**Issue Number: 016**

Unit of Presentation in the Canadian Clinical Drug Data Set

### The Issue

Not all NTPs can be uniquely described using only substance-(presentation) strength set and dosage form; for some products, unit of presentation information is required.

1. Background Information

#### NTP supporting model

In the original thoughts for the NTP, the “grouping concept” for use primarily for electronic prescribing without having to specify a manufactured product, we suggested that “unit of presentation” would be needed explicitly for some types of medicinal products (see diagram below).



An NTP represents the aggregation of a unique set of:

* dosage form
* substance-strength set
* *unit of presentation (possibly)*

The products needing unit of presentation are the products that are presented in a “continuous phase” dosage form (liquids and semi-solids) as opposed to those presented in a “discrete solid” dosage form (tablets, capsules, dry powder vials (as the manufactured dosage form prior to any transformation). This is because products presented in a continuous phase must have their strength represented as a concentration ratio, with the denominator usually an SI unit (e.g. “25 mg per 2 mL”, or for the semi-solids, this is converted to a percentage, “2.5%”). In contrast the discrete solid dosage forms express their strength as the amount per unit of presentation, and since the unit of presentation is so closely related to the dosage form, it is not restated (e.g. 500 mg **per tablet** for a clotrimazole vaginal tablet presentation).

Unit of presentation in the Identification of Medicinal Products (IDMP’s) 11615 is defined as “a qualitative term describing the discrete countable entity in which a pharmaceutical product or manufactured item is presented, in cases where strength of quantity is expressed referring to one instance of this countable entity”.

In the discussion at the time, the Advisory Group felt that including the unit of presentation in the NTP was probably not necessary, and given the time constraints it was removed from the working model. In order to circumvent the problems this might cause, the expression of strength for the affected product groups in the Canadian Clinical Drug Data Set (CCDD) has been to explicitly use presentation strength. This “manages” the problem for the vast majority of products, especially when coupled with providing separate Manufactured Product (MP) codes for products currently identified with a single DIN and described in DPD using concentration strength.

#### Problem concepts

Unfortunately, using presentation strength alone cannot differentiate between different units of presentation when the presentation strength is the same. An example (admittedly unlikely to be prescribed in primary care) is amiodarone injection:

* amiodarone hydrochloride 150 mg per 3 mL solution for injection **vial**
* amiodarone hydrochloride 150 mg per 3 mL solution for injection **pre-filled syringe**

BUT the CCDD is encountering problems where two products with the same presentation strength have different units of presentation, which is important for prescribers to know, because they need to select the correct one. The classic example here is the insulins where the presentation strength cannot be used; it must be 100 unit per 1 mL to be clinically safe and recognizable.

For example, the CCDD needs Non-proprietary Therapeutic Products (NTPs) for LANTUS and BASAGLAR products that separate:

* insulin glargine 100 unit per 1 mL solution for injection **3 mL cartridge**
* insulin glargine 100 unit per 1 mL solution for injection **3 mL prefilled pen**
* insulin glargine 100 unit per 1 mL solution for injection **10 mL vial**

and there is also a TOUJEO product whose NTP should be

* insulin glargine **300 unit per 1 mL** solution for injection **1.5 mL prefilled pen**

Providing unique and clinically recognisable NTP concepts for testosterone gel *can* be overcome by using presentation strength:

* testosterone 25 mg per 2.5 g cutaneous gel
* testosterone 50 mg per 5 g cutaneous gel
* testosterone 12.5 mg per actuation cutaneous gel (is OK anyway, because is a metered dose presentation, so strength is per actuation)

But, this does not show that the first two products are individual sachets unless the unit of presentation is also provided (similar to the amiodarone example). If the description of strength is given as is normal for most semi-solid dosage forms (i.e. as a percentage), then “the insulin problem” arises; the need to indicate the amount present in the unit of presentation

* testosterone 1% cutaneous gel 2.5g sachet
* testosterone 1%cutaneous gel 5g sachet

#### Data sources

Unit of presentation information is not easily accessible in the DPD, especially not in a machine-processable format.

