

# Characterization of an extemporaneous liquid formulation of lisinopril

KAREN C. THOMPSON, ZHONGXI ZHAO, JESSICA M. MAZAKAS,  
CHRISTOPHER A. BEASLEY, ROBERT A. REED, AND CHERYL L. MOSER

Lisinopril is an orally active angiotensin-converting enzyme (ACE) inhibitor used for the treatment of hypertension, heart failure, and acute myocardial infarction. It is currently supplied as 2.5-, 5-, 10-, and 20-mg tablets in two brand-name products, Prinivil (Merck Research Laboratories, West Point, PA) and Zestril (AstraZeneca UK Ltd., London, England). Recent clinical studies have been completed with pediatric patients using a suspension of lisinopril prepared from 20-mg Zestril or Prinivil tablets.<sup>1</sup> An extemporaneously compounded oral suspension allows physicians to adjust the dose for pediatric patients and provides easier administration for patients who have difficulty swallowing tablets. Pharmacokinetic studies have demonstrated the bioequivalence between lisinopril suspension and 20-mg Prinivil tablets in adults.<sup>2</sup> This article describes the development of a lisinopril 1-mg/mL oral suspension.

The vehicle used for the lisinopril suspension was selected with several specific objectives. First, only vehicles readily available to pharmacies for pharmaceutical compounding were considered. Second, the desired product would be used over the

**Abstract:** The stability of lisinopril in an extemporaneously prepared suspension stored at or below 25 °C for 28 days under ambient light exposure was studied.

A formulation of 1-mg/mL oral suspension was prepared from commercially available 20-mg lisinopril tablets, using Bicitra and Ora-Sweet SF as the compounding vehicles to make a final volume of 200 mL. Individual samples, stored in 8-oz amber polyethylene terephthalate bottles, were used for each test performed. All samples were stored at 25 °C. Appropriateness of the extemporaneous preparation method was performed by shaking three lots of each suspension for 30, 60, and 90 seconds. To test the robustness and reproducibility of the method, two chemists prepared the suspensions from the same three lots of lisinopril tablets. Chemical and physical stability were established by analyzing duplicate samples at time zero and after one, two, four, and six weeks. The solubility of lisinopril was tested from suspensions stored for four weeks. In-use stability was also examined over four weeks. Photochemical stability was examined by expos-

ing three batches of the suspension to maximum light stress in accordance with the International Conference on Harmonization. Antimicrobial-effectiveness testing was also conducted with freshly prepared suspensions and suspensions stored for six weeks.

The preparation method used was appropriate and effective. Lisinopril is fully dissolved in the suspension matrix. Satisfactory chemical, physical, and microbiological results were obtained after the suspensions were stored for six weeks at 25 °C and 35% relative humidity.

Lisinopril suspensions extemporaneously prepared from tablets are stable for at least four weeks when stored at or below 25 °C under ambient light exposure.

**Index terms:** Angiotensin converting enzyme inhibitors; Compounding; Containers; Contamination; Formulations; Lisinopril; Photodecomposition; Polyethylene terephthalate; Solubility; Stability; Storage; Suspensions

**Am J Health-Syst Pharm.** 2003; 60:69-74

course of one month, with multiple doses taken from a single bottle, so preservation of the vehicle was necessary to minimize microbial growth over the shelf life of the suspension. Vehicles preserved with sodium benzoate increased the risk of adverse

events for pediatric patients and were not considered for use in this suspension.<sup>3</sup> Compounding vehicles preserved with parabens and potassium sorbate were pursued as they provided less risk to low-birth-weight infants and term infants with signifi-

KAREN C. THOMPSON, PH.D., is Senior Research Fellow, Formulation Design and Characterization; ZHONGXI ZHAO, PH.D., is Research Fellow; JESSICA M. MAZAKAS, B.S., is Staff Chemist; CHRISTOPHER A. BEASLEY, B.S., is Chemist; ROBERT A. REED, PH.D., is Director; and CHERYL L. MOSER, M.S., is Senior Research Associate, Pharmaceutical Analysis and Control, Merck Research Laboratories, West Point, PA.

