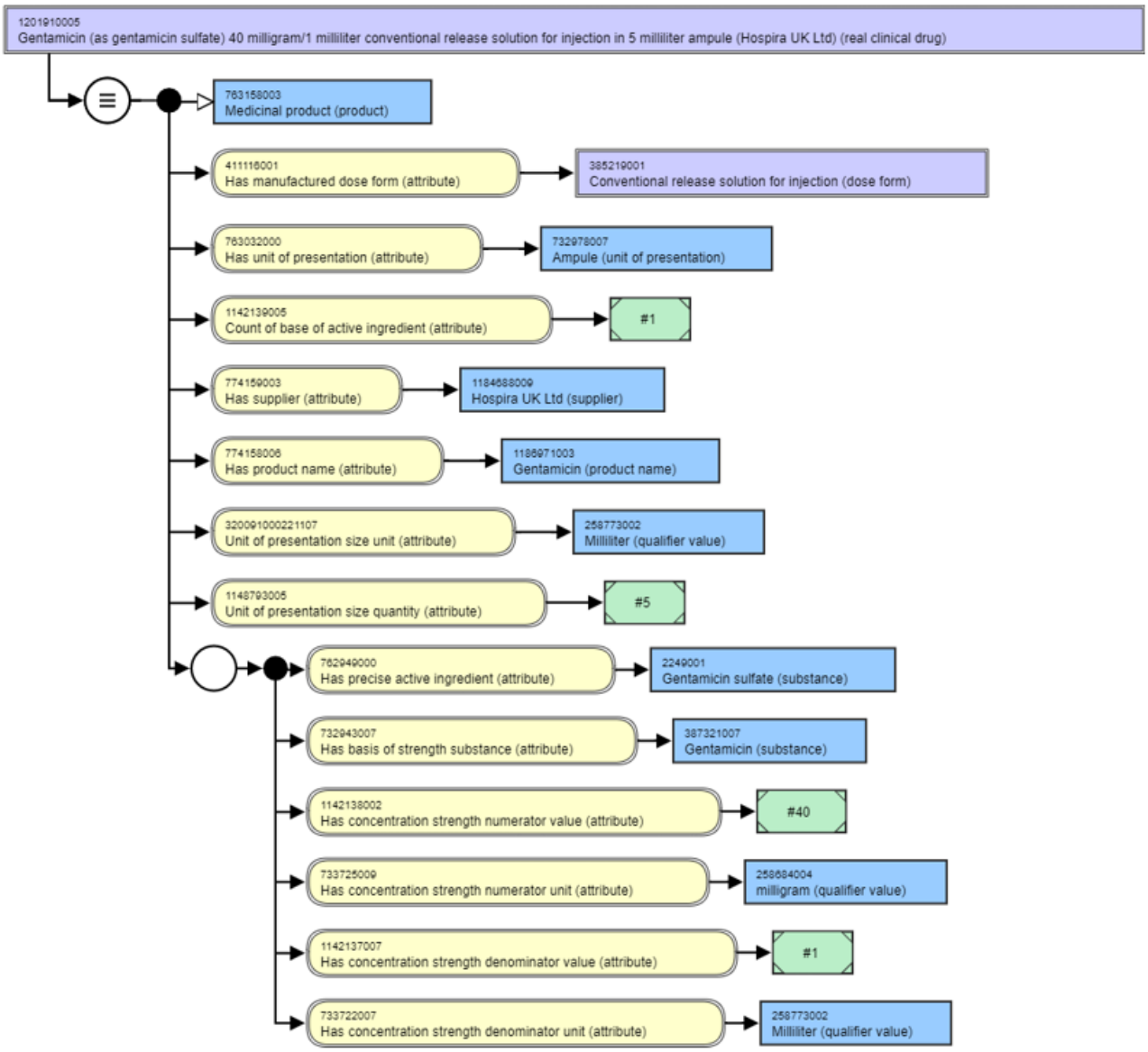

Figure 30: Single active ingredient substance (concentration and presentation strength) <u>without</u> equivalent clinical drug - real clinical drug example - stated view

Figure 31: Single active ingredient substance (concentration and presentation strength) <u>without</u> equivalent clinical drug - real clinical example - inferred view

Optional Additional Information

National extensions that function as national medicinal product dictionaries may require information that extends beyond the characteristics of the product as described here in this specification for real clinical drugs. Product characteristics can be included *within* the SNOMED CT structure using attributes and values, whereas knowledge about the product should be managed *alongside* the SNOMED CT structure (e.g., in a reference set), and relationships between identification systems should be managed in cross maps.

- Product characteristics may include describing excipient substances to support allergy or intolerance checking. Excipient substance roles may include flavours, colours, preservatives, and stabilisers/fillers.
- Knowledge about the product may include usage information, such as availability within the supply chain, licensing/authorization category and/or legal status of supply and prescribability information including reimbursement categories
- Other identification systems for a real clinical drug may include licensing/authorization number or Global Trade Identification Number (GTIN)

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.

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, whereas this model describes combination products as packaged products only. 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.

2.5 Packaged Clinical Drug (PCD)

Definition

An abstract 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 lefthand 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 below.

Use Cases

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 Real Packaged Clinical Drug 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

Discussion

Packs of medicinal products must be represented using the closed world view; they contain ***only*** the clinical drug content stated. The packaged clinical drug class is related to the clinical drug class by a composition relationship, the package *contains* the clinical drug. To correctly describe this and so to ensure that pack concepts classify correctly, and 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 "clinical drug count" attribute as a proxy for the closed world view, in a similar way to the use of the active ingredient count attribute used for MP only concepts, MPF only concepts, and clinical drug concepts. By using a "count" attribute in the definition of closed world concepts, the count information is machine processable, and therefore, if/when a more expressive description logic becomes available to properly represent the closed world view, then all the count attributes can be used to transfer to the closed world description logic consistently.

