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## Evaluation of the USP Risedronate Sodium Assay

### INTRODUCTION

Bisphosphonates are a class of molecules that consist of two phosphonate groups linked to a carbon atom. These molecules are analogues of pyrophosphates that were found to be biologically active in 1969<sup>1</sup> and currently these analogues are widely used in the treatment of bone-resorption diseases, such as osteoporosis.<sup>2</sup> Three generations of bisphosphonate products have been developed for the treatment of bone-resorption diseases; each generation more potent than its predecessor. Risedronate is a third-generation bisphosphonate, which is 5000 times more potent than a first-generation bisphosphonate.<sup>3</sup>

Risedronate (Figure 1) is a pyridinyl bisphosphonate and is one of the most popular first-line drugs available for the prevention and treatment of osteoporosis, a debilitating disease estimated by the National Osteoporosis Foundation to affect 61 million Americans age 50 and older by 2020.<sup>4</sup> Risedronate is available as a tablet for oral administration that contains the equivalent of 5, 30, 35, or 75 mg of anhydrous risedronate sodium in the hemi-pentahydrate form with small amounts of the monohydrate. In October 2010, a second-generation risedronate in a delayed-release formulation was approved by the U.S. Food and Drug Administration (FDA).

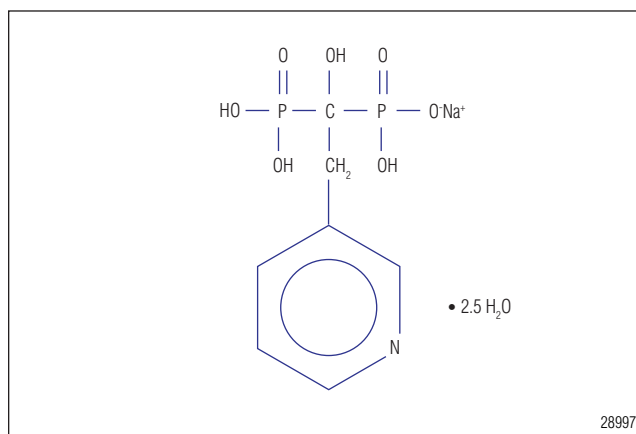


Figure 1. Risedronate sodium hemi-pentahydrate chemical structure.

Risedronate poses analytical challenges for reversed-phase (RP) high-performance liquid chromatography (HPLC) due to the presence of two polar phosphonate groups. This makes retention on commonly used RP columns (e.g., the Thermo Scientific Acclaim™ 120 C18 column) difficult. In addition, the metal chelation property of risedronate can cause poor peak shape and analyte recovery in systems that are not metal-free. Chelating agents, such as edetate disodium (EDTA), are added to the mobile phase to prevent metal contaminants from chelating with risedronate.

In addition, ion-pairing reagents typically are added to the mobile phase to enable retention and separation on a RP column. However, ion-pairing RP methods typically are not as robust as ion-exchange methods.<sup>5</sup> The multiple interactions between the ion-pairing reagent and the different phases, longer equilibration times, and the need for dedicating columns for specific ion-pair applications, increases the complexity of ion-pairing methods compared to ion-exchange methods.

Assay of the active pharmaceutical ingredient (API) and determining the presence of impurities and other related compounds is critical to ensure the formulation is safe and effective. The U.S. Pharmacopeia (USP) monograph describes an ion chromatography (IC) method to assay risedronate in the drug substance and product (Actonel, 35 mg tablets). This study evaluates and validates the USP monograph method for risedronate analysis and identifies the critical points of the method for successful chromatography.

The method specifies the USP L48 column with an EDTA eluent at pH  $9.5 \pm 0.1$  followed by UV detection at 263 nm.<sup>6</sup> The Thermo Scientific Dionex IonPac™ AS7 column meets the description of USP L48<sup>7</sup> and is used in this method. EDTA in the mobile phase prevents risedronate from chelating with metals and improves peak shape. The Dionex IonPac AS7 column is a high-capacity, high-efficiency, hydrophobic, anion-exchange column specifically developed for the analysis of a wide range of polyvalent anions, including polyphosphonates, hexavalent chromium, cyanide, and iodide. This study demonstrates the linearity, detection limits, precision, and accuracy of the assayed amount of risedronate in the drug substance and drug product, thus showing the method to be simple, rugged, and accurate.

