MEETING THE GAP IN PARENTERAL PACKAGING

The primary packaging market for parenteral formulations is dominated by a few established and well characterised containers, says Ralf Künzi, Medical Business Development, Hoffmann Neopac. Here, he outlines the benefits and drawbacks of each container type, revealing a clear gap in available parenteral packaging options.

AMPOULES

Ampoules are available in many different sizes and shapes and also made from several materials, however specifically for parenteral applications glass is by far the most common material. The main benefit of ampoules is their low cost of goods. Especially in developing economies the glass ampoule is therefore the most common type of primary packaging for parenteral formulations. Due to the good barrier properties of glass, ampoules provide a high level of protection at minimum cost.

The main disadvantage is user handling as ampoules have to be cut and broken to be opened and the drug has to be transferred into a syringe using a transfer needle. In addition to this being a cumbersome procedure, cutting and breaking glass creates small glass particles which may enter into the blood stream and if the break is not clean, dangerous glass sharps are generated. Moreover, ampoules are mostly made from thin-walled glass which easily breaks when dropped. Due to their tall narrow shape ampoules easily fall over leading to costly and sometimes dangerous spillage of contents once the ampoule has been opened. Furthermore, the contents of the container are exposed after it has been opened, posing a significant risk of contamination if not handled with utmost care.

Ampoules should thus only be considered as a viable packaging option if cost of goods is the only selection criterion. Ampoules are not ideal if the drug is administered to patients very frequently due to high time consumption for the caregiver. In the case of drugs requiring particular care when handled, such as cytotoxic drugs, ampoules should be ruled out as a primary packaging option altogether.

CRIMP VIALS

As with ampoules, crimp vials exist in many different sizes. The main difference to ampoules is the rubber septum used to close the vial. This design aspect resolves the main disadvantages of ampoules and in addition allows for multiple administrations from the same container. Cost of goods is higher due to the additional number of components and the thicker glass required ensuring that the crimp-sealing process does not cause the glass to break.

Crimp vials are predominantly made from glass except for the rubber septum, with the latter component leading to more challenging drug compatibility characteristics compared with ampoules. Crimp vials entirely made from plastic are becoming more popular for parenteral applications and are predominantly made from cyclic olefin copolymer (COC). This material does however not provide the same barrier properties as glass especially for oxygen and water vapour permeation.

The handling procedure for crimp vials is clearly improved compared to ampoules but still requires numerous steps as the drug has to be transferred into a syringe requiring a dedicated transfer needle.

Crimp vials are thus a viable packaging option for many types of drugs. But as for ampoules, the complex handling procedure is a limiting characteristic of this primary packaging option. Crimp vials are therefore a suboptimal choice for drugs administered very frequently and/or to a very large number of patients.

PREFILLED SYRINGES

Over the last 20 years the popularity of prefilled syringes has increased significantly. The main reason for this trend is the substantially higher level of convenience for the user. If equipped with a staked-on needle a prefilled syringe requires minimal preparation and can easily be used by care givers as well as patients themselves. As for crimp vials, prefilled syringes are to-date also mainly made of glass with COC versions slowly gaining market acceptance. There are however also some clear drawbacks of prefilled syringes, the main ones being comparatively high unit costs especially for delivery volumes above 2 ml, and the other being the need for silicone lubrication. Also the fact that a rubber plunger is required poses challenges for certain ingredients. And tungsten residues on the inner glass surface have caused some undesirable interactions in the past.

Prefilled syringes are thus a viable packaging option for drugs which are frequently administered. To compensate for the comparatively high cost of goods, prefilled syringes are mainly used for high-priced pharmaceutical preparations; this is especially true for larger delivery volumes. In addition, special attention needs to be paid to compatibility aspects related to rubber materials and silicone oil.