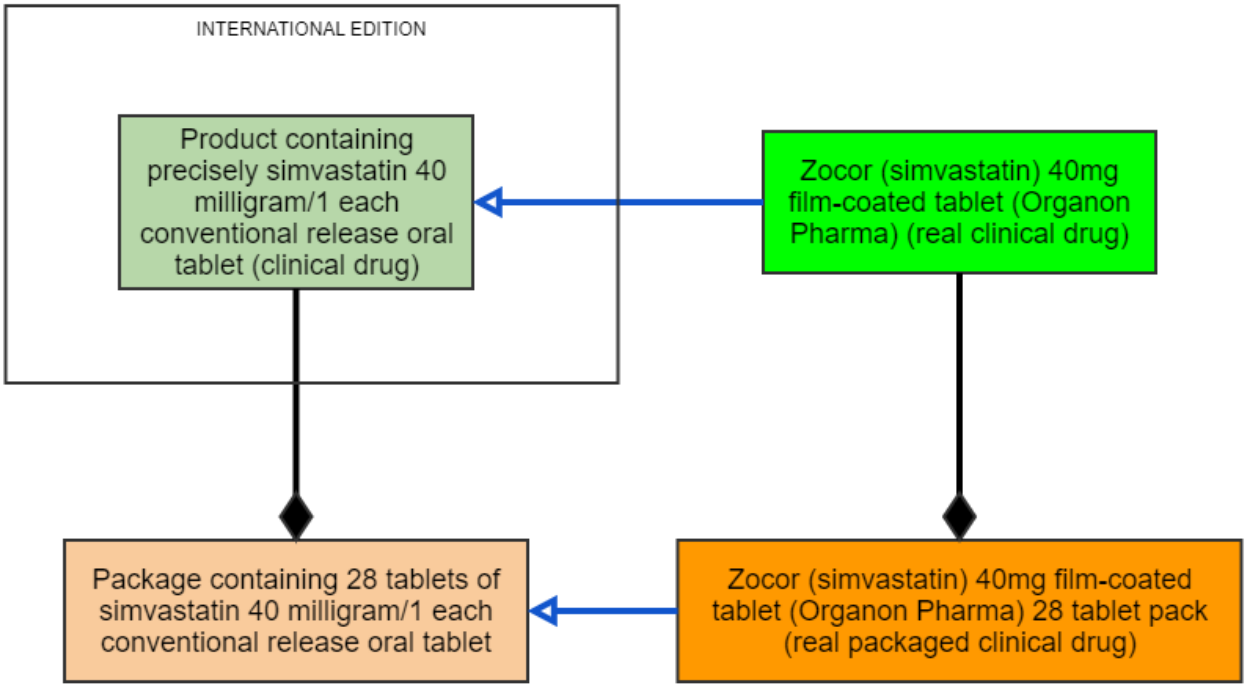

Figure 32: Diagram of the packaged clinical drug class and its composition relationship to clinical drug, with an example (Zocor)

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 and is currently out of scope for this initial version of the national extension specification. In most nations, sub-packs are 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.

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

Attributes

The following table describes the attributes for packaged clinical drugs that contain one type of clinical drug only. That is they are NOT combination (multi-component or kit) products.

The packaged clinical drug class is related to the clinical drug class by a composition relationship, and therefore, the 774160008 | Contains clinical drug (attribute)| 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 is for continuous products such as semi-solid

dose forms of creams, gels, etc. where strength pattern 3a is used (see International Medicinal Product Model). In all cases the pack size and pack size unit should relate to the denominator unit of the strength.

<table>
<tr><td colspan="2">Semantic tag</td><td>(packaged clinical drug)</td></tr>
<tr><td colspan="2">Definition status</td><td>900000000000073002 |Sufficiently defined concept definition status (core metadata concept)|</td></tr>
<tr><td colspan="2">Attribute: 1142143009 |Count of clinical drug type|</td><td>Range INT (integer) Cardinality 1..1 Note This attribute provides the number (count) of distinct clinical drug (concepts) present in the package. For all non-combination packages, this value should be "one".</td></tr>
<tr><td rowspan="2">Role Group
[1..*]
(although for all packages other than combination products it is 1..1)</td><td>Attribute: 774160008 |Contains clinical drug|</td><td>Range < 763158003 |Medicinal product (product)| Cardinality 1..1 Note This attribute value represents the clinical drug that is contained in the packaged product.
It is currently not possible to explicitly specify an expression to describe the range of clinical drugs to populate this attribute, since a range cannot currently recognise a set of concepts with a particular semantic tag - in this case, (clinical drug). Alternative range expressions could be used, based on the definitional attributes of a clinical drug. For the interim, the range is specified as the descendants of the root medicinal product concept: 763158003 |Medicinal product (product)|.</td></tr>
<tr><td>Attribute: 1142142004 |Has pack size|</td><td>Range INT (integer) Cardinality 1..1 Note This attribute represents the amount or quantity of clinical drug present in the package; for presentation strength it is the number of countable units of presentation in the package; for concentration strength it is the mass or volume of the continuous dose form in the package</td></tr>
</table>

	Attribute: 774163005 |Has pack size unit|	**Range** • < 767524001 |Unit of measure (qualifier value)| **Cardinality** • 1..1 **Note** • This attribute value represents the unit of measure of the pack size; for presentation strength it is the unit of presentation in the package; for concentration strength it is the unit of mass (e.g. gram) or volume (e.g. millilitre) of the continuous dose form in the package. More specific range expressions such as "One of EITHER <732935002 | Unit of presentation (unit of presentation) - OR <258680008 | Unit of mass (qualifier value) OR <258769000 | Unit of volume (qualifier value)" 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".

Example Diagrams

Some examples of packaged clinical drug (PCD) concepts are shown below.

Stated template view:

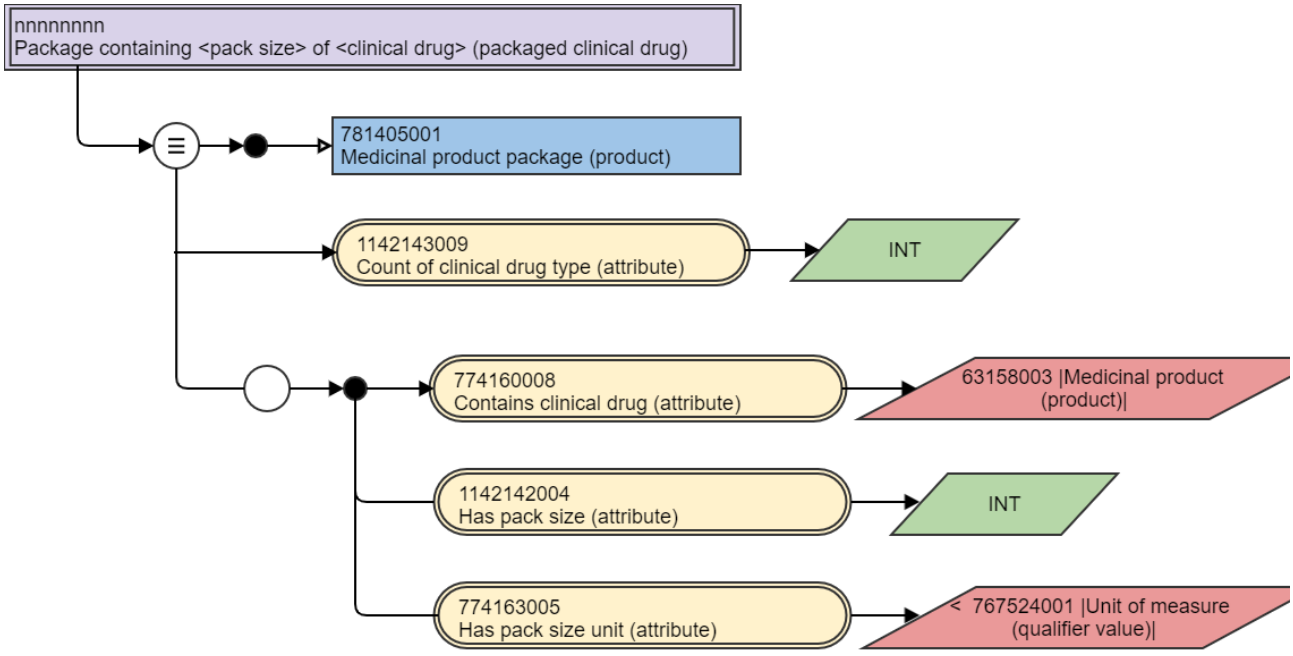

Figure 33: Template for simple packaged clinical drug

Example: single active ingredient substance presentation strength packaged clinical drug: stated view followed by the inferred view