## **EQUIPMENT**

Thermo Scientific Dionex ICS-3000 system\* including:

SP Single Pump or DP Dual Pump module

DC Detector/Chromatography module

(single- or dual-temperature zone configuration)

AS Autosampler with 2 mL vial tray (PN 062481)

Dionex ICS Variable Wavelength Detector (VWD), single or multiple wavelength with deuterium lamp (P/N 066347) and 11  $\mu$ L, 10 mm path length PEEK™ cell (P/N 066346)

Thermo Scientific Dionex Chromeleon™ software, 6.8 or higher

Polypropylene injection vials with caps, 1.5 mL (Vial Kit, P/N 079812)

Vacuum pump (Gast Manufacturing Corp. P/N DOA-P104-AA) or equivalent, for degassing eluents

Nalgene™ Filter Unit, 0.2  $\mu$ m nylon membrane, 1 L capacity (Nalgene P/N 164-0020)

Helium or nitrogen; 4.5-grade (99.995%) or better, <5 ppm oxygen (Praxair)

\*A Dionex ICS-5000 system can also be used for this application.

## **REAGENTS AND STANDARDS**

Deionized (DI) water, Type I reagent grade, 18 M $\Omega$ -cm resistivity or better

pH buffer, 7.00 (VWR P/N BDH5046-500ML)

pH buffer, 10.00 (VWR P/N BDH5072-500ML)

Risedronate sodium, hemi-pentahydrate, USP RS

C<sub>7</sub>H<sub>10</sub>NNaO<sub>7</sub>P<sub>2</sub> • 2.5 H<sub>2</sub>O, F.W. 350.13 (US Pharmacopeia Cat # 1604610)

USP Risedronate Related Compound A RS, F.W. 283.12 (US Pharmacopeia Cat # 1604621)

USP Risedronate Related Compound C RS, F.W. 267.11 (US Pharmacopeia Cat # 1604643)

Sodium hydroxide, 50% w/w (Fisher Chemical Cat # SS254-500)

Edetate disodium [EDTA, disodium salt, dihydrate USP grade (VWR Cat # 1395-04)]

## **Samples**

Drug substance: Risedronate sodium, hemi-pentahydrate

Drug product: Tablets containing 35 mg risedronate sodium per tablet.

Samples were donated by a pharmaceutical company.

## **CONDITIONS**

Column: Dionex IonPac AS7 analytical,  
4 × 250 mm (P/N 035393)  
Dionex IonPac AG7 guard, 4 × 50 mm  
(P/N 035394)

Mobile Phase: 4.8 mM EDTA,  
pH = 9.5 ± 0.1

Flow Rate: 0.8 mL/min

Inj. Volume: 20 µL

Temperature: 25 °C

Detection: UV absorbance, 263 nm

System

Backpressure: ~1430 psi

Noise: ~0.016 mAU

Run Time: 20 min

## **PREPARATION OF SOLUTIONS AND REAGENTS**

### **Sodium Hydroxide, 5 M**

To prepare 5 M sodium hydroxide (NaOH) solution, pipette 26.2 ml of 50% w/w NaOH into a 100 mL polypropylene volumetric flask containing approximately 50 mL of DI water, then dilute to the mark with DI water. Stir gently to mix well.

### **Mobile Phase**

Weigh and transfer 1.80 g of EDTA to a 1 L polypropylene bottle and dilute to a final weight of 1000 g with degassed DI water. Mix the solution until all the EDTA is dissolved. Adjust the pH of the resulting 4.8 mM EDTA disodium solution to 9.5 ± 0.1 by adding 1.16 mL of 5 M NaOH solution. Set aside 500 mL of the mobile phase to use as diluent.