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CARTRIDGES

A cartridge is basically a combination of a prefilled syringe and a crimpl vial. The cartridge is typically used for multi-dose applications, such as for administering anaesthetics in dental care and for the self-administration of hormone replacements such as insulin, growth hormone etc. They allow for accurate deliveries of small amounts of liquids (<0.5 ml). Like the other parenteral containers, glass is by far the most widely used material for the cartridge barrel. Similar to the prefilled syringes the drawbacks are mainly related to comparatively high unit costs, the need for siliconisation inside the barrel, and compatibility aspects due to the use of rubber components.

Cartridges are thus a viable packaging option for drugs which are frequently administered in small doses and which have a sufficiently high price tag to absorb the higher total cost of goods. As for pre-filled syringes, special attention needs to be paid to compatibility aspects related to rubber materials and silicone oil.

MATERIAL CONSIDERATIONS

As already stated in this article, glass is by far the most common material used for parenteral packaging. This is for good reason as the barrier properties of glass are unmatched by anything else and the material is inert to a wide range of ingredients. However, besides obvious drawbacks of glass such as the risk for breakage, glass can pose substantial challenges such as delamination e.g. due to acidic pH or protein adsorption for biologic APIs. Therefore, polymer-based packaging materials such as COC, Cyclic Olefin Polymer (COP) and polypropylene are becoming more widely accepted as primary packaging materials for injectable drugs. However, these materials provide insufficient barrier properties for a large range of sensitive ingredients. And especially for larger containers the cost of goods is prohibitive for many applications.

LIQUID UNSTABLE DRUGS

Formulation scientists are confronted with special challenges if drugs are not stable in liquid form over prolonged periods. The goal for any new drug must be to achieve liquid stability as this is always the better option in terms of cost of goods, packaging complexity and logistics and most of all user handling. However, despite all modern formulation technologies, liquid stability cannot be achieved in many cases. Therefore, the primary packaging should reduce the formulation-related challenges and drawbacks.

Unfortunately, to date very few viable primary packaging options exist. In most cases the dry component is filled either as a powder or granulate into a crimpl vial, or as a liquid followed by lyophilisation. The liquid components have to be stored in a separate crimpl vial resulting in a particularly complicated and time-consuming handling process. To simplify this process special add-on devices are available, but these devices are not reducing the actual number of steps but still add further delivery costs. The most convenient options to date are dual chamber cartridges and syringes, which clearly reduce the number of steps and makes drug delivery almost as easy as for liquid stable drugs. But for many applications the resulting high total cost of goods is prohibitive, and in addition due to their comparatively large-size dual chamber cartridges and syringes are rarely used for delivery volumes greater than 1ml.

FLEXIMED® FILLING THE GAP

From the above considerations it becomes clear that current parenteral packaging options do not fully cover current market needs. The greatest need is apparent for frequently administered drugs which are not fully liquid stable. For many applications the resulting high total cost of goods is prohibitive, and in addition due to their comparatively large-size dual chamber cartridges and syringes are rarely used for delivery volumes greater than 1ml.

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From the above considerations it becomes clear that current parenteral packaging options do not fully cover current market needs. The greatest need is apparent for frequently administered drugs which can not be formulated as liquids for stability reasons. To-date, most such drugs are therefore packed in suboptimal primary containers.

To meet this substantial need Hoffmann Neopac has developed the innovative Fleximed® tube. Fleximed® provides a combination of packaging characteristics which is absolutely unique in the field of parenteral packaging:

- Ease of use: requiring substantially fewer handling steps compared with ampoules and crimpl vials, no need of a transfer needle
- Multi-layer laminates for tailor-made barrier properties
- Different protein adsorption behaviour compared with glass
- Packaging does not break when dropped
- Low cost of goods, especially for larger fill volumes >3 ml.
- By adding a frangible middle seam two or more components can be stored in one tube.
- State-of-the-art bulk freeze drying technologies also allow Fleximed® to be used for lyophilised drugs.

The following illustration (Figure 1) visualises how Fleximed® completes the gap for parenteral containers when considering the key challenges and demands in the parenteral world.

Figure 1: Key demands for primary parenteral containers which are ideally met with Fleximed®.