

To the editor:

This note is in response to a recent patient information page (Good to Know: Using U-500 insulin. *Clinical Diabetes* 30:86, 2012). Our practice has quite a large cohort of patients on U-500, and I have spent quite a bit of time this year analyzing our database, where we have 70 patients on multiple daily injections with at least one follow-up visit and also a smaller group on continuous subcutaneous insulin infusion. (As an aside, I often combine U-500 with pramlintide, in part to help deal with the blunted peak of U-500 and also because the typical U-500 patient is usually coping with excessive adiposity.)

My first concern has to do with the patient information page description of the U-500 vial/packaging. We emphasize this a lot with our patients to make sure that a potentially disastrous substitution is not made. The article states that the stripes on the U-500 vial are orange, but I believe they are, in fact, brown. We inform patients that the vial is 20 ml and contains a total of 10,000 units. We also emphasize that they should look for the red "U-500 (Concentrated)" verbiage on the package. Finally we tell them to watch for the gray cap as yet another way of double-checking that they are, in fact, using U-500 insulin.

My second concern has to do with the description of how to draw up the insulin and, in particular, the statement that each mark represents 5 units. We are very cautious with our patient education and very cognizant of the harm that can be done by transitions between U-500 and U-100 insulins because we do not really have a proper delivery system for U-500 insulin at this point in time.

Various patients use different insulin syringes for the delivery of U-500. Depending on the volume

and make of the insulin syringe, the actual markings can be in 2-, 1-, or ½-unit increments. In our practice, we instruct patients in "U-100 equivalents." For example, if we desire to give 50 units with a meal, we simply tell them to draw 10 units with an insulin syringe. We combine this, however, with detailed counseling about the fact that they are actually giving 5 times the insulin. We also discuss the fact that there have been fatalities when doses have been mistranslated, and we provide an example of how this could happen.

I have modified our electronic medical record system so that U-500 is highlighted distinctly, providing staff with a clear flag that this type of insulin is being used. I realize that our approach is not what is recommended by Eli Lilly [which manufactures U-500 insulin], and when we write the prescription, it would read, "50 units given before the meal delivered as 10 units by an insulin syringe." I know that we are supposed to tell our patients the actual dose and then translate it, but when we are reviewing glucose levels and adjusting regimens regularly, this is cumbersome and excessively complex for patients (and I worry that there is an increased risk of mistakes as opposed to a reduced risk from this practice). It is far simpler for patients to just think in terms of the actual units drawn and to KNOW that they cannot translate this directly to U-100 insulin (or vice versa) if their type of insulin is changed.

In the patient information piece, I think patients would assume that each marking is 5 units regardless of whether their specific syringe has the 2-, 1-, or ½-unit markings and, as a result, might be drawing their insulin up in increments of 10, 5, or 2.5 units. It is very frustrating that we do not have a specific U-500 delivery device and that all of us in clinical

practice who use U-500 have to deal with this.

The job of an editor or author addressing this issue is particularly daunting because there are different ways of dealing with this, and you are left with the need to come up with a consensus. I don't envy anyone that task. I hope this letter provides food for thought.

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To the editor:

We would like to respond to the thoughtful letter from Dr. Robert Hood regarding the recently published patient information page about U-500 insulin. In addition to responding to his concerns, we would like to propose distinct wording to more accurately explain unit-to-unit dosing of U-500 insulin in relation to U-100 insulins.

One of the concerns voiced by Dr. Hood pertains to accurate U-500 administration using syringe unit markings since there is no delivery device specifically designed for U-500 insulin on the market. We agree with Dr. Hood's comments regarding the difference between the actual U-500 units delivered and the unit markings (the recommended terminology to use instead of referring to "units"),<sup>1</sup> which vary depending on the scales on the particular U-100 insulin syringe being used. For example, each syringe unit marking equals 10 units of U-500 when using a 1-ml U-100 insulin syringe, whereas each syringe unit marking equals 5 units of U-500 when using a 0.5-ml U-100 insulin syringe. Finally, for a 0.3-ml U-100 insulin syringe with half-unit mark-

ings, each syringe unit marking equals 2.5 units of U-500.

As Dr. Hood mentions, the Eli Lilly U-500 product label<sup>1</sup> and education materials do emphasize the need for patients to understand their actual U-500 dose and syringe markings, whether they are using U-100 insulin syringes (unit markings) or volumetric syringes (milliliter markings). Eli Lilly materials also highlight the need for providers to prescribe U-500 in actual units as well as syringe markings. The rationale for this recommendation is that, when patients transition between health care facilities or providers, it is important for them to understand their dose in actual units as well as in specific syringe unit markings

to accurately communicate their U-500 dose.

The recently published patient information page introduces the complex concept of U-500's concentration by stating, "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."

However, U-500 contains five times as much insulin in 1 ml as standard (U-100) insulin. Therefore, U-500 provides more insulin in a smaller volume of solution. The difference between U-500 and U-100 insulin is a difference of volume, not units. Following is a suggested revision of the patient education page to improve its accuracy on this issue. "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."

#### REFERENCE

<sup>1</sup>Eli Lilly and Co.: Humulin R U-500 [product label]. Indianapolis, Ind., Eli Lilly and Company, 2011

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