## **PREPARATION OF STANDARDS AND SAMPLE SOLUTIONS**

Risedronate sodium can be either a monohydrate containing one molecule of water or a hemi-pentahydrate containing 2.5 molecules of water. The hemi-pentahydrate form has 12.9% water, which equals 0.871 g of anhydrous risedronate sodium per 1.0 g of risedronate sodium hemi-pentahydrate. This must be considered when preparing the standards and samples on an anhydrous basis. All standard and sample solutions are stable for at least 30 days when stored at 4 °C.

## **DRUG SUBSTANCE ASSAY**

### **USP Related Compound A Stock Solution**

Weigh 10.0 mg of compound A into a 20 mL polypropylene bottle and tare the balance. Add 10.0 g of diluent to make 1.0 mg/mL USP risedronate-related compound A stock solution. Close the bottle cap and agitate using a vortex mixer for approximately 1 min to dissolve the solid material.

### **USP Risedronate Standard**

Weigh 11.5 mg of USP risedronate sodium hemi-pentahydrate into a 20 mL polypropylene bottle and tare the balance. Add 1.0 g of 1 mg/mL USP related compound A stock solution and bring the final weight to 10.0 g with diluent. Close the bottle cap and agitate using vortex mixer for 1 min to obtain a homogenous solution of 1.0 mg/mL anhydrous risedronate sodium with 0.1 mg/mL of USP related compound A.

### **Assay Preparation**

Weigh 11.5 mg of risedronate sodium hemi-pentahydrate sample into a 20 ml polypropylene bottle and tare the balance. Add 10 g of diluent to make a sample solution of approximately 1.0 mg/mL anhydrous risedronate sodium. Agitate using a vortex mixer for approximately 1 min to dissolve the solid material.

## **DRUG PRODUCT ASSAY**

### **USP Risedronate Sodium Stock Standard**

Weigh 11.5 mg of USP risedronate sodium hemi-pentahydrate into a 20 mL polypropylene bottle, tare the balance, and add 10.0 g of diluent. Close the bottle cap and agitate using vortex mixer for 1 min to obtain a homogenous solution of 1.0 mg/mL anhydrous risedronate sodium.

### **USP-Related Compound C Stock Solution**

Weigh 10.0 mg of USP risedronate-related compound C into a 20 mL polypropylene bottle and tare the balance. Add 10.0 g of diluent to obtain 1.0 mg/mL USP risedronate-related compound C stock solution. Close the bottle cap and agitate using vortex mixer for approximately 1 min to ensure the solid is completely dissolved.

### System Suitability Standard

Transfer 1.5 mL of risedronate sodium stock solution and 75  $\mu$ L of USP risedronate-related compound C stock solution into a 20 mL polypropylene bottle, tare the balance, and add 10.0 g of diluent. Close the bottle cap and agitate using vortex mixer to obtain a homogenous solution of 0.15 mg/mL anhydrous risedronate sodium with 7.5  $\mu$ g/mL of related compound C.

### USP Risedronate Sodium Working Standard

Transfer 1.0 mL of risedronate sodium stock solution into a 20 mL polypropylene bottle, tare the balance, and bring the final weight to 10.0 g with diluent. Close the bottle cap and agitate using vortex mixer for a few seconds to obtain a homogenous solution of 0.1 mg/mL anhydrous risedronate sodium.

### Assay Preparation

Risedronate sodium tablets are available in 5, 30, 35, or 75 mg strength dosage forms. For this study, 35 mg strength tablets were used. To assay risedronate in tablets, dissolve 5 tablets in 350 g diluent by shaking continuously for 10 min, then sonicate for 5 min to obtain a 0.5 mg/mL solution. Decant approximately 10 mL of the supernatant into a centrifuge tube, discarding the insoluble material, and centrifuge at 5000 rpm for 15 min. Dilute 2 mL of the supernatant from the centrifuge tube to 10 mL with diluent to obtain a final solution of 0.1 mg/mL of risedronate sodium.