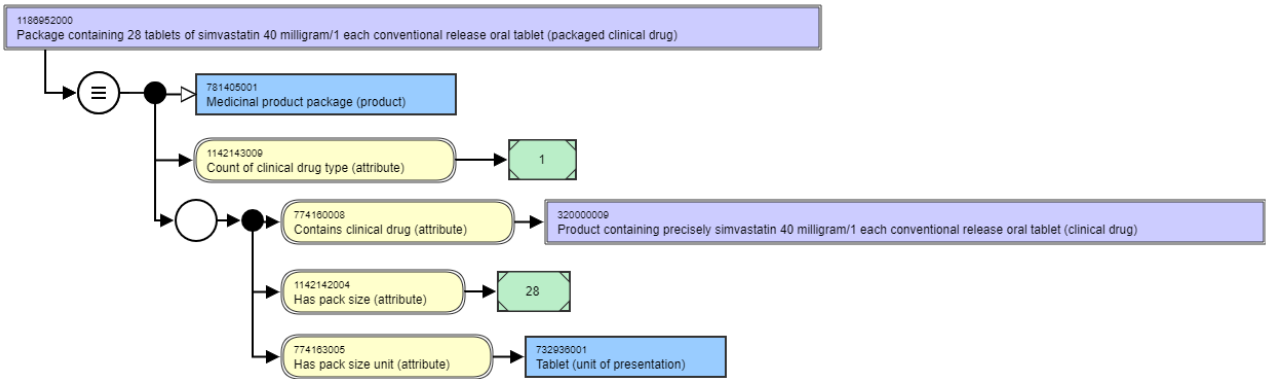

Figure 34: Example of a presentation strength packaged clinical drug - stated view

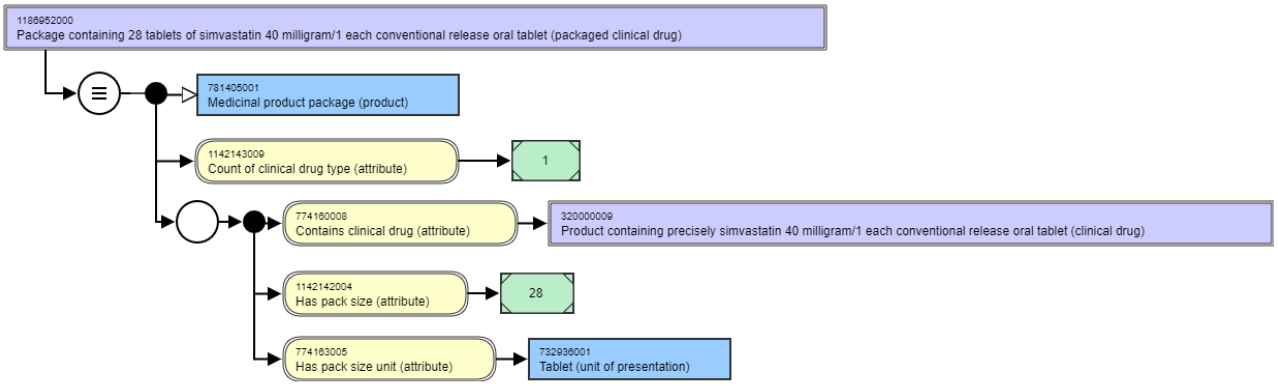

Figure 35: Example of a presentation strength packaged clinical drug - inferred view

Example: single active ingredient substance presentation strength packaged clinical drug: stated view followed by the inferred view

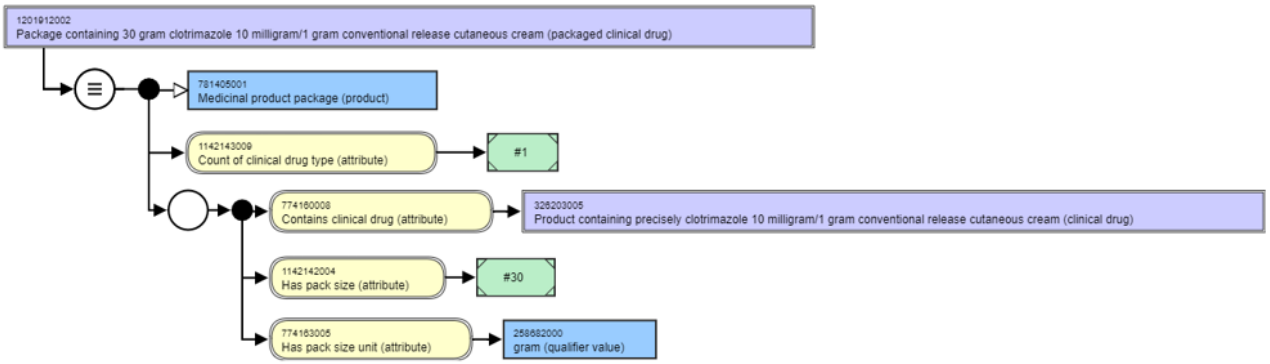

Figure 36: Example of a concentration strength packaged clinical drug - stated view

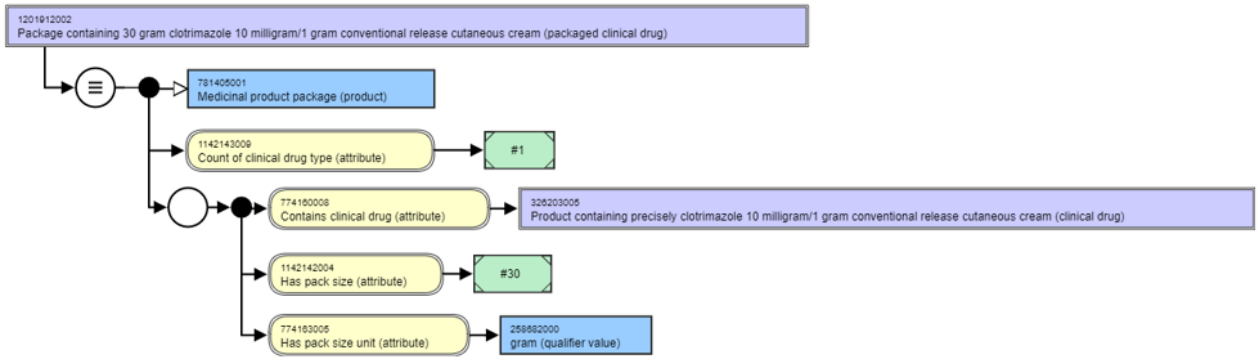

Figure 37: Example of a concentration packaged clinical drug - inferred view

Optional Additional Information

The following information may be additionally used to describe characteristics of the packaged clinical drug concept in a national extension:

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

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.

2.6 Real Packaged Clinical Drug (RPCD)

Definition

The representation of a medicinal product as it is 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. It is a subtype of, and real world equivalent to, the Packaged Clinical Drug (PCD) class.

Use Cases

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

- 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 automatic identification and data capture (AIDC), for example, scanning the bar code on the package)
- Compliance monitoring, using pack size information to calculate whether a patient is following the dosage instructions correctly (how quickly a repeat supply of a package of medication is required)
- Anti-counterfeiting: in support of initiatives such as the Falsified Medicines Directive (see amended Directive 2001/83/EC) using AIDC and which requires 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 labeling issues

- The association between the clinical representation of medicinal products and their representation in the supply chain for supply chain management

Discussion

The real packaged clinical drug represents the product as its packaged products that are marketed into the supply chain in any jurisdiction. A small number of regulatory authorities license medicines at this level, with each package having a separate authorisation; others allow all the different package sizes to be authorised by the single authorisation of the RCD. Real packaged clinical drugs must be represented using the closed world view; they contain ***only*** the content as stated in the logical definition. Since this class represents real product packages 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 packaged clinical drug concepts, should a national extension wish to do this.

