

U-500 Insulin: Clinical Comments From the Experts

John R. White, Jr., PA-C, PharmD

Twenty or thirty years ago, U-500 insulin was a product that, for the most part, sat in the corner and moldered. Relative to other pharmaceuticals, it was almost a curiosity. A patient treated with U-500 was a rarity and would likely end up with “grand rounds” status.

Today, unfortunately, the picture is different. As the obesity and type 2 diabetes epidemics continue and

we witness a relentless burgeoning of severely insulin-resistant patients, the use of U-500 insulin has escalated.

Still, the use of U-500 insulin is not an everyday occurrence in most practices, and when it is used, health care providers must be vigilant in terms of both accurate prescribing and thorough patient education. Consistency and precision in the

use of terminology surrounding the management of patients with U-500 insulin is obligatory.

This journal recently published a “Practical Pointers” article (Valentine V: Don’t resist using U-500 insulin and pramlintide for severe insulin resistance. *Clinical Diabetes* 30:80–84, 2012) and a corresponding patient information page (Good to Know: Using U-500

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insulin. *Clinical Diabetes* 30:86, 2012) on the topic of U-500 insulin. These articles prompted both a letter to the editor from Dr. Robert C. Hood of Beaumont, Tex., and an editor-invited response to that letter from Jennal L. Johnson and her colleagues at Lilly Diabetes in Indianapolis, Ind., which manufactures U-500 insulin. Both of these letters, published at the end of this commentary (p. 51–52), raise points worth considering.

Dr. Hood's letter is based on a great deal of personal experience with the use of U-500 in his practice. Several of his points warrant comment. First, he echoes the potential value of using U-500 insulin combined with pramlintide, which was described in the article by Valentine.

Dr. Hood also offers a correction of the statement describing the stripes on the U-500 insulin vial as orange, saying they are, in fact, brown. His description of stripes is consistent with the U-500 insulin product package insert. In reality, however, the label color might be perceived as either orange or brown and could potentially be a point of confusion. Therefore, it would be prudent to explain that some see the label stripes as orange, while others tend to see these markings as brown.

Dr. Hood also points out that patients should be encouraged to look for the red "U-500 (Concentrated)" verbiage on the package and reminds us that the cap on the vial is grey. He notes the importance of patients double-checking to make sure that they are in fact holding a vial of U-500 insulin. This is excellent advice.

He then describes the potential confusion that could result from a patient using different volume insu-

lin syringes, because the markings may be in 2-, 1-, or ½-unit increments (using a U-100 standard). He also describes the particular method that he uses in his practice to handle the use of U-500 insulin.

In a response to Dr. Hood's letter, Ms. Johnson and her colleagues make several important points. They underscore the potential problems involved with the use of insulin syringes of various volumes. The package insert (and the table included in the previously published patient information page) describe the use of a U-100 syringe and a tuberculin syringe. It should be noted that these volume/dosage rubrics are based on the assumption of a 1-ml syringe in both cases. This was not, however, explicitly stated.

Ms. Johnson and her colleagues also point out a potentially confusing statement in the patient information page: "U-500 is 5 times more concentrated than U-100 insulin. This means that every 1 unit of U-500 is the same as 5 units of your usual insulin. This makes it a more powerful medicine." As they point out, this statement is not accurate because 1 unit is 1 unit. The difference between U-100 and U-500 is that, with U-500 insulin, each unit is delivered in one-fifth the volume. Johnson et al. propose a more accurate revision to the statement: "U-500 is 5 times more concentrated than U-100 insulin. This means that every 1 unit of U-500 is the same as 1 unit of your usual insulin, but U-500 is delivered in one-fifth the volume compared to your usual insulin. This makes it a more powerful medicine."

The timely information in the previously published "Practical Pointers" and patient information articles, as well as the two let-

ters written in response to them, highlight the potential difficulty and complexity involved in using U-500 insulin. In summary, several important points can be garnered or extrapolated from these two informed and thoughtful letters.

In describing the product to a patient, it would be a good idea to have an actual vial of U-500 on hand (perhaps an empty vial). The label should be described as "brown or orange." One should emphasize the red labeling on the vial that says "Concentrated" and "Warning—High Potency Not for Ordinary Use." It might also be helpful to note that this particular insulin has a grey cap.

The use of U-500 insulin will be simplified by pairing it with a 1-ml syringe (U-100 or tuberculin) and thinking in terms of volume. For example, 125 units of U-500 is contained in 0.25 ml in a tuberculin syringe or in a 1-ml U-100 syringe filled to the 25 marking. Use of smaller-volume syringes, if absolutely necessary, must be undertaken with a great deal of care on the part of health care providers and patients with the understanding that the package insert chart no longer applies.

U-500 insulin is a potent and effective tool to treat hyperglycemia, but it must be used very cautiously and treated with a great deal of respect.

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