### Precautions

Use polypropylene bottles instead of glassware for mobile phase preparation. Calcium and other metal ions can leach from glassware, making it difficult to accurately adjust the pH of the EDTA solution. In addition, maintaining the mobile phase pH within the specified range and adding a consistent volume of NaOH to adjust pH is critical to avoid retention time shifts and decreased resolution between risedronate and its related compounds. If the resolution does not meet the USP specification, verify that the mobile phase pH is within  $9.5 \pm 0.1$ . Due to the strong chelation character of risedronate with metals, risedronate determination requires a metal-free system for efficient peak shapes.

## RESULTS AND DISCUSSION

### Separation and Detection

Separation of risedronate from its related substances is achieved on a Dionex IonPac AS7 ( $4 \times 250$  mm) column with 4.8 mM EDTA mobile phase adjusted to pH 9.5. The Dionex IonPac AS7 column is specially designed for determining polyvalent anions, such as bisphosphonates. At  $\text{pH } 9.5 \pm 0.1$ , risedronate is readily ionized into a polyvalent anion and EDTA is predominantly trivalent. Separation is likely achieved by the trivalent EDTA anion eluting the polyvalent risedronate anion. The EDTA in the mobile phase also helps prevent metal contaminants from chelating with risedronate. Risedronate and its related compounds elute within 15 min and the detection is by UV absorbance at 263 nm.

Figure 2, trace A, shows the separation of risedronate from related compound C, and trace B shows the separation of risedronate and its related compound A using the conditions described in the monograph. The retention times of related compound C, related compound A, and risedronate were approximately 9.4, 10.2, and 11.9 min, respectively. Figure 3 shows a risedronate peak in the drug product (Actonel<sup>®</sup>, 35 mg tablet) preparation.

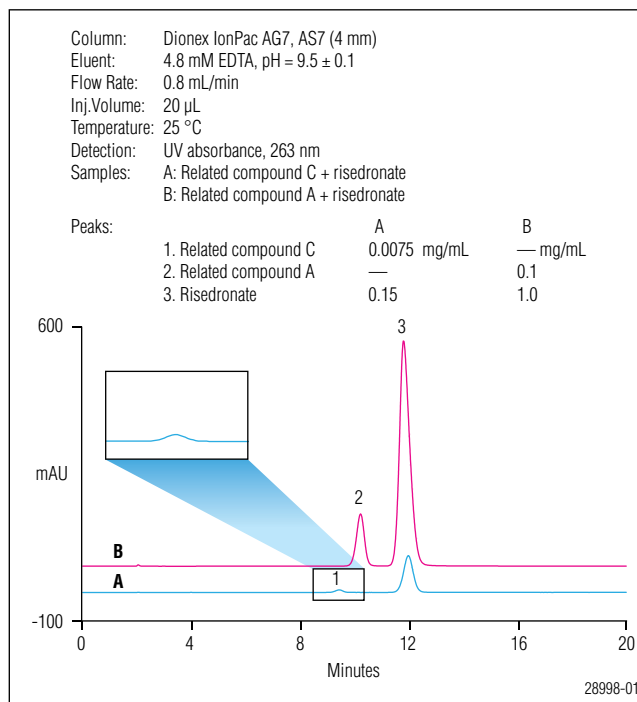


Figure 2. Overlay of chromatograms of risedronate standard with related compound C in trace A and related compound A in trace B.

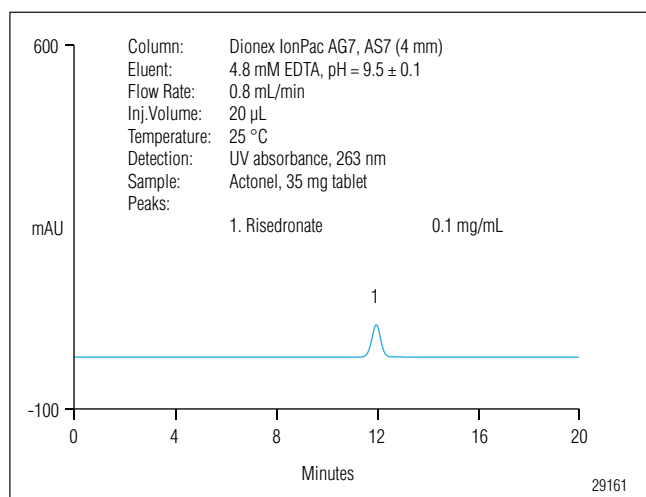


Figure 3. Chromatogram of Actonel, 35 mg tablet preparation showing risedronate.

