



Louisiana

C1 Esterase Inhibitor (Cinryze[®], Haegarda[®])

Policy # 00277

Original Effective Date: 02/16/2011

Current Effective Date: 02/08/2021

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: C1 Esterase Inhibitor (Berinert[®]) is addressed separately in medical policy 00276.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider the use of C1 esterase inhibitor (Cinryze[®], Haegarda[®])[†] for routine prophylaxis against hereditary angioedema (HAE) attacks to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility will be considered for the use of C1 esterase inhibitor (Cinryze, Haegarda) for routine prophylaxis against HAE attacks when the following criteria are met:

- Patient has a diagnosis of HAE confirmed by appropriate laboratory test(s); AND
- Patient has a history of laryngeal edema or airway compromise with an episode of HAE OR a history of at least 2 HAE attacks per month.

*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of C1 esterase inhibitor (Cinryze, Haegarda) in the absence of a history of laryngeal edema or airway compromise with an episode of HAE OR in the absence of a history of at least 2 HAE attacks per month to be **not medically necessary**.**

©2021 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

C1 Esterase Inhibitor (Cinryze[®], Haegarda[®])

Policy # 00277

Original Effective Date: 02/16/2011

Current Effective Date: 02/08/2021

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of C1 esterase inhibitor (Cinryze, Haegarda) for routine prophylaxis against HAE attacks without a confirmed diagnosis of HAE by appropriate laboratory tests to be **investigational**.*

Background/Overview

Human plasma-derived C1 esterase inhibitor is available in three products: Berinert^{®†}, Cinryze, and Haegarda. Berinert is indicated for treatment of acute abdominal, facial, or laryngeal attacks of HAE, while Cinryze and Haegarda are both indicated for routine prophylaxis of HAE attacks in pediatric, adolescent, and adult patients. Cinryze is for intravenous use only. In patients 12 years of age and older, a dose of 1000 units of Cinryze can be administered at a rate of 1 mL per minute every 3 or 4 days, but may be increased to a maximum dose of 2500 units (not to exceed 100 units/kg) every 3 or 4 days based on individual patient response. In patients 6 to 11 years of age, the starting dose is 500 units every 3 or 4 days and it may be increased up to 1,000 units every 3 to 4 days. Haegarda is for subcutaneous administration only and should be dosed at 60 units per kilogram body weight twice weekly in patients 6 years of age and older. Haegarda is intended for patient self-administration.

Hereditary Angioedema (HAE)

HAE is a potentially life-threatening autosomal dominant genetic disease in which there is inadequate or nonfunctional complement-1 esterase inhibitor (C1-INH) in the blood. HAE is characterized by episodic, sudden, acute attacks of intense localized edema causing swelling. The swelling can occur almost anywhere but is commonly found in the following body parts: extremities, intestines (abdomen), face, larynx and genitals. Swelling attacks can occur unpredictably and vary in severity and frequency.

The prevalence of HAE is uncertain but is estimated to range from 1 in 10,000 to 1 in 50,000 persons worldwide. It is estimated that HAE affects 6,000 to 30,000 individuals in the U.S. HAE has been reported in all races. No sex predominance has been found between the two main types of HAE (Type I and Type II). Type I HAE accounts for 85% of all cases and results in both decreased

©2021 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

C1 Esterase Inhibitor (Cinryze[®], Haegarda[®])

Policy # 00277

Original Effective Date: 02/16/2011

Current Effective Date: 02/08/2021

antigenic and functional levels of C1-inhibitor. Type II HAE accounts for 15% of all cases and results in normal antigenic C1-inhibitor levels but decreased functional C1 inhibitor levels. Type III HAE is found predominantly in women and was initially associated with therapeutic estrogen. It has been suggested that HAE Type III is caused by activating mutations in the gene for coagulation factor XII. Thus, Type III HAE is not a disease of C1-esterase deficiency and will not be considered further in this review. The disease is inherited in an autosomal dominant manner, and family history is a strong predictor of the disease. However, spontaneous mutation accounts for up to 25% of newly diagnosed cases.

Symptