



Liposomal forms of drugs: now specified in the brand name, but no improvement to the INN

● Some drugs, such as injectable *amphotericin B*, *doxorubicin* and *irinotecan*, are marketed in liposomal and non-liposomal forms, but these forms are not interchangeable. The European Union has taken action to prevent errors in this situation, by adding “liposomal” or “pegylated liposomal” to the brand name. As an added precaution, it is useful to refer to these drugs on prescriptions and in other healthcare documents by their INN + the form (liposomal or non-liposomal) + the brand name.

Liposomes are small spherical vesicles with a lipid bilayer wall enclosing an internal aqueous cavity, in which drugs can be encapsulated to obtain a liposomal form of the drug. As of 2020, this technique is mainly used for injectable antineoplastic or anti-infective drugs. Another technique involves incorporating polyethylene glycol (PEG) into the lipid bilayer, to form pegylated liposomes. The intention behind the liposomal or pegylated liposomal form of a drug is generally to modify its pharmacokinetics, for example to increase the concentration of the drug in a target tissue or prolong its duration of action (1,2).

Liposomal and non-liposomal forms of the same drug are not interchangeable. Some drugs are marketed in the European Union in conventional (non-liposomal), liposomal and pegylated liposomal forms. These products are not interchangeable. Confusion between these products can cause dosing errors or administration errors with potentially serious consequences (3-6). For example, three injectable forms of *amphotericin B* are marketed in France: a conventional, *amphotericin B* deoxycholate form (Fungizone°), and two lipid forms, one liposomal (Ambisome°) and one non-liposomal, in which *amphotericin B* is incorporated into a phospholipid matrix (Abelcet°). Cases of confusion between the three forms of this antifungal drug have been reported since the late 1990s, including overdose caused by the use of conventional *amphotericin B* at doses prescribed for a lipid form, resulting in serious or even fatal renal and cardiac disorders. These errors occurred at the prescribing, dispensing, preparation and administration stages of the medication use process (4,5).

Brand names indicate whether the product is a liposomal form. In 2019, the European Medicines Agency (EMA) asked pharmaceutical companies that market liposomal or pegylated liposomal forms of drugs to modify the brand name of the products concerned if a risk of medication errors through confusion with non-liposomal forms had been identified. This involved adding the qualifier “liposomal” or “pegylated liposomal” to the brand name.

As of 13 October 2020, the pharmaceutical companies we approached informed us that the qualifier “pegylated liposomal” is displayed in English on the packaging of products marketed in France: “Ambisome° liposomal” for the liposomal form of *amphotericin B*, “Caelyx° pegylated liposomal” for the pegylated liposomal form of *doxorubicin*, “Onivyde° pegylated liposomal” for the pegylated liposomal form of *irinotecan*, and “Vyxeos° liposomal” for the liposomal form of the *daunorubicin* + *cytarabine* combination (3). Some of these names have not yet been updated on the website of the French Health Products Agency (ANSM) as of 13 October 2020 (7-9).

Conventional forms of *doxorubicin* and *irinotecan* are also marketed in France (2,5-11).

In practice A half measure. A drug’s real name is its international nonproprietary name (INN). When the INN is insufficiently informative, any modifications required to prevent errors would be better added to the INN than to a brand name that conveys no information about the product’s composition. Adding the qualifier to the brand name does not eliminate the risk of confusing one product for another, for example when selecting a treatment from a drop-down menu in an electronic prescribing system.

Healthcare professionals must take great care at every stage of the medication-use process when dealing with drugs that are available in liposomal and non-liposomal forms. In such cases, it is advisable to refer to the product by its INN + form + brand name on prescriptions, and to make sure that the form being dispensed or administered is the prescribed form, and that the dose and method of administration match.

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