Address correspondence to Dr. Thompson at Merck Research Laboratories, P.O. Box 4, WP78-302, West Point, PA 19486 (karen\_thompson@merck.com).

Supported in part by AstraZeneca Pharmaceuticals LP.

Copyright © 2003, American Society of Health-System Pharmacists, Inc. All rights reserved. 1077-0002/03/0101-0069\$06.00

## REPORTS Lisinopril

cant hyperbilirubinemia.<sup>4</sup> Ora-Sweet and Ora-Sweet SF were considered as compounding vehicles on the basis of their preservatives. Of the two, Ora-Sweet SF was chosen as the primary vehicle for long-term administration in pediatric patients because it is sugar free.

The extemporaneous formulation was prepared from 20-mg Prinivil or Zestril tablets. Although these tablets contain calcium phosphate, after preparing the suspension the pH was high enough to decrease the antimicrobial effectiveness of potassium sorbate.<sup>5</sup> Bicitra (Alza Corporation, Mountain View, CA), an oral solution containing sodium citrate and citric acid, was used to control the pH and effectively adjust the calcium phosphate. This vehicle was added to the Ora-Sweet SF and the stability of the resulting suspension was analyzed.

### Methods

For every test performed and described below, separate bottles were freshly made and discarded immediately after high-performance liquid chromatography (HPLC) analysis, except for the in-use stability test. For that test, bottles of lisinopril suspension were repeatedly sampled and returned to storage.

**Preparation of samples.** Each oral suspension of lisinopril 1 mg/mL was prepared by placing 10 20-mg lisinopril (Prinivil<sup>a</sup> or Zestril<sup>b</sup>) tablets and 10 mL of purified water into an 8-oz amber polyethylene terephthalate (PET) bottle,<sup>c</sup> shaking by hand, and gradually adding the compounding vehicles (Bicitra solution<sup>d</sup> and Ora-Sweet SF<sup>e</sup>), shaking the bottle after each addition, to achieve a final volume of 200 mL. The suspensions were shaken before each use and stored at or below 25 °C for 28 days. The detailed procedure for this extemporaneous compounding is provided in the appendix.

**Assay of lisinopril suspension.** A gradient HPLC method was developed to assay lisinopril, its degradation

product diketopiperazine, methylparaben and propylparaben, and the chromatographically rich matrix of Bicitra and Ora-Sweet SF. Commercial HPLC instruments<sup>f</sup> equipped with a photodiode array detector were used for sample assay analyses. A C-8 column<sup>g</sup> was used because of its extended polar selectivity to separate hydrophilic species around lisinopril and diketopiperazine. Column temperature was maintained at 40 °C. Two reservoirs contained the mobile phases of (A) 91% 30-mM phosphate buffer<sup>h</sup> with a pH of 2.2 and 9% acetonitrile<sup>i</sup> and (B) acetonitrile<sup>i</sup>, which were pumped through the column at a flow rate of 1.0 mL/min. The gradient conditions were isocratic, with 100% mobile phase A for 16 minutes, followed by a linear gradient from 0 to 45% mobile phase B over the next 9 minutes, and remained at 45% mobile phase B over the next 15 minutes. The injection volume was 50  $\mu$ L, and the detection wavelength was 215 nm.

The analytical standard was prepared in mobile phase A. An analytical standard consisting of lisinopril,<sup>j</sup> diketopiperazine,<sup>k</sup> methylparaben,<sup>l</sup> and propylparaben<sup>m</sup> was prepared at concentrations of 31, 0.3, 12, and 3.2  $\mu$ g/mL, respectively. Satisfactory chromatographic resolution was obtained for all four species in the standard solution. Lisinopril, methylparaben, diketopiperazine, and propylparaben eluted at 7.4, 13.1, 17.8, and 26.0 minutes, respectively. Analytical sample solutions were prepared by pipetting 5 mL of the lisinopril suspension into 200-mL flasks and diluting to volume with mobile phase A.