For the Top 250 moieties for the initial delivery of the CCDD, most of the data required is available as a result of collecting it during an initial QA process. , The data was sourced primarily from the product monographs. There may be other sources within Health Canada (e.g. the labelling files).

In the long term, this data will be provided by the manufacturers to the regulatory agency in a structured manner as core part of IDMP (ISO 11615). It will therefore be available to be used directly into the CCDD auto-generation process.

For the interim, as CCDD content expands beyond the Top 250 to include more products (especially hospital products) affected by these issue, it is accepted that sourcing this data may be challenge.

### *Proposed actions and Options for resolution*

#### Do nothing

This is not really an option, as the CCDD must have unambiguous NTP formal name descriptions for concepts such as the insulin glargine products above (which have different DINs) so that they can be accurately mapped and the CCDD can function as the interchange terminology to underpinning PrescribeIT.

#### Add additional information related to unit of presentation to the descriptions for those products that need it (e.g. “pseudo-DINs”)

#### Manual Exceptions

Do manual exceptions for the insulins in the Top 250 only; manage the testosterones using presentation strength and ignore about the amiodarone issue, at least initially. This could be an option for the September delivery (insulins are key prescribable products in primary care and must be properly described) but this is not viable going forward.

#### Repurpose the DPD Packaging Table to provide machine processable data

Currently, the DPD Packaging Table has only a very small amount of data, which has not been maintained (30-40 rows of data out of 16405 possible rows). But it has a set of structured fields that could be used to store unit of presentation data in a way that would allow it to be used in the NTP generation process and provide the NTPs needed. These fields could be repurposed as follows:

* The unit of presentation could be stored in the Package\_Type field
  + Unit of presentation type (vial, ampoule, sachet, pre-filled syringe) would be a controlled set of terms, drawn from the EDQM unit of presentation terminology
* The unit of presentation “amount value” could be stored in the Package\_Size field (e.g. ‘3’, ‘1.5’, ‘10’) *for only those products like the insulins where presentation strength is not enough*
* The unit of presentation “amount unit” could be stored in the Package\_Size\_Unit field (e.g. ‘mL’) *for only those products like the insulins where presentation strength is not enough*
* This data is then available for use in the auto-generation of the MPs and the rules for unique NTPs with their formal name
  + When there is data in the Package\_Size field and Package\_Size\_Unit field, use this to prefix the unit of presentation from the Package\_Type field (to give 3 mL pre-filled syringe) then use this to generate unique NTPs and append the information to the currently patterned NTP formal name
  + When there is NO data in the Package\_Size field and Package\_Size\_Unit field, use **only** the unit of presentation from the Package\_Type field and use this to generate unique NTPs and append this to the currently patterned NTP formal name
  + When there is NO data in any field for a product in the DPD Packaging Table, there is no requirement for explicit unit of presentation information in the MP or NTP

Some possible worked examples are shown in the table at the end of this document.

### *Recommendation*

That Option 3 (2.2.2) be pursued.