The USP specifies values for the assay amount, resolution between risedronate and its related compounds, tailing factor, and peak area RSD in both drug product and drug substance monographs. All these parameters were evaluated and proven to meet or exceed the USP specifications. To obtain the specified resolution of  $\geq 2.3$  between related compound A and risedronate in the analysis of the drug substance, it is critical to prepare the mobile phase as outlined here. Typically, the amount of 5 M NaOH solution required to adjust the mobile phase pH to  $9.5 \pm 0.1$  is less than 1.2 mL. If more NaOH is required to obtain the correct pH, there is a possibility of not meeting the USP resolution specification. In this case, the mobile phase should be prepared fresh with attention to the amount of NaOH added. Peak asymmetry or tailing factor for risedronate was 1.3, which meets the USP specification of  $\leq 1.5$ . A tailing factor  $> 1.5$  can indicate metal contamination in the solutions and/or the system.

For three replicate injections of risedronate standard, peak area precision of 0.32% was obtained, which is within the USP specification limit of  $\leq 1.0\%$ . The USP specifications and the experimental values obtained are presented in Table 1.

Table 1. Specifications				
Drug Substance				
	Tailing Factor	Resolution <sup>a</sup>	% RSD <sup>c</sup>	% Risedronate
USP Spec.	$\leq 1.5$	$\geq 2.3$	$\leq 1.0$	98.0%–102.0%
Experimental	1.3	2.5	0.32	99.6%
Drug Product				
	Resolution <sup>b</sup>	% RSD <sup>c</sup>	% Risedronate	
USP Spec.	$\geq 2.5$	$\leq 1.0$	90.0%–110.0%	
Experimental	4.4	0.19	98.3%	

<sup>a</sup>Related compound A and risedronate

<sup>b</sup>Related compound C and risedronate

<sup>c</sup>n = 3

#### Linearity, Limit of Detection (LOD), and Limit of Quantification (LOQ)

To determine linearity, the system was calibrated using duplicate injections of five concentrations covering the range of 0.5 to 1.5 mg/mL anhydrous risedronate sodium for the drug substance and 0.05 to 0.15 mg/mL anhydrous risedronate sodium for the drug product. Peak area response was plotted versus the risedronate concentration, and linear regression analysis was performed. The baseline noise for LOD was determined by measuring the peak-to-peak noise in a representative 1 min segment of the baseline where no peaks elute. The method demonstrated a very low LOD and LOQ of 0.08  $\mu\text{g/mL}$  and 0.3  $\mu\text{g/mL}$ , respectively, for risedronate. Table 2 shows the linearity, LOD, and LOQ for risedronate determined in the drug substance and drug product using UV detection.

Table 2. Linearity, LOD, LOQ for Risedronate					
	Analyte	Range (mg/mL)	Coefficient of Determination ( $r^2$ )	LOD ( $\mu\text{g/mL}$ )	LOQ ( $\mu\text{g/mL}$ )
Substance	Risedronate	0.5–1.5	1.00	0.08	0.3
Product	Risedronate	0.05–0.15	0.9999	0.08	0.3

## Accuracy and Precision

Method accuracy was tested by preparing risedronate sodium drug substance and tablets (drug product) in triplicates at 75%, 100%, and 125% of the monograph concentration, which is 1.0 mg/mL anhydrous risedronate for the drug substance and 0.1 mg/mL for the drug product. The % assay for the samples was calculated using the following formula found in both the USP monographs:

$$\% \text{ risedronate} = 100 (C_s/C_u) (r_u/r_s)$$

$C_s$  is concentration, in mg/mL, of anhydrous  $R_s$  in the standard preparation.