Method validation was performed for specificity, recovery, linearity, limits of detection and quantitation, solution stability, and method precision. For lisinopril, the mean  $\pm$  S.D. recovery for samples with concentrations ranging from 50% to 150% of the testing concentration (0.025 mg/mL) was 99.1%  $\pm$  0.3% ( $n = 10$ ) and the correlation coefficient for lineari-

ty was 0.9999. The mean  $\pm$  S.D. recovery for diketopiperazine samples with concentrations ranging from 0.1% to 1.5% of the nominal lisinopril concentration (0.025 mg/mL) was 105.6%  $\pm$  2.6% ( $n = 10$ ) and the correlation coefficient for linearity was 0.999.

The linear response of methylparaben and propylparaben was examined by diluting appropriate amounts of Ora-Sweet SF, which contained both parabens from 50% to 150% of the final target composition and yielded a correlation coefficient greater than 0.99. The precision of measurement was examined using multiple injections of a standard solution, resulting in acceptable values for lisinopril, diketopiperazine, methylparaben, and propylparaben with standard deviations of 0.2%, 0.6%, 0.2%, and 0.4%, respectively ( $n = 10$ ). The precision of the method was examined by preparing 10 lisinopril suspension samples, yielding standard deviations of 0.6%, 0.4%, and 2.0% for lisinopril, methylparaben, and propylparaben, respectively. Diketopiperazine levels in all samples were below quantitation limits. The method's limits of detection and quantitation were 0.03% and 0.1%, with a minimum signal-to-noise ratio of 3 and 13, respectively. Both sample and standard solutions were stable for one week under ambient temperature and light conditions.

**Formulation appropriateness.** *Shaking time.* Initial studies were performed to examine the sensitivity of the extemporaneous sample preparation to the recommended one minute of shaking time. Three sample preparations were independently made from different lots of Prinivil tablets.<sup>a</sup> Bottles were shaken for 30, 60, and 90 seconds to disperse the tablets. The sample preparations were completed as previously described and assayed by HPLC.

*Robustness.* Three different lots of Prinivil tablets<sup>a</sup> were used by two different chemists to prepare oral

suspensions to demonstrate the reproducibility and robustness of the extemporaneous preparation. The robustness of the preparation method for lisinopril pediatric suspension using Zestril tablets was also established by using three different lots of Zestril tablets.<sup>b</sup> All samples were analyzed by HPLC.

**Stability studies.** *Chemical and physical stability.* Bottles of suspension were prepared from three different lots of Prinivil tablets,<sup>a</sup> stored in a stability chamber at 25 °C and 35% relative humidity, and analyzed in duplicate at time zero (preparation) and after one, two, four, and six weeks. Each bottle was sampled only once, and the bottles were discarded after sampling.

*Solubility.* Lisinopril solubility in the suspensions was evaluated by studying four-week samples made from Prinivil tablets<sup>a</sup> both before and after shaking the sample for 30 seconds. Four weeks after the suspensions were prepared, samples were carefully removed from the stability chambers to avoid further mixing the suspension. A 5-mL sample was pipetted from the clear upper portion of the solution. The same bottle was then shaken for about 30 seconds to resuspend the insoluble portion of the formulation to yield a uniform suspension. Another 5-mL sample of the suspension was taken. Both 5-mL samples were assayed.

*In-use stability.* To test the formulation's in-use stability, lisinopril suspensions generated from Prinivil tablets<sup>a</sup> from three different lots were tested immediately after preparation. Subsequently, one bottle from each lot was stored at 25 °C and 60% relative humidity. The same bottles were repeatedly sampled and returned to the chamber after one, two, and four weeks of storage. All samples were assayed by HPLC.

*Photochemical stability.* Three batches of lisinopril suspensions generated from each of the Prinivil tablet lots<sup>a</sup> were prepared and exposed to

maximum light stress, in accordance with the International Conference on Harmonization (ICH) (a minimum of 1.2 million lux-hours of visible light, followed by a minimum of 200 W-hours/m<sup>2</sup> of ultraviolet light), in a photostability chamber<sup>n</sup> at 25 °C. One bottle from each preparation lot was wrapped in aluminum foil and placed in the light chamber to act as a control. All samples were then analyzed by HPLC.