The real clinical packaged drug is the marketed (therefore "real") instantiation in any one country of the abstract packaged clinical drug in the international edition, and as such, real packaged clinical drugs classify as child concepts of the packaged clinical drug, if the national extension has authored these concepts.

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 real packaged clinical drug concepts are advised to define their real packaged clinical drug concepts using real clinical drug concepts from their national extension. This allows grouping of package concepts with their associated real clinical drug using the 774160008 |Contains clinical drug (attribute)| value and information from that (for example, excipient information) can be transferred through that composition relationship if required.

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
- "Product" class in the Dutch Z-Index

Attributes

The following table describes the attributes for real packaged clinical drugs (RPCDs) that contain one type of clinical drug only. That is, they are NOT combination (multi-component or kit) products.

The real packaged clinical drugs class is related to the real clinical drug class by a composition relationship, and therefore the attribute |Contains real clinical drug (attribute)| is used to make the association between the real packaged clinical drug and the (real) clinical drug it contains.

Representation of real packaged medicinal products should use 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 is for continuous products such as semi-solid dose forms of creams, gels, etc. where strength pattern 3a is used (see International Medicinal Product Model). 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 real clinical drugs and/or product names and manufacturer / supplier organisations
Attribute: 1142143009 |Count of clinical drug type|	**Range**

		• INT (integer) **Cardinality** • 1..1 **Note** • This attribute provides the number (count) of distinct clinical drug (concepts) present in the package. For all non-combination packages, this value should be "one"
Role Group [1..*] (although for all packages other than combination products it is 1..1)	**Attribute:** 774160008 |Contains clinical drug|	**Range** • < 763158003 |Medicinal product (product)| **Cardinality** • 1..1 **Note** • This attribute value represents the real clinical drug that is contained in the packaged product It is currently not possible to explicitly specify an expression to describe the range of real clinical drugs from a national extension to populate this attribute, since a range cannot currently recognise a set of concepts with a particular semantic tag - in this case "(real clinical drug)". For the interim, the range is specified as the descendants of the root medicinal product concept: 763158003 |Medicinal product (product)|.
	Attribute: 1142142004 |Has pack size|	**Range** • INT (integer) **Cardinality** • 1..1 **Note** • This attribute represents the amount or quantity of clinical drug present in the package; for presentation strength it is the number of countable units of presentation in the package; for concentration strength it is the mass or volume of the continuous dose form in the package
	Attribute: 774163005 |Has pack size unit|	**Range** • < 767524001 |Unit of measure (qualifier value)| **Cardinality** • 1..1 **Note**

		• This attribute value represents the unit of measure of the pack size; for presentation strength, it is the unit of presentation in the package; for concentration strength, it is the unit of mass (e.g. gram) or volume (e.g. millilitre) of the continuous dose form in the package. More specific range expressions such as "One of EITHER <732935002 | Unit of presentation (unit of presentation) - OR <258680008 | Unit of mass (qualifier value) OR <258769000 | Unit of volume (qualifier value)" 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".

Example Diagrams

Some examples of real packaged clinical drugs are shown below.

Stated template view:

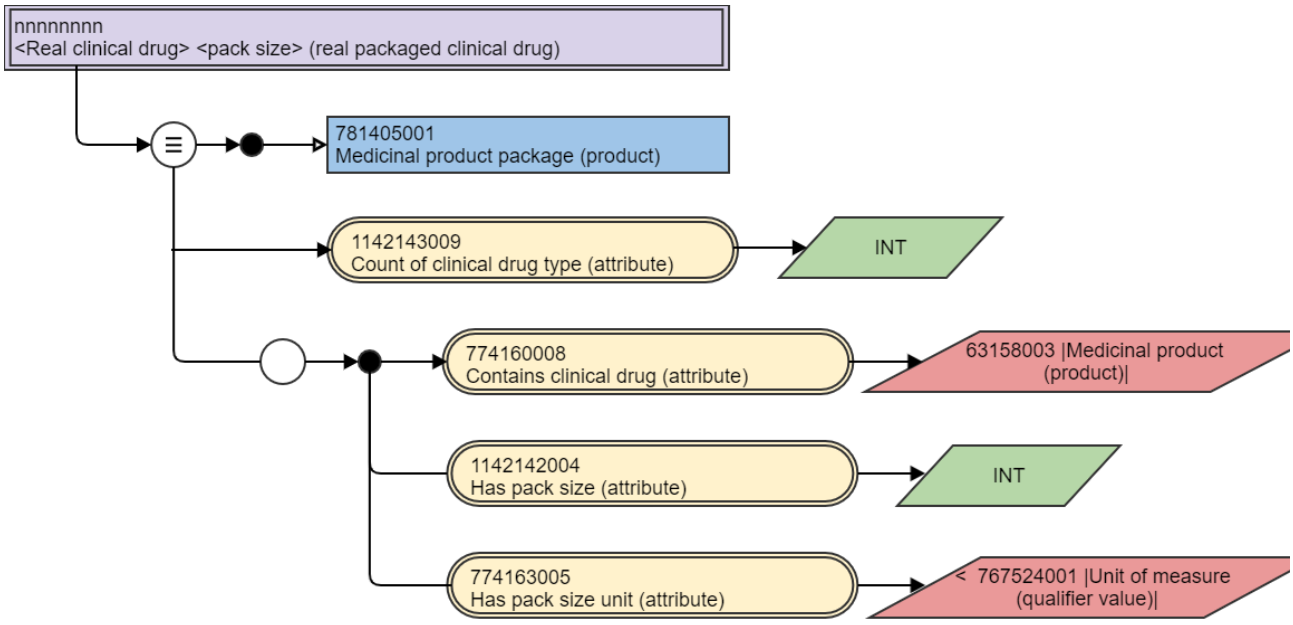

Figure 38: Template for a simple real packaged clinical drug

Example: simple real packaged clinical drug: stated view followed by the inferred view

