

## U-500 Regular Insulin

### Dosage and Administration

#### SUMMARY

*Information on dosage and administration of U-500 regular human insulin is summarized below. More detailed information is available in the sections that follow.*

- Information on dosage and administration included in this letter may contain information that does not completely match the current US prescribing information for U-500 regular insulin. **Please see prescribing information for approved label information.**
- U-500 regular insulin is not approved for use in CSII. **Please see prescribing information for approved indication(s).**
- Because a single dose of U-500 regular insulin has a relatively long duration of action (up to 24 hours) as compared to other regular insulins (Humulin package insert, 2007), it should be dosed differently than U-100 regular insulin. Most patients will need 2 to 3 injections daily (Humulin package insert, 2007; Lane, 2009). Additional information on dosing is provided in Table 1 (Lane, 2009).
- It is recommended that a U-100 insulin syringe or tuberculin syringe be used for measurement of dosage (Humulin package insert, 2007; Lane, 2009; Davidson, 2010). Conversion information on both syringes is available in Table 2 (Lane, 2009).
- U-500 regular insulin takes effect within 30 minutes; therefore, the injection of U-500 regular insulin should be followed by a meal within approximately 30 minutes of administration (Khan, 2007; Davidson, 2010). U-500 regular insulin should only be administered subcutaneously. Intravenous administration is not advised because of possible inadvertent overdosage (Humulin package insert, 2007).
- Mixing U-500 regular insulin with other insulin preparations cannot be recommended. Additionally, concurrent use of oral hypoglycemic agents with U-500 regular insulin is not recommended due to limited study data (Humulin package insert, 2007).
- Unlike other forms of insulin, the actual unit dose of U-500 regular insulin does not correspond to the unit markings on a U-100 insulin syringe. When prescribing U-500 regular insulin, the amount of insulin to be taken should be written in actual insulin units and unit markings on the U-100 insulin syringe or actual insulin units and volume if using a tuberculin syringe (Cochran, 2008; Lane, 2009; Davidson, 2010).
- When administering U-500 regular insulin in the hospital setting, it is recommended to store, dispense and administer U-500 regular insulin separately from U-100 insulins to reduce administration errors (Garg, 2007; Cochran, 2008; Lane, 2009).



## DOSING OF U-500 REGULAR INSULIN

U-500 regular insulin contains 500 units of biosynthetic human insulin per mL. Because a single dose of U-500 regular insulin has a relatively long duration of action (up to 24 hours) as compared to other regular insulins (Humulin package insert, 2007), it should be dosed differently than U-100 regular insulin.

A 2009 review article in *Endocrine Practice* proposes a U-500 regular insulin dosing algorithm utilizing the patient's previous required daily insulin dose, with dosage distribution based on percentages of the total daily dose (Table 1). For patients with baseline A1C levels between 8 and 10%, a dose-for-dose conversion from U-100 is recommended. If baseline A1C is  $\leq 8\%$ , a reduction of the conversion dose by 10 to 20 % is recommended. For baseline A1C  $\geq 10\%$ , an increase by 10 to 20% in the conversion dose should be considered (Lane, 2009).

**Table 1. Dosing Algorithm for U-500 Regular Insulin Therapy<sup>a</sup> (Lane, 2009)**

Total Daily Insulin Dose (units/day)	Injection Frequency/ Delivery Method	Dosage Distribution (% of TDD)
150-300	2 injections/day (AM and PM) with or without basal insulin  3 injections/day (AM, noon, and PM) with or without basal insulin	AM injection = 60% TDD PM injection = 40% TDD (i.e., 60/40)  40/30/30 or 45/35/20 or 40/40/20
300-600	CSII  3 injections/day (AM, noon, and PM) with or without basal insulin  4 injections/day (AM, noon, PM, and bedtime)	24-hour basal insulin infusion + 3 mealtime boluses (e.g., 50% TDD for basal rate and 20/15/15 for mealtime boluses or 20% TDD for basal rate and 30/25/25 for mealtime boluses)
>600	CSII 4 injections/day (AM, noon, PM, and bedtime)	40/30/30 or 45/35/20 or 40/40/20  30/30/30/10  Same as above 25/25/25/25 or 30/30/30/10

Abbreviations: AM = pre-breakfast; CSII = continuous subcutaneous insulin infusion; noon = pre-lunch; PM = pre-evening meal; TDD = total daily insulin dose.

<sup>a</sup> Conversion to U-500 regular insulin therapy based on a patient's previous total daily insulin requirements.

Adapted from: Lane WS, Cochran EK, Jackson JA, et al. High-dose insulin therapy: is it time for U-500 insulin? *Endocr Pract.* 2009;15(1):71-79.

## ADMINISTRATION OF U-500 REGULAR INSULIN

It is recommended that a U-100 insulin syringe or tuberculin syringe be used for measurement of dosage (Humulin package insert, 2007; Lane, 2009; Davidson, 2010). The table below contains conversion information using both types of syringes (Lane, 2009).