**Antimicrobial-effectiveness testing.** Antimicrobial-effectiveness testing was performed on lisinopril suspensions in accordance with *USP* requirements<sup>6</sup> at Lancaster Laboratories (Lancaster, PA) and the Pharmaceutical Analysis and Control Division at Merck Research Laboratories (West Point, PA). Testing was conducted on freshly prepared suspensions and suspensions stored for six weeks at 25 °C and 35% relative humidity in an 8-oz PET bottle.

**Results and discussion**

**Appropriateness of extemporaneous preparation.** After the suspension was prepared, the bottles were shaken individually for 30, 60, or 90 seconds. Table 1 summarizes the effect of shaking time on the solubility of

lisinopril. The entire content of lisinopril in Prinivil tablets dissolved into water after 30 seconds of shaking; therefore, the recommended shaking time of one minute is more than adequate.

The reproducibility and robustness of the extemporaneous preparation are illustrated in Table 2. Lisinopril dissolved completely after 60 seconds of shaking. Low standard deviations were obtained by both chemists for each suspension. The developed extemporaneous preparation for Prinivil tablets can also be easily applied to Zestril tablets, as shown in Table 3, and yields similar reproducibility and robustness results to those suspensions prepared with Prinivil tablets.

**Stability.** Table 4 summarizes the chemical and physical results of lisinopril, methylparaben, propylparaben, and diketopiperazine. Methylparaben and propylparaben contents were monitored to assess their chemical stability. Lisinopril, methylparaben, and propylparaben concentrations; pH; and appearance were unchanged throughout the six-week period for all three suspensions. A 0.1% increase in the levels of diketopiperazine was observed and considered inconsequen-

Table 1. Lisinopril Concentrations in Oral Suspensions Prepared from Prinivil Tablets with Different Shaking Times

Lot	% Nominal Concentration (1 mg/mL)		
	30-sec Shake	60-sec Shake	90-sec Shake
1	101.7	103.1	101.7
2	99.7	103.1	102.2
3	101.3	100.5	101.2

Table 2. Lisinopril Concentrations in Oral Suspensions Prepared from Prinivil Tablets by Different Chemists

Lot	% Nominal Concentration (1 mg/mL)		
	Chemist 1	Chemist 2	Mean (% RDS) <sup>a</sup>
1	103.8	101.6	102.6 (1.9)
	104.5	100.3	
2	99.6	100.8	100.4 (0.6)
	100.6	100.7	
3	101.6	100.0	100.9 (0.8)
	101.5	100.5	

<sup>a</sup>n = 4. % RSD = % relative standard deviation.

## REPORTS Lisinopril

tial to the safety and efficacy of lisinopril. This formulation can be stored for up to six weeks at 25 °C and 35% relative humidity.

Because the suspended solid particles precipitate over time, a clear supernatant forms that was sampled to determine the amount of lisinopril in the supernatant solution. The same bottle was then shaken to resuspend the solids, a second sample was taken, and both samples were analyzed by HPLC. The data clearly show that the soluble drug does not settle out with insoluble excipients after sitting undisturbed for four weeks and that lisinopril remains quantitatively fully dissolved in the extemporaneous

preparations (Table 5). These data were expected because Bicitra and Ora-Sweet SF are water-based diluents and because lisinopril has an aqueous solubility almost 100 times higher than the targeted 1-mg/mL concentration in the targeted pH range (4–5).

The in-use stability study simulated actual usage by patients. Each suspension was removed from the stability chamber, sampled, and returned to the chamber at each time point. The suspension's chemical and physical integrity were then monitored after each repeated sampling. The properties of these suspensions remained unchanged, sup-

porting the multidose use of this extemporaneously compounded product (Table 6).

Duplicate samples of extemporaneous preparations from each lot were exposed to 1.2 million lux of visible light and 200 W/m<sup>2</sup> of ultraviolet light and agreed within experimental error (Table 7). Further, no significant differences between the control samples and the full ICH light-stressed samples were observed. Therefore, precautions against exposure to ambient light are not necessary for lisinopril oral suspensions prepared and stored in PET bottles.