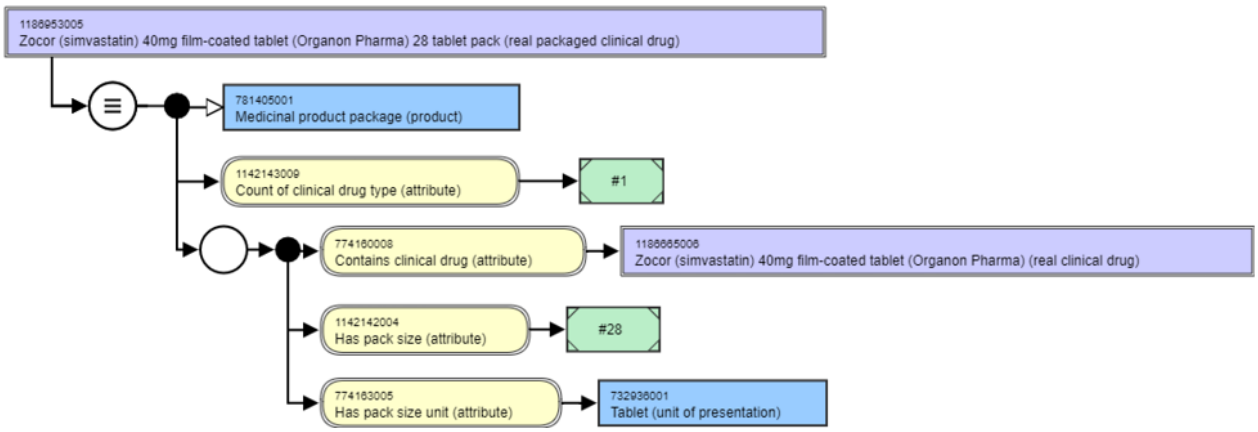

Figure 39: Example of a real packaged clinical drug - stated view

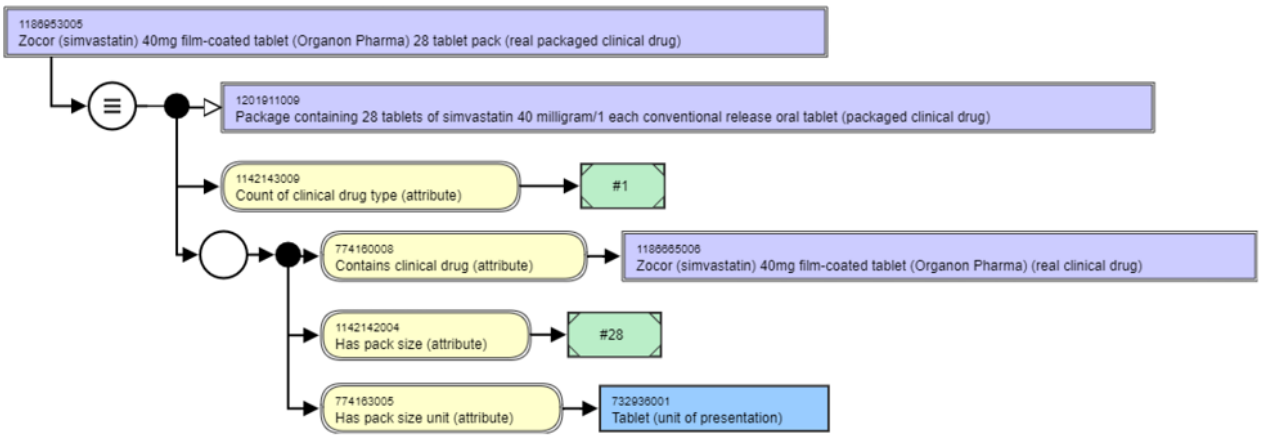

Figure 40: Example of a real packaged clinical drug - inferred view

Optional Additional Information

As with the real clinical drugs, national extensions may require additional information to be associated with real packaged clinical drugs. This may include characteristics of the packaged product that can be described *within* the SNOMED CT structure using attributes and values, managed *alongside* the SNOMED CT structure (e.g., in a reference set) and/or relationships between identification systems should be managed in cross maps.

- Packaged product characteristics may include package/container types (e.g. bottle, box, jar, tube - to support various use cases including robotic dispensing) and administration device supplied in the package (e.g. medicine spoon, vaginal applicator, applicator brush for cutaneous liquid products)
- Knowledge about the product may include usage information such as availability within the supply chain, licensing/authorization category and/or legal status of supply, and prescribability information including reimbursement categories
- Other identification systems for a real packaged clinical drug may include licensing/authorization number, if this is provided for individual packages or Global Trade Identification Number

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 packaged clinical drug and the real clinical drug supplied by the original manufacturer, if that is present within the jurisdiction.

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).

2.7 Combination (Real) Packaged Clinical Drugs

Definition

The representation of a medicinal product as it is supplied in a package that contains within the package more than one type of clinical drug.

Use Cases

The use cases supported by the Combination (Real) Packaged Clinical Drug concept type are the same as those for the basic real packaged clinical drug with the additional detail that administration records may wish to identify which of the particular component clinical drugs were administered at any particular point in time of the administration event (using AIDC or similar).

Discussion

For abstract concepts, the combination packaged clinical drug contains two or more different clinical drugs.

For real concepts, the combination real packaged clinical drug contains two or more different real clinical drugs. The package is placed in the supply chain using a single name (which may be a trade or brand name) by a single supplier organisation, even if one or more of the component real clinical drugs is sourced from a different organisation. For this reason, the 774158006 |Has product name| and 774159003 |Has supplier| attributes are optionally included.

A combination packaged clinical drug 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* or a *combination medicinal product*. Occasionally a combination packaged clinical drug may be known as a *compound product*, but this 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 clinical drug include a package each containing:

- clotrimazole cutaneous cream and one or more clotrimazole vaginal tablets for treatment of vaginal candidiasis
- clotrimazole cutaneous cream and one or more fluconazole oral capsules for treatment of vaginal candidiasis
- combinations of ethinylestradiol 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)
- amoxicillin, clarithromycin and lansoprazole for treatment of Helicobacter infection
- a budesonide dispersible tablet and the vehicle to disperse it in to make a rectal solution for treatment of colitis
- rasburicase 1.5 mg powder for solution for injection and the diluent solution

This specification for national drug extensions recommends that a combination packaged clinical drug should be represented only as packaged products (real packaged clinical drugs, and if an abstract representation is 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 include combination packaged clinical drug 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:

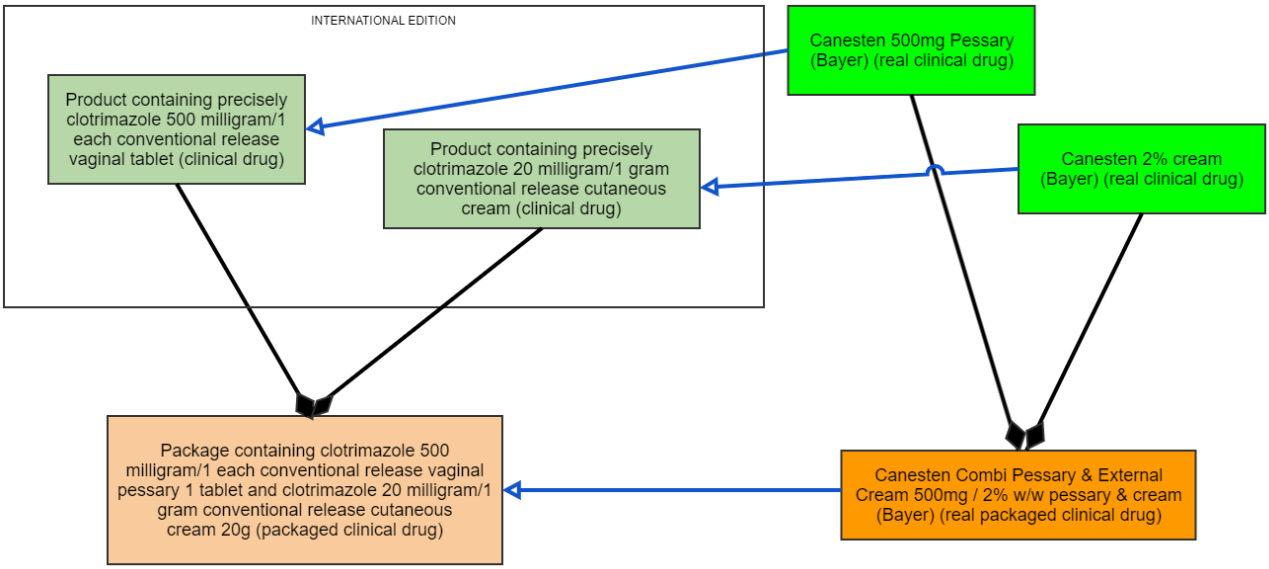

Figure 41: Diagram of options for a national extension describing combination real packaged clinical drugs

In some representations of combination packages, 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 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.

