Table 4-4 Novel Injectable Packaging Delivery Systems for Human Growth Hormone

- Eli Lilly (Humatrope®)
  - HumatroPen™
    - Reusable pen with lyophilized powder in a cartridge with diluent connector and prefilled diluent syringe
- Genentech (Nutropin®)
  - Nutropin AQ® Pen (reusable)
- Novo-Nordisk (Norditropen®)
  - NordiPen®
    - Reusable pen with cartridges
  - NordiPenmate®
    - Slides over pen for automated insertion and injection
  - Nordiflex®
    - First and only disposable pen for human growth hormone
- Pfizer (Genotropin®)
  - MiniQuick
    - Lyophilized powder in dual chamber syringe
  - Reusable pen with clip-on color panels
  - Reusable mixer for dual chamber cartridge
  - Intra-Mix®
    - Reconstitution device prefilled with dual-chambered cartridge
- Serono (Saizen®)
  - One.click™ autoinjector
  - Click.easy™ reconstitution aid
  - Cool.click™ resusable needle-free device

have a "dial-a-dose" feature. Of course, the drug manufacturer is responsible for validating the dependability of the device to deliver the right dose every time, all the time. The device manufacturer is not responsible for submitting these data to regulatory authorities. Single-dose disposable pens and fixed-dose pens also are commercially available. Major pen manufacturers included Becton-Dickinson (Fig. 4-8), Owen-Mumford (Fig. 4-9), West Pharma (Fig. 4-10), and Ypsomed (Fig. 4-11).

Reusable autoinjector, like reusable pens, requires several steps for preparation and injection. Autoinjectors can inject a fixed dose of 1 mL or less. Autoinjectors have been used primarily for treatment of multiple sclerosis and osteoarthritis, as they are quite suitable for home health care. Disposable autoinjector systems have been used historically for emergency uses, for example, the EpiPen®, but now are used for rheumatoid arthritis, anemia, and oncology purposes. Disposable injectors are single use and simple to operate. They are relatively expensive ($1–$4 per injection) and better serve less frequent administered drug products.

RECONSTITUTION PACKAGING SYSTEMS

Historically, lyophilized drugs were available in vials where the diluent, used to reconstitute the freeze-dried powder, was either provided with the vial package (combination package of vial and syringe) or the pharmacist used a common diluent in a vial (usually Sterile Water for Injection) to withdraw the appropriate volume of diluent from a vial using an empty sterile syringe and then reconstituting the drug-containing vial product.

Currently, while the classic way of reconstituting freeze-dried powders still is routinely practiced, two advances have gained popularity. One is the use of vial adapters and preassembled systems (Figs. 4-12 and 4-13) that facilitate the combination and transfer of diluents into the freeze-dried product vial. The other is the design of dual-chambered vials or syringes where the freeze-dried powder and the diluent are contained in the same packaging system separated by a rubber septum, where at the time of reconstitution the rubber septum is moved toward the powder compartment and the diluent combines with the powder via a bypass design in the syringe. The Vetter Lyo-Ject® (Fig. 4-14) has been the major player in this market although by the time of the publication of this book, other systems might be available. Dual-chambered vials such as Solu-Medrol® Mix-O-Vial™ are marketed, but other dual-chambered vials like Redi-Vial™ were removed from the market due to excessive costs.