**Antimicrobial effectiveness.** Microorganisms, including *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Candida albicans*, and *Aspergillus niger*, were monitored in the samples, and the resulting data are summarized in Table 8. Both initial and six-week samples passed the *USP* antimicrobial-effectiveness test for a category-1C product.

### Conclusion

Lisinopril suspensions extemporaneously prepared from tablets are stable for at least four weeks when stored at or below 25 °C under ambient light exposure.

Table 3.  
Lisinopril Concentrations in Oral Suspensions Prepared from Zestril Tablets by Different Chemists

Lot	% Nominal Concentration (1 mg/mL)		
	Chemist 1	Chemist 2	Mean (% RSD) <sup>a</sup>
1	101.6	103.1	102.3 (0.7)
	102.0	101.4	
2	101.8	102.8	102.5 (0.4)
	102.0	102.2	
3	101.3	102.2	101.4 (0.8)
	100.7	100.5	

<sup>a</sup>n = 4. % RSD = % relative standard deviation.

Table 4.  
Stability of Lisinopril 1-mg/mL Oral Suspensions and Content of Degradation Product and Preservatives

Time	% Initial Concentration Remaining <sup>a</sup>				pH (n = 1)	Appearance
	Lisinopril	Diketopiperazine	Methylparaben	Propylparaben		
<i>Lot 1</i>						
Initial	100 (0.72)	<0.1	100 (0.15)	100 (0.63)	4.4	Unchanged
Week 1	99.9 (0.98)	<0.1	98.5 (0.36)	101.2 (1.4)	4.3	Unchanged
Week 2	100 (0.21)	<0.1	98.2 (0.07)	100.5 (0.08)	4.3	Unchanged
Week 4	99.9 (0.42)	<0.1	98.0 (2.6)	100.9 (1.1)	4.3	Unchanged
Week 6	98.4 (0.78)	0.1 (141)	96.1 (0.74)	98.8 (1.8)	4.4	Unchanged
<i>Lot 2</i>						
Initial	100 (0.40)	<0.1	100 (0.76)	100 (1.5)	4.3	Unchanged
Week 1	99.7 (0.57)	<0.1	98.8 (0.43)	101.2 (0.60)	4.4	Unchanged
Week 2	100 (0.78)	<0.1	97.6 (0.07)	99.7 (0.15)	4.3	Unchanged
Week 4	100.5 (0.21)	<0.1	97.7 (0.73)	100.6 (0.45)	4.4	Unchanged
Week 6	99.6 (0.14)	0.1 (141)	94.9 (0.22)	96.6 (0.31)	4.4	Unchanged
<i>Lot 3</i>						
Initial	100 (0.51)	0.1 (14.0)	100 (0.32)	100 (1.1)	4.4	Unchanged
Week 1	100.3 (0.70)	0.2 (3.9)	98.1 (1.2)	101.6 (1.0)	4.4	Unchanged
Week 2	99.8 (0.14)	0.2 (18.6)	99.2 (0.51)	101.4 (1.3)	4.3	Unchanged
Week 4	100.6 (0.49)	0.2 (141)	99.2 (0.22)	101.4 (0.67)	4.4	Unchanged
Week 6	99.4 (0.21)	0.2 (141)	96.0 (0.22)	98.5 (0.77)	4.4	Unchanged

<sup>a</sup>Data reported as mean (% relative standard deviation). All samples tested in duplicate, except for initial concentrations, which were measured in triplicate.

Table 5.  
Lisinopril Concentrations in Oral Suspensions with and without Shaking

Lot	% Nominal Concentration (1 mg/mL)	
	Unshaken <sup>a</sup> (n = 2)	Shaken (n = 1)
1	100.8 (0.07)	99.9
2	100.0 (0.28)	99.3
3	100.8 (0.35)	99.5

<sup>a</sup>Data reported as mean (% relative standard deviation).