### *Decision*

Recommendation approved. CCDD Editorial Guidelines will be updated

### *Document History*

|  |  |  |
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|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **DIN** | **DIN name** | **BoSS** | **Strength** | **Dosage form** | **Package Type**  **becomes Unit of presentation type** | **Package Size**  **becomes Presentation amount** | **Package Size Unit**  **becomes Presentation amount unit** | **NTP** |
| 02245689 | LANTUS SANOFI-AVENTIS CANADA INC | insulin glargine | 100 unit per mL | solution for injection | vial | 10 | mL | insulin glargine 100 unit per mL solution for injection 10 mL vial |
| 02251930 | LANTUS SANOFI-AVENTIS CANADA INC | insulin glargine | 100 unit per mL | solution for injection | cartridge | 3 | mL | insulin glargine 100 unit per mL solution for injection 3 mL cartridge |
| 02444844 | BASAGLAR ELI LILLY CANADA INC | insulin glargine | 100 unit per mL | solution for injection | cartridge | 3 | mL |
| 02294338 | LANTUS SANOFI-AVENTIS CANADA INC | insulin glargine | 100 unit per mL | solution for injection | pen | 3 | mL | insulin glargine 100 unit per mL solution for injection 3 mL pen |
| 02444852 | BASAGLAR ELI LILLY CANADA INC | insulin glargine | 100 unit per mL | solution for injection | pen | 3 | mL |
| 02246953 (needs pseudoDIN) | AMIODARONE FOR INJECTION 50MG/ML [TEVA CANADA L](https://health-products.canada.ca/dpd-bdpp/search-fast-recherche-rapide.do?lang=en&code=14318)IMITED | amiodarone hydrochloride | 150 mg per 3 mL | solution for injection | vial |  |  | amiodarone hydrochloride 150 mg per 3 mL solution for injection vial |
| 02242325 (needs pseudoDIN) | AMIODARONE HYDROCHLORIDE FOR INJECTION SANDOZ CANADA INCORPORATED | amiodarone hydrochloride | 150 mg per 3 mL | solution for injection | vial |  |  |
| 02242325 (needs pseudoDIN) | AMIODARONE HYDROCHLORIDE FOR INJECTION SANDOZ CANADA INCORPORATED | amiodarone hydrochloride | 150 mg per 3 mL | solution for injection | syringe |  |  | amiodarone hydrochloride 150 mg per 3 mL solution for injection syringe |
| 02242325 (needs pseudoDIN) | AMIODARONE HYDROCHLORIDE FOR INJECTION SANDOZ CANADA INCORPORATED | amiodarone hydrochloride | 450 mg per 9 mL | solution for injection | vial |  |  | amiodarone hydrochloride 450 mg per 9 mL solution for injection vial |
| 02246953 (needs pseudoDIN) | AMIODARONE FOR INJECTION 50MG/ML [TEVA CANADA L](https://health-products.canada.ca/dpd-bdpp/search-fast-recherche-rapide.do?lang=en&code=14318)IMITED | amiodarone hydrochloride | 900 mg per 18 mL | solution for injection | vial |  |  | amiodarone hydrochloride 900 mg per 18 mL solution for injection vial |
| 02242325 (needs pseudoDIN) | AMIODARONE HYDROCHLORIDE FOR INJECTION SANDOZ CANADA INCORPORATED | amiodarone hydrochloride | 900 mg per 18 mL | solution for injection | vial |  |  |

* Note: not all presentations for insulin glargine or amiodarone are shown in the table

### *Appendices*

## Observations from the UK’s NHS dm+d (Dictionary of Medicines and Devices)

One of the things that was useful to help folk understand the role of the unit of presentation in defining the VMP (the equivalent to the NTP) was to say that the VMP concept represented “**the one thing you hold in your hand**” without any outer packaging. Sometimes that meant that there needed to be something extra, beyond ‘substance-strength set and dosage form’, to fully describe what that “one thing” was:

* For **discrete solid dosage forms**: tablet, capsule, suppository, pessary, vial/ampoule of dry powder for injection; sachet of powder or granules (where the strength is amount per sachet), the one thing you hold in your hand can be explicitly identified just using ‘substance-strength set and dosage form’ because the dosage form tells you what type of thing the ‘one thing’ is
* For **discrete presentations of solid dosage forms** such as sachets of powder or granules the one thing you hold in your hand (the sachet) can be explicitly identified just using ‘substance-strength set and dosage form’ because the strength denominator is explicit (exotocillin 250 mg per 1 sachet oral powder)
* For **discrete presentations of solid dosage forms** such as vials/ampoules of dry powder for injection the one thing you hold in your hand is a vial or ampoule of some sort; this is the unit of presentation, NHS dm+d expresses explicitly (exotamumab 100 mg powder for solution for injection vial)
* For **continuous** **dosage forms**: such as: a 5 mL teaspoonful; vials/ampoules/cartridges of solution/suspension/emulsion for injection; oral solutions/suspensions presented as drops; prefilled syringes; “nebules”/unit dose vials; Expression of presentation strength is explicit for what is held in the hand…*for everything but insulins* etc. where presentation strength is not used. NHS dm+d is explicit in providing the unit of presentation type with the presentation strength when this is sufficient (e.g. methotrexate 12.5mg/0.5ml solution for injection pre-filled syringe) but for those products like the insulins when this is not sufficient, it provides unit of presentation type and amount (e.g. insulin lispro 100units/ml solution for injection **10ml vial** and insulin lispro 100units/ml solution for injection **3ml cartridge**)
* For continuous **dosage forms** **where strength is expressed as a percentage**, this is just “continuous stuff”; creams, ointments, gels, eye drops, ear ointments. The “one thing you hold in your hand is a squidge or a drop” so a unit of presentation does not usually get stated formally (sometimes a drop does, particularly for products that can reliably say a strength per drop). This is OK, unless you have unit dose presentations…*like the testosterone gels in sachets* NHS dm+d uses presentation strength in these cases: testosterone 50mg/5g unit does sachet or testosterone 50mg/5g unit does tube