**Table 2. Conversion Information for U-500 Regular Insulin Dose When Using a U-100 Insulin Syringe or a Tuberculin Syringe (Lane, 2009)**

U-500 Regular Insulin Dose (actual units)	U-100 Insulin Syringe (unit markings)	Tuberculin Syringe (volume [mL])
25	5	0.05
50	10	0.10
75	15	0.15
100	20	0.20
125	25	0.25
150	30	0.30
175	35	0.35
200	40	0.40
225	45	0.45
250	50	0.50
275	55	0.55
300	60	0.60
325	65	0.65
350	70	0.70
375	75	0.75
400	80	0.80
425	85	0.85
450	90	0.90
475	95	0.95
500	100	1.0

Adapted from: Lane WS, Cochran EK, Jackson JA, et al. High-dose insulin therapy: is it time for U-500 insulin? *Endocr Pract.* 2009;15(1):71-79.

The onset of action is similar to that of U-100, so injection of U-500 regular insulin should be followed by a meal within approximately 30 minutes (Khan, 2007; Davidson, 2010). It should only be administered subcutaneously. It is inadvisable to inject U-500 regular insulin intravenously because of possible inadvertent overdosage (Humulin package insert, 2007).

The effects of mixing U-500 regular insulin with other insulin preparations have not been studied, and therefore cannot be recommended. The concurrent use of oral hypoglycemic agents with U-500 regular insulin is not recommended since there are no data to support such use (Humulin package insert, 2007).

Extreme caution should be used in measurement of U-500 regular insulin dosage. Inadvertent overdose may result in serious adverse reaction or life-threatening hypoglycemia. U-500 regular insulin is distinctively labeled to differentiate it from U-100 regular insulin. Both the carton and the vial label are marked with diagonal brown and white stripes and a black and white label without any additional color differentiation. Additionally, the U-500 regular insulin vial label contains the following statement in bold, red letters: “Warning- High Potency Not For Ordinary Use”. The U-500 regular insulin vial has a grey flip top (as opposed to the orange flip top on the U-100 regular insulin vial) and contains 20 mL (10,000 units) versus 10 mL (1000 units) for U-100 insulin vials (Humulin package insert, 2007).

### **PRESCRIBING U-500 REGULAR INSULIN**

Unlike all other forms of insulin, the dose of U-500 regular insulin does not correspond to the unit markings on a U-100 insulin syringe. Since tuberculin syringes have volume (mL) markings rather than unit markings, they may be used for administration to help avoid confusion. In an effort to avoid dosing errors, the amount of insulin to be taken should be written in actual insulin units and unit markings on the U-100 insulin syringe or actual insulin units and volume if using a tuberculin syringe (e.g., U-500 regular insulin: inject 50 units [0.1 mL or 10 units on a U-100 insulin syringe] subcutaneously 3 times daily before meals) (Cochran, 2008; Lane, 2009; Davidson, 2010).

### **USE OF U-500 REGULAR INSULIN IN THE HOSPITAL**

When administering U-500 regular insulin in the hospital setting, it is recommended to store, dispense and administer U-500 regular insulin separately from U-100 insulins to reduce administration errors. Additionally, highlighting the strength on the front of the patient chart and in the medication record may help minimize drug-dispensing errors (Garg, 2007; Cochran, 2008; Lane, 2009).

HUMULIN® R U-500, (concentrated, insulin human injection, USP [rDNA origin]), Lilly

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*Based on feedback that health care providers wanted to receive a response to their question supported with peer-reviewed, published literature, publication(s) are attached/linked for additional reference (indicated by bolded text in the reference list). The attached/linked publication(s) were selected using the following criteria; however, all published references listed are available upon request by contacting 1-800-LillyRx. The method used to select the relevant publication(s) included a preference for peer-reviewed journals, the ability for the publication(s) to best answer the question from a clinical perspective, and publications that would provide scientific and/or fair balance. The most current publications meeting these criteria were considered.*

## REFERENCES

- Cochran E, Gorden P. Use of U-500 insulin in the treatment of severe insulin resistance. *Insulin*. 2008;3(4):211-218. [HIRTCCOCHRAN]**
- Davidson MB, Navar MD, Echeverry D, Duran P. U-500 regular insulin: clinical experience and pharmacokinetics in obese, severely insulin-resistant type 2 diabetic patients. *Diabetes Care*. 2010;33(2):281-283.
- Garg R, Johnston V, McNally PG, et al. U-500 insulin: why, when and how to use in clinical practice. *Diabetes Metab Res Rev*. 2007;23(4):265-268.
- Humulin R U-500 [package insert]. Indianapolis, IN: Eli Lilly and Company; 2007.
- Khan M, Lee YY. The pharmacokinetic and pharmacodynamic properties of regular U500 insulin in health non-obese subjects [abstract]. *Diabetes*. 2007;56(Suppl 1):1294-P.
- Lane WS, Cochran EK, Jackson JA, et al. High-dose insulin therapy: is it time for U-500 insulin? *Endocr Pract*. 2009;15(1):71-79. [HIRTLANE]**