Table 6.  
Stability of Lisinopril 1-mg/mL Oral Suspension with Multiple Usage

Time	% Initial Concentration Remaining				pH	Appearance
	Lisinopril	Diketopiperazine	Methylparaben	Propylparaben		
<i>Lot 1</i>						
Initial	100	<0.1	100	100	4.4	Unchanged
Week 1	99.6	<0.1	98.9	98.9	4.5	Unchanged
Week 2	100.3	0.1	100.5	106.1	4.5	Unchanged
Week 4	98.8	0.1	100.2	103.2	4.4	Unchanged
<i>Lot 2</i>						
Initial	100	<0.1	100	100	4.4	Unchanged
Week 1	98.6	<0.1	98.8	100.4	4.5	Unchanged
Week 2	99.4	<0.1	100	106.2	4.5	Unchanged
Week 4	97.8	0.1	98.8	103	4.4	Unchanged
<i>Lot 3</i>						
Initial	100	0.1	100	100	4.4	Unchanged
Week 1	99.9	0.1	100.2	99.8	4.5	Unchanged
Week 2	100	0.2	100.1	102.9	4.4	Unchanged
Week 4	98.8	0.2	100.1	101.8	4.4	Unchanged

<sup>a</sup>Data reported as mean±S.D. All samples tested in duplicate, except for initial concentrations, which were measured in triplicate.

Table 7.  
Photochemical Stability of Lisinopril 1-mg/mL Oral Suspension Prepared with Prinivil Tablets

Sample	% Nominal Concentration Remaining <sup>a</sup>				pH	Appearance
	Lisinopril	Diketopiperazine	Methylparaben	Propylparaben		
<i>Lot 1</i>						
Control	100	<0.1	100	100	4.4	Unchanged
Full light-stress	98.6 (0.93)	<0.1	99.2 (0.50)	99.5 (0.30)	4.4	Unchanged
<i>Lot 2</i>						
Control	100	<0.1	100	100	4.4	Unchanged
Full light-stress	99.8 (0.07)	<0.1	100.2 (0.58)	100.3 (1.2)	4.4	Unchanged
<i>Lot 3</i>						
Control	100	<0.1	100	100	4.4	Unchanged
Full light-stress	99.3 (0.28)	<0.1	98.8 (0.43)	96.9 (0.75)	4.4	Unchanged

<sup>a</sup>Data reported as mean (% relative standard deviation) for light-stressed samples, which were tested in duplicate. Full light-stressed = exposure to 1.2 million lux of visible light and 200 W/m<sup>2</sup> of ultraviolet light.

<sup>a</sup>Prinivil 20-mg tablets, Merck & Co., West Point, PA, lots HBB738, HBB754, and J8227.

<sup>b</sup>Zestril 20-mg tablets, AstraZeneca Pharmaceuticals LP, Wilmington, DE, lots CSH871, CSJ151, and CSJ281.

<sup>c</sup>Polyethylene terephthalate 8-oz bottles, Owens Brockway, Brookville, PA.

<sup>d</sup>Bicitra, Alza Corporation, Mountain View, CA, lots 9A008 and 8B131.

<sup>e</sup>Ora-Sweet SF, Paddock Laboratories,

Minneapolis, MN, lots 0D6302, 9F6726, and 8K6273.

<sup>f</sup>HPLC, model HP 1100, Agilent Technologies, Palo Alto, CA.

<sup>g</sup>Alltech Platinum EPS C-8 column, 250-mm × 4.6-mm inner diameter, 5-µm packing, Alltech Associates, Deerfield, IL.

<sup>h</sup>Potassium bisphosphate and phosphoric acid 85%, HPLC grade, Fisher Scientific, Fair Lawn, NJ.

<sup>i</sup>Acetonitrile, Optima grade, Fisher Scientific.

<sup>j</sup>Lisinopril standard, Merck & Co., Rahway, NJ, lot L-154, 826-000T.

<sup>k</sup>Diketopiperazine, Merck & Co., lot L-659, 199-000L.

<sup>l</sup>Methylparaben, Aldrich, Milwaukee, WI, lot L-474, 898-000V.

<sup>m</sup>Propylparaben, Aldrich, lot L-510, 208-000V.

<sup>n</sup>Photostability chamber, model ES 2000, Environmental Specialties, Raleigh, NC.

# Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

## Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

## Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

## Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

## API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

## LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

## FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

## E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.