

# UNIT-II

## DDD & INN



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*Shaping Lives...  
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# Daily defined doses (DDD)

The basic **definition** of the defined daily dose (DDD) is:

- *The DDD is the **assumed average maintenance dose per day for a drug used for its main indication in adults.***
- The DDD is a **unit of measurement and does not necessarily reflect the recommended or Prescribed Daily Dose (PDD).**

- **Therapeutic doses for individual patients and patient groups will often differ from the DDD as they will be based on individual characteristics (such as age, weight, ethnic differences, type and severity of disease) and pharmacokinetic considerations.**
- **Only one DDD is assigned per ATC code and route of administration (e.g. oral formulation). The DDD is nearly always a compromise based on a review of available information including doses used in various countries when this information is available.**

- The DDD is sometimes a “dose” that is rarely if ever prescribed, because it might be an average of two or more commonly used doses.
- Drug utilization data presented in DDDs only give a rough estimate of consumption and not an exact picture of actual use.
- DDDs provide a fixed unit of measurement independent of price, currencies, package size and strength enabling the researcher to assess trends in drug consumption and to perform comparisons between population groups.

## **Objectives of DDD: By applying DDD it is possible to**

- Examine changes in drug utilization over time.
- Make international comparisons.
- Evaluate the effect of an intervention on drug use.
- Document the relative therapy intensity with various groups of drugs.
- Follow the changes in the use of a class of drugs.
- Evaluate regulatory effects and effects of interventions on prescribing patterns.

## General principles for DDD assignment

- DDDs are **only assigned to drugs with an ATC code** and a DDD will normally **not be assigned for a substance before a product is approved and marketed in at least one country.**
- The basic principle is to assign **only one DDD per route of administration within an ATC code.**
- **DDDs for single substances** are normally based on **monotherapy.**
- Exceptions to this rule are given in the guidelines of the relevant ATC groups.

- For substances **indicated for rare disorders** with highly individual dosing schedules, the Working Group could decide **not to assign a DDD.**
- **DDDs are not established for topical products, sera, vaccines, antineoplastic agents, allergen extracts, general and local anesthetics** and contrast media.
- When a new DDD is assigned, various sources are used to get the best overview of the actual or expected use of a substance. The assigned DDD is based on the following principles:

- The **average adult dose recommended for the main indication** as reflected by the ATC code. When the recommended dose refers to body weight, an adult is considered to be a person of 70 kg. It should be emphasized that **even special pharmaceutical forms mainly intended for children** (e.g. mixtures, suppositories) are assigned the DDD used for adults. Exceptions are made for some products only used by children, e.g. growth hormones and fluoride tablets.
- For some **groups of medicinal products specific principles for DDD assignment are established** (e.g. the DDDs for **the selective serotonin agonists in the treatment of migraine** are based on the **approved initial dose**). These principles are given in the guidelines for the relevant ATC groups.



- The **recommended maintenance dose** (long term therapeutic dose) is usually **preferred when establishing the DDD**. The **initial dose may differ from the maintenance dose** but this is **not reflected in the DDD**.
- If the **approved dose recommendation** provides **limited information about maintenance dose**, the **DDD** will usually be **the average of the maintenance dose range**. Examples of interpretation of approved dose titration recommendations:
  - “Titrate up to a high dose if it is tolerated”: the high dose would normally be chosen as the DDD.
  - “Consider to increase the dose only if efficacy is not satisfactory with initial dose”: the **DDD would normally be based on the initial dose**.

- The treatment dose is generally used. If, however, prophylaxis is the main indication, this dose is used, e.g. for fluoride tablets (A01AA01) and some anti malaria.
- A DDD is usually **established** according to the **declared content (strength) of the product**. **Various salts of a substance** are usually **not given different DDDs**.
- **Different stereoisomeric forms** are normally assigned separate DDDs and ATC codes. The DDDs for stereoisomeric forms are described in the respective ATC groups.
- **Prodrugs**, have **not been given a separate ATC code**.

- The DDD is often identical for various dosage forms of the same drug. Different DDDs can be **established when the bioavailability is substantially different for various routes of administration** (e.g. oral and parenteral administration of morphine) or if the dosage forms are used for different indications.
- The **DDDs are frequently used as indicators for antibacterial use** in hospitals, and it has been decided that assigning **different DDDs for oral and parenteral formulations** could be important in some cases to improve the usefulness of the methodology in drug utilization monitoring and research.
- **Parenteral products with different routes of administration** (e.g. i.v. and i.m.) have the **same DDD**.