$C_u$  is concentration, in mg/mL, of anhydrous  $R_s$  in assay preparation.

$r_u$  is assay preparation peak area response.

$r_s$  is standard preparation peak area response.

The average percent assay of risedronate in the drug substance prepared at 0.75, 1.00, and 1.25 mg/mL anhydrous risedronate is 99.5%, 99.6%, and 99.1%, respectively. Average percent assay of risedronate in the drug product (tablets) prepared at 0.075, 0.100, and 0.125 mg/mL anhydrous risedronate is 97.1%, 98.3 %, and 97.7%, respectively. The USP monograph specifies % assay for risedronate in the drug substance to be  $100.0 \pm 2.0\%$  and in the drug product to be  $100.0 \pm 10.0\%$ . All the values obtained in this validation successfully meet the specifications.

Method precision was calculated from the peak area values at three different concentrations. For both substance and product analysis, the method shows a peak area precision of <1.0% at the test concentration (100%) and <2.0% for concentrations at 75% and 125% of the test method concentration. The accuracy and precision values are reported in Tables 3 and 4.

**Table 3. Accuracy and Precision for the Determination of Risedronate in the Drug Substance**

Drug Substance Preparation	Concentration (mg/mL)	Average Peak Area Response (mAU*min)	% RSD	% Risedronate	Average % Assay
75%-1	0.75	172.1	1.0	98.6	99.5 ± 0.8
75%-2	0.75	175.6		99.9	
75%-3	0.75	174.8		99.9	
100%-1	1.00	233.7	0.3	99.9	99.6 ± 0.5
100%-2	1.00	233.3		99.9	
100%-3	1.01	234.7		99.0	
125%-1	1.25	289.5	1.0	99.6	99.1 ± 0.9
125%-2	1.25	284.5		98.0	
125%-3	1.25	289.6		99.6	
<b>1.01 mg/mL anhydrous USP risedronate standard response 235.9 mAU*min</b>				<b>Average</b>	<b>99.4</b>
				<b>Std. Dev.</b>	<b>0.3</b>

**Table 4. Accuracy and Precision for the Determination of Risedronate in the Drug Product (Tablet)**

Drug Product Preparation	Concentration (mg/mL)	Average Peak Area Response (mAU*min)	% RSD	% Risedronate	Average % Assay
75%–1	0.075	17.5	2.0	98.6	97.1 ± 1.5
75%–2	0.075	17.3		97.2	
75%–3	0.075	16.8		95.6	
100%–1	0.100	23.1	0.6	98.0	98.3 ± 0.6
100%–2	0.100	23.1		98.0	
100%–3	0.100	23.3		99.0	
125%–1	0.125	29.0	1.8	98.8	97.7 ± 1.8
125%–2	0.125	29.0		98.8	
125%–3	0.125	28.1		95.6	
<b>0.101 mg/mL anhydrous USP risedronate standard response 23.8 mAU*min</b>				<b>Average</b>	<b>97.7</b>
				<b>Std. Dev.</b>	<b>0.6</b>

### Method Robustness

According to the International Conference on Harmonization (ICH): "The robustness of an analytical procedure is a measure of its capacity to remain unaffected by small but deliberate variations in method parameters and provides an indication of its reliability during normal usage."<sup>8,9</sup> Although not required in the USP monograph, this method was evaluated for its ability to pass USP specifications with slight changes in the parameters that can be expected during routine analysis. Column temperature, mobile phase pH, and the

condition of the column were variables selected for this study. Column temperature was varied by  $\pm 2$  °C from the control temperature of 25 °C and the pH was varied within the USP specified range of  $9.5 \pm 0.1$  units. In addition, two Dionex IonPac AS7 columns from the same manufactured lot were compared for this analysis. The results from this study are presented in Table 5. All the USP specifications were still met despite the variations in the test method parameters. Resolution between related compound A and risedronate is affected most significantly by these variations.

**Table 5. Robustness for the Analysis of the Drug Substance**

Parameter	Resolution <sup>a</sup> (spec $\geq 2.3$ )	Difference (%)	Resolution <sup>b</sup> (spec $\geq 2.5$ )	Difference (%)	Tailing Factor <sup>c</sup> (spec $\leq 1.5$ )	Difference (%)	Risedronate Peak Area (mAU*min)	Difference (%)
<b>Column Temperature</b>								
<b>23 °C</b>	3.0	+20	4.5	+2	1.18	-8	233.1	-1
<b>25 °C</b>	2.5	—	4.4	—	1.28	—	236.5	—
<b>27 °C</b>	2.9	+16	4.6	+5	1.25	-2	232.7	-2
<b>Mobile Phase pH</b>								
<b>9.38</b>	3.4	+36	4.7	+7	1.15	-10	231.5	-2
<b>9.52</b>	2.5	—	4.4	—	1.28	—	236.5	—
<b>9.63</b>	2.6	+4	4.4	0	1.28	0	231.0	-2
<b>Column Condition</b>								
<b>Column 1 After ~ 550 Injections</b>	2.5	—	4.4	—	1.28	—	236.5	—
<b>Column 2</b>	3.3	+32	5.1	+16	1.45	+13	236.7	+0.1

<sup>a</sup>Resolution between related compound A and risedronate

<sup>b</sup>Resolution between related compound C and risedronate

<sup>c</sup>Tailing factor of risedronate peak

## CONCLUSION

The USP monograph for risedronate sodium was used to assay the API in the drug substance and product, which is available from 5–75 mg strength tablets. This method is based on an anion-exchange separation with a 4 × 250 mm Dionex IonPac AS7 (USP L48) column using EDTA eluent to resolve risedronate from related compounds. As shown in Table 1, the results exceeded the USP monograph specifications. The method separated risedronate in <15 min and it was well resolved from related compounds A and C. Although not specifically required in the USP monograph, the method ruggedness was also evaluated by varying the column temperature, eluent pH, and using different Dionex IonPac AS7 columns from the same lot. For each variable in the range tested, the results met or exceeded the USP specifications to demonstrate method ruggedness. The results from this study demonstrated a simple, rugged, and accurate method to assay risedronate sodium in the drug substance and product. Therefore, the method is suitable for quality control labs to ensure that the drug meets the approved specifications.

## SUPPLIERS

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Rockville, Maryland 20852-1790, U.S.A.  
Tel: 800-227-8772.  
<http://www.usp.org>

## REFERENCES

1. Graham, R.; Russell, G. *Bisphosphonates: The First 40 Years*. The Mellanby Centre for Bone Research, University of Sheffield, Sheffield, U.K. doi:10.1016/j.bone.2011.04.022 (accessed July 29, 2011).
2. Russell, R.G. Bisphosphonates: Mode of Action and Pharmacology. *Pediatrics* **2007**, *119* (Suppl. 2:S), 150–62.
3. DeRuiter, J.; Clark, R. Bisphosphonates: Calcium Antiresorptive Agents. *Endocrine Module*, **2002**, (Spring).
4. America's Bone Health: The State of Osteoporosis and Low Bone Mass in Our Nation; National Osteoporosis Foundation: Washington, DC, 2002.
5. Dolan, J.W. Ion Pairing—Blessing or Curse? *LCGC Europe* **2008**, *21* (5).
6. U.S. Pharmacopeia 34, National Formulary 29, 2011, p 4166.
7. *Validation of Analytical Procedures, Q2A Definitions and Terminology*, Guidelines prepared within the International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use, ICH, 1995, 1–5.
8. U.S. Pharmacopeia Forum 34 (5) 2010, pp 1183, 1186.
9. *Validation of Analytical Procedures, Q2B Methodology*, Guidelines prepared within the International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use, ICH, 1996, 18.

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