For those combination packages that contain a diluent as an 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.

Attributes

The following table describes the attributes for combination (real) packaged clinical drugs in a national extension.

The (real) packaged clinical drug class is related to the clinical drug class by a composition relationship, and therefore, the 774160008 | Contains clinical drug (attribute)| 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 is for continuous products such as semi-solid dose forms of creams, gels, etc. where strength pattern 3a is used (see International Medicinal Product Model). In all cases, the pack size and pack size unit should relate to the denominator unit of the strength.

Semantic tag		(packaged clinical drug) OR (real packaged clinical drug)
Definition status		900000000000073002 |Sufficiently defined concept def **Note**: This can only be the case if extensions author co manufacturer / supplier organisations
Attribute: 1142143009 |Count of clinical drug type (attribute)|		**Range** • INT (integer) **Cardinality** • 1..1 **Note** • This attribute provides the number (cou package. For combination packages, th
Attribute Attribute: 774158006 |Has product name (attribute)|		< 774167006 |Product name (product name)| ▪ Extensions must author product 774167006 | Product name (proc **Cardinality** • 0..1 **Notes** • The attribute value should represent th trademarked name and is often referre • This attribute should only be valued in t combination product is known to be dif clinical drugs
Attribute: Attribute: 774159003 |Has supplier (attribute)| 774159003 |Has supplier (attribute)|		< 774164004 |Supplier (supplier)| ▪ Extensions must author concept their extension using the root of hierarchy **Cardinality** • 0..1 **Notes** • The attribute value should represent th authorisation for supply; this may or ma manufacture of the product (see section • This attribute should only be valued in t combination product is known to be dif drugs
Role Group 1..* for combination packaged clinical drugs	**Attribute:** **774160008 |Contains clinical drug (attribute)|**	< 763158003 |Medicinal product (product)| **Cardinality** • 1..1 **Note** • This attribute value represents the real It is currently not possible to explicitly s

		clinical drugs from a national extension currently recognise a set of concepts wi drug)". For the interim, the range is spe concept: 763158003 |Medicinal product
	Attribute: **1142142004 |Has pack size (attribute)|** 1142142004 |Has pack size (attribute)|	**Range** • INT (integer) **Cardinality** • 1..1 **Note** • This attribute represents the amount or in the package; for presentation strengt the package; for concentration strength the package
	Attribute: **774163005 |Has pack size unit (attribute)|**	< 767524001 |Unit of measure (qualifier value)| **Cardinality** • 1..1 **Note** • This attribute value represents the unit presentation strength it is the unit of pr is the unit of mass (e.g. gram) or volume package. More specific range expressions such as of presentation) OR <258680008 | Unit o (qualifier value)" are currently not supp (for example) assert "if the clinical drug Has_pack_size_unit will be valued as 't

Example Diagrams

Example: combination packaged clinical drug: stated view followed by the inferred view

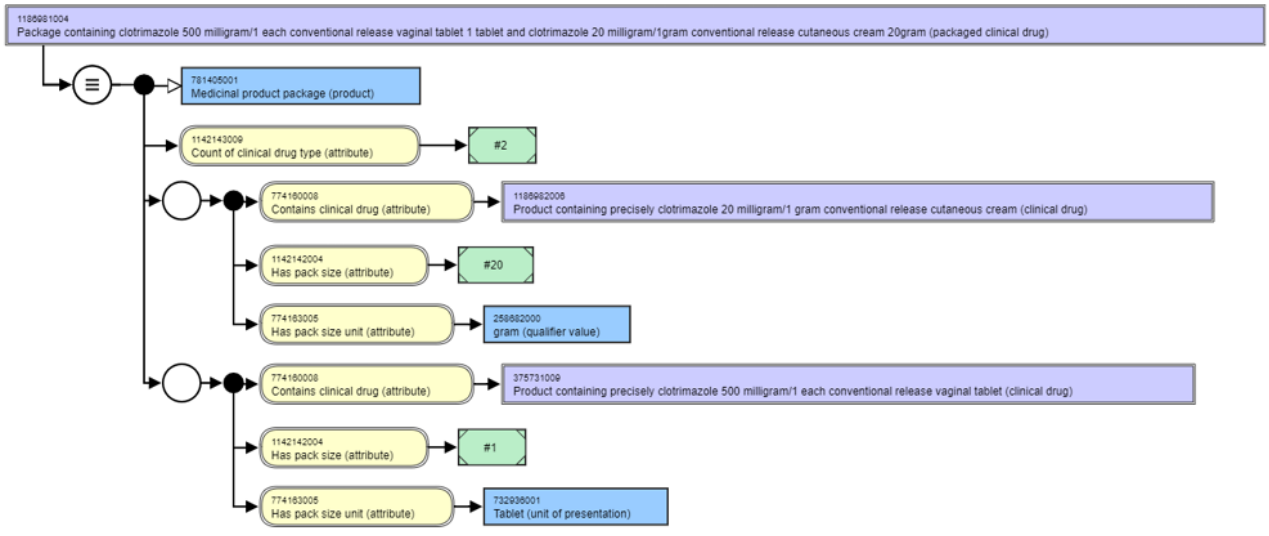

Figure 42: Example of a combination packaged clinical drug - stated view

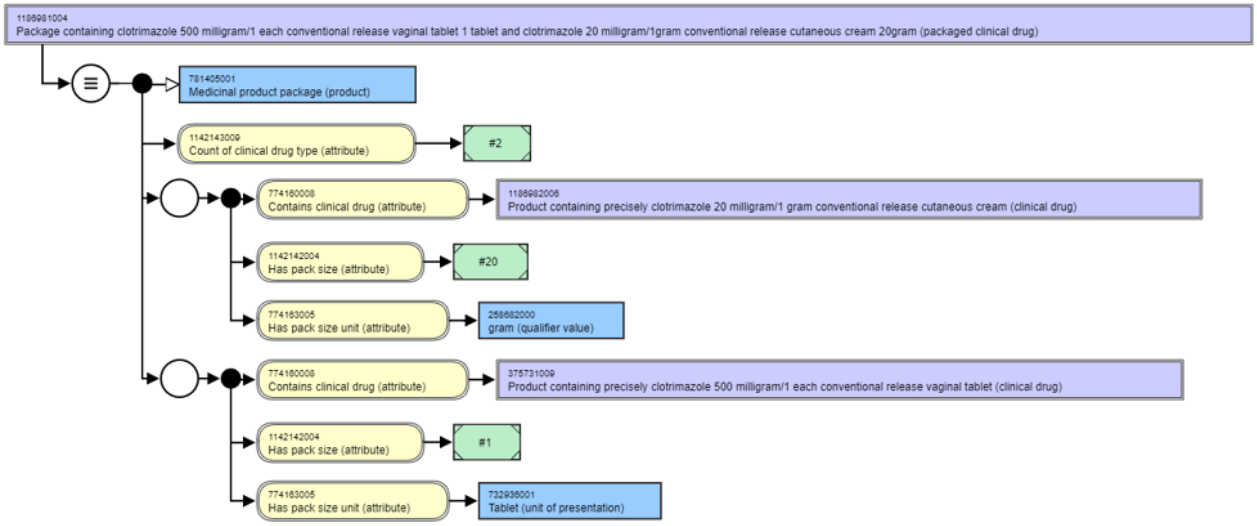

Figure 43: Example of a combination packaged clinical drug - inferred view

Example: combination real packaged clinical drug: stated view followed by the inferred view