## Avoiding confusion with pack (size) description

Pack size description should provide the information on how many units of presentation are present in the licensed and supplied package. Some terminologies include this as one of their classes, usually called something like “packaged product” (e.g. NHS dm+d and AMT); to date that requirement has not been presented for CCDD (or indeed for RxNorm). Pack size information usually supports reimbursement and supply chain use cases – for example it provides a link to one of the main types of GS1 identifier. It is also important in cultures where there is ‘original pack prescribing and dispensing’ (which is not the case in Canada); to support this practice, prescribers need to know pack size as well as dispensers.

IDMP is more detailed, dealing with both intermediate packs (e.g. 14 tablets in a blister strip) and what in clinical care would be the main “package” (of 28 tablets - 2 blister strips in the box). IDMP does not specify how many levels of recursion, so it can deal with pre-filled syringes (unit of presentation), individually wrapped in sterile bags (next layer) in a blister strip of 5 bags (next layer), in a box of 25 (5 blisters of 5 strips) – the “package”.

The following table gives some examples of the relationship between package size/quantity, intermediate packaging, unit of presentation and exemplar dose form.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Pack size quantity** | **Unit of presentation** | **Intermediate package** | **Intermediate package quantities** | **Out pack description** | **Original pack description (text)** | **Exemplar dose form (info only)** |
| 28 | tablets | blister strip | 2 x 14 tablets | Box | “Box of 28 tablets” | oral tablet, prolonged release oral tablet, gastro-release tablet, chewable tablet, dispersible oral tablet; vaginal tablet |
| 100 | capsules | NA | NA | Bottle | “Bottle of 100 capsules” | oral capsule, modified release oral tablet, |
| 10 | suppositories | blister strip | 2 x 5 suppositories | Carton | “Carton of 10 suppositories” | suppository |
| 30 | sachets | NA | NA | Box | “Box of 30 sachets” | oral powder, oral granules |
| 50 | actuations | NA | NA | Bottle | “Spray bottle of 50 actuations” | nasal spray, cutaneous spray, mouthwash, gingival spray |
| 200 | actuations | NA | NA | Inhaler | “200 actuation inhaler” | pressurised inhalation, inhalation powder |
| 20 | (unit dose) vials | vial strip | 4 x 5 vial strips | Box | “Box of 20 vials” | nebuliser solution, nebuliser suspension |
| 10 | vials | NA | NA | Carton | “Carton of 10 vials” | powder for solution for injection, powder for suspension for injection |
| 5 | cartridges | blister strip | 1 x 5 cartridge strip | Box | “Box of 5 cartridges” | solution for injection, suspension for injection |
| 10 | syringes | NA | NA | Box | “Box of 10 pre-filled syringes” | solution for injection, suspension for injection |
| 100 | mL | bottle | NA | Box | “100 mL bottle” | oral solution, oral suspension |
| 5 | mL | NA | NA | Bottle | “10 mL bottle” | ophthalmic drops, otic drops, nasal drops |
| 30 | g | NA |  | Tube | “30 g tube” | cutaneous cream, cutaneous ointment, cutaneous gel |