## **DDDs for combinations products:**

- The DDDs assigned for combination products are **based on the main principle of counting the combination as one daily dose**, regardless of the **number of active ingredients included in the combination**.
- If a treatment schedule for a patient includes e.g. **two single ingredient** products, then the consumption will be measured by counting the **DDDs of each single ingredient product separately**.

- **Example I:**

Treatment with two products, each containing one active ingredient:

- Product A:

Tablets containing 20 mg of substance X (DDD = 20 mg)

- Product B:

Tablets containing 25 mg of substance Y (DDD = 25 mg)

- The dosing schedule 1 tablet of A plus 1 tablet of B daily will be calculated as a consumption of 2 DDDs.

- **Example II:**

Treatment with a combination product containing two active ingredients:

- Product C:

Tablets containing 20 mg of substance X and 12.5 mg of substance Y. The DDD of the combination products is assigned as 1 UD = 1 tablet.

- The dosing schedule 1 tablet of C daily will be calculated as 1 DDD (even though it will be equivalent to 1.5 DDD of the single active ingredients).

# International Nonproprietary Name

- An international nonproprietary name (INN) is an **official generic and non-proprietary name given to a pharmaceutical drug or an active ingredient**
  - to make communication **more precise** by providing a **unique standard name for each active ingredient**
  - to **avoid prescribing errors**.
- The INN system has been coordinated by the **World Health Organization (WHO)** since **1953**.
- Drugs are generally marketed by their **brand names**. Countries have their own systems of **generic nomenclature** for pharmaceutical substances. However owing to the various languages, there is a **need to have a uniform standardized system of generic names** that are accepted worldwide.

- The WHO administers an **international generic nomenclature system** called INNs also known as **rINN**, for **recommended International Nonproprietary Name** or **p INN** for **proposed International Nonproprietary Name**).
- **A nonproprietary name** is also known as a **generic** name.
- Initiated in 1950 by a World Health Assembly resolution
- Cumulative list of INN now stands at some 7000 names designated since that time .

# AIMS OF INN SYSTEM

- To provide **health professionals with a unique and universally available designated name**
- To **identify** each pharmaceutical substance.
- For the **clear identification, safe prescription and dispensing of medicines** to patients.
- For **communication and exchange of information** among health professionals and scientists worldwide.
- **Nonproprietary** names are **intended for use in Pharma, labeling, product information, advertising and other promotional material, drug regulation and scientific literature**, and as a basis for product names, e.g. for generics.



# SELECTION OF INN

- The names are selected by the World Health Organization on the advice of experts from the WHO Expert Advisory Panel.

## STEPS:

- **a request/application** is made by the **manufacturer or inventor**; after a review of the request **a proposed INN** is selected and published for comments.
- after a time-period for objections has lapsed, the name will obtain the status of a recommended INN and will be published as such if no objection has been raised.
- Since the name is available in the **public domain it may be used freely**. However, it **should not be registered as a trade-mark** since this would prevent its use by other parties.

## **NAMING**

- INN is designated for the active part of the molecule only to avoid the multiplication of entries in cases where several salts, esters, etc. are actually used. In such cases, the user of the INN has to create a modified INN (INN<sub>M</sub>).
- Ex: mepyramine maleate (a salt of mepyramine with maleic acid)

### **The primary principles for selection:**

- Distinctive in sound and spelling; Not too long
- Not liable to confusion with other names in common use.
- Ex: -ac for anti-inflammatory agents, ibufenac derivatives -coxib for COX-2 inhibitors, a type of anti-inflammatory drugs (e.g. celecoxib)
- Do not select names for mixtures of substances.
- Do not select names for those substances that have a long history of use for medical purposes under well established names such as those of alkaloids (e.g. morphine, codeine), or trivial chemical names (e.g. acetic acid)

## USE OF INNs IN INDIA

- In India, Section 13 (b) of the Trade Marks Act, 1999 prohibits the registration of names of chemical elements or INNs which have been declared by the World Health Organization (WHO) and notified by the Registrar of Trade Marks.
- Nevertheless, there are reported incidents of marketing of drugs under names that are similar to INNs. The WHO has brought the same to the attention of the Drug Controller General of India.
- The basic requirement of Section 13 (b) of the Trade Marks Act, 1999 is that INNs must be notified by the Registrar.