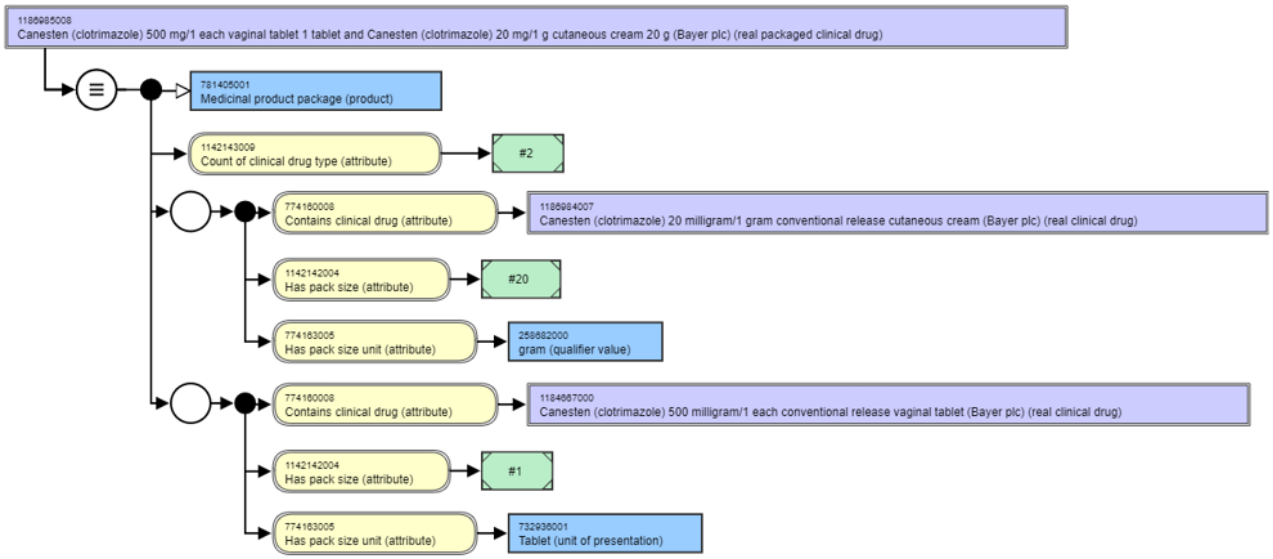

Figure 44: Example of a combination real packaged clinical drug - stated view

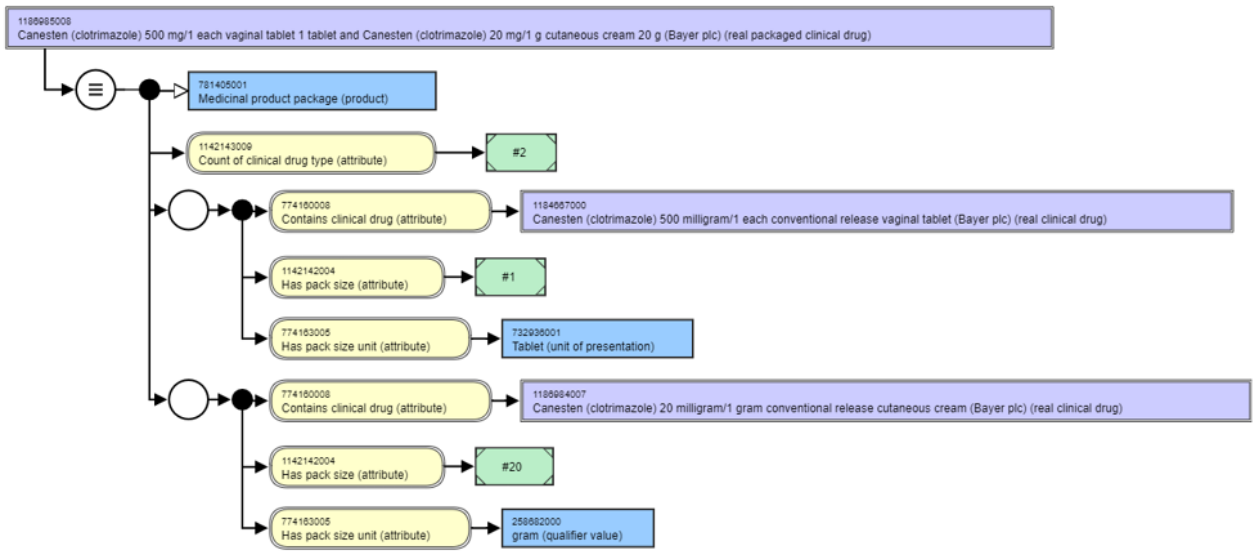

Figure 45: Example of a combination real packaged clinical drug - inferred view

IDMP Compatibility

Since the ISO 11615 standard treats all Packaged Medicinal Products in the same manner whether they are standard products or combination products, and 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 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.

2.8 Supporting Attributes

The section describes the attributes used in the definition of the concepts classes in the national extension model. Descriptions of the attributes used in both the international content and the national extension are given in the international Medicinal Product Hierarchy Specification.

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*.

Discussion

The 774158006 | Has product name (attribute)| is used in the definition of the real medicinal product and the real clinical drug. It is not used in the real packaged clinical drug, as this brings the relevant information via the real clinical drug it contains.

It is not essential that the product name be an invented or brand name; it can be a generic name (for example, using one or more international non-proprietary therapeutic substance names). The product name concepts are authored to value the definitional attribute for the real medicinal products and real clinical drugs in the national extension, and since real packaged clinical drugs contain real clinical drugs, this set of concepts does also.

It is possible for an extension that wishes to author a hierarchy of product name concepts to choose to value the 774158006 | Has product name (attribute)| differently for the different classes of real medicinal product and real clinical drug.

For example,

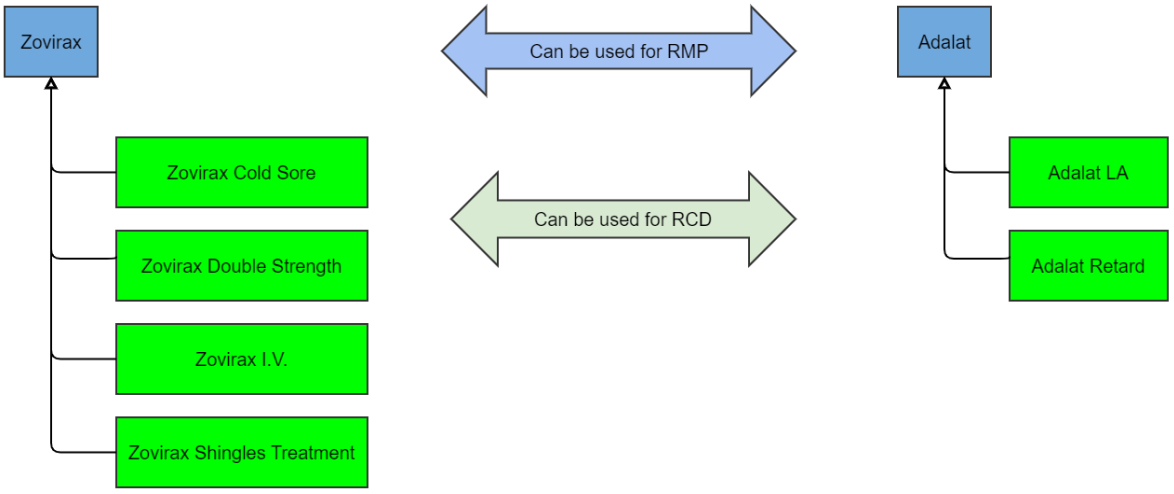

Figure 46: Diagram of examples of a product name hierarchy

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 and associated real clinical drug concepts. It is therefore most useful if the parent product name does not include any reference to dose form (e.g., "LA" or "Retard") or to strength (e.g., "Double Strength") 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.

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 can have a different meaning in different jurisdictions.

The 774158006 |Has product name (attribute)| is available from the concept model attribute hierarchy; values for 774158006 | Has product name (attribute)| should be authored in the national extension using the root of 774167006 | Product name (product name)| from the Qualifier hierarchy.

Has supplier

Definition

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

Discussion

The 774159003 | Has supplier (attribute)| is used in the definition of the real medicinal product and the real clinical drug. It is not used in the real packaged clinical drug, as this brings the relevant information via the real clinical drug it contains.

Medicinal products, like other complex products, are rarely *manufactured* by one single organisation; the substances in a product 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 professional and public facing information about the product. To avoid confusion in this specification, the term *manufacturer* has not been used; instead , *supplier* is the term used and 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 management of all adverse event information relating, or possibly relating to, the product in use. All of those are the responsibility of the organisation that is authorised to *supply* the product into the supply chain. Some healthcare cultures allow agreements whereby an organisation may obtain stocks of a medicinal product and then to repackage or relabel 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 repackaging/relabeling 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 must decide the principles under which to populate the 774159003 |Has 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 repackaging or relabeling 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* in Europe) or whether both are allowed, and how the authorisations for these are managed and therefore which organisation (the licensed repackager 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/or 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

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. For those extensions that populate the real medicinal product concept class, in situations where individual real clinical drugs share the same product name but have different supplier organisations, two real medicinal products will exist, as shown in the example below:

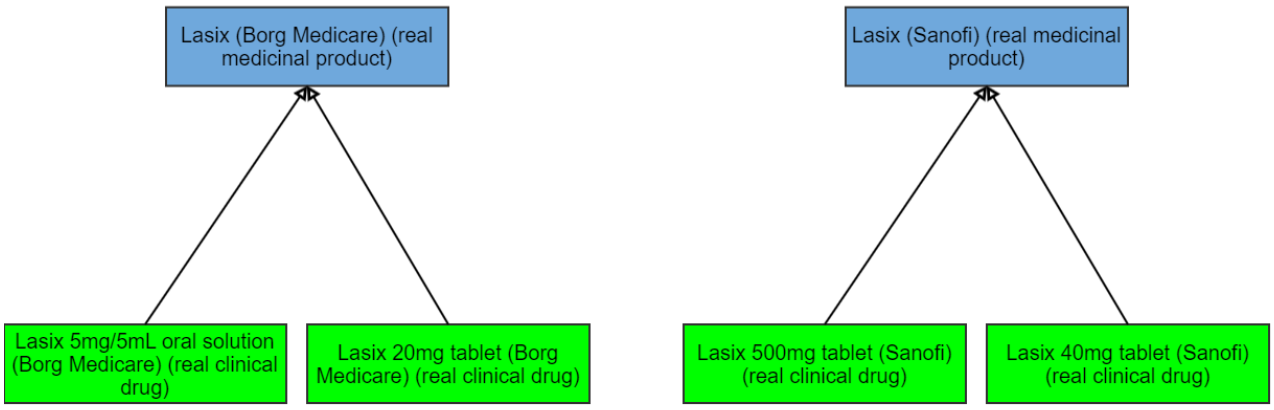

Figure 47: Diagram to show RCDs sharing a single product name associated with different RMPs due to having different suppliers

The 774159003 | Has supplier (attribute) | is available from the concept model attribute hierarchy. 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 using 774164004 | Supplier (supplier) | from the Qualifier hierarchy as the root concept.

Count of clinical drug type

Definition

The number (count) of of distinct clinical drug (concepts) present in the package. For all non-combination packages, this value should be "one".

Discussion

The 1142143009 | Count of clinical drug type (attribute)| is used in the definition of the packaged clinical drug and the real packaged clinical drug.

Count attributes are used for all medicinal product and package concepts that must be represented using the closed world view as a proxy for and until a more expressive description logic becomes available to properly represent the universal restriction. Packaged medicinal products must be described as containing *only* those clinical drugs that are stated in the logical definition; no other content is to be contemplated (no open world view). A package containing 500mg paracetamol tablets must contain explicitly and only 500mg paracetamol tablets (not paracetamol capsules, or paracetamol and codeine tablets). To correctly describe this, and particularly 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 *clinical drug count*. This follows a similar pattern to the use of the active ingredient count attribute used for MP only concepts, MPF only concepts, and clinical drug concepts.

By using a *count* attribute in the definition of closed world concepts, the count information is machine processable, and therefore if/when a more expressive description logic becomes available to properly represent the closed world view, then all the count attributes can be used to transfer to the closed world description logic consistently.

Standard packs containing a single clinical drug type have a count of "one" for the 1142143009 | 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.

Contains clinical drug

Definition

The (real) clinical drug contained in the packaged product.

Discussion

The 774160008 | Contains clinical drug (attribute)| is used in the definition of the packaged clinical drug and the real packaged clinical drug.

For packaged clinical drug concepts, the 774160008 | Contains clinical drug (attribute)| should be valued with a clinical drug from the international release or from the national extension (for example, if a liquid presentation has concentration and presentation strength clinical drug representation in the national extension).

For real packaged clinical drug concepts, the 774160008 | Contains clinical drug (attribute)| should be valued with a real clinical drug from the national extension.

As noted in the attribute tables for packaged clinical drug and real packaged clinical drug, it is not possible currently to explicitly specify an expression to describe the range of (real) clinical drugs to populate this attribute since (for example) a range cannot currently recognise a set of concepts with a particular semantic tag. Alternative range expressions could be developed based on the attributes that are unique to a (real) clinical drug. For example:

- For clinical drugs: all products with a dose form, precise ingredient substance, and basis of strength substance
- For real clinical drugs: all products with a dose form, precise ingredient substance, basis of strength substance, product name, and supplier name.

Has pack size and Has pack size unit

Definition

Has pack size: The amount or quantity of clinical drug present in the package

Has pack size unit: The unit of measure appropriate for the pack size

Discussion

For (real) clinical drugs described with a unit of presentation and either a presentation strength or and concentration and presentation strength, 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 (real) clinical drugs with a continuous dose form, described with concentration strength, the pack size is the amount of the clinical drug present in the package with pack size units of either weight or volume as appropriate.

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" - sachet, vial etc.	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"	concentration strength and presentation strength)	"intimate container"	number of units of presentation present in package	same as unit of presentation

Product type	CD strength type	Unit of presentation	Pack size	Pack size unit
Metoclopramine hydrochloride 5 mg per 1 mL solution for injection 20mL 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 3mL cartridge, package of 5 cartridges		*cartridge*	*5*	*cartridge(s)*
Continuous preparation No unit of presentation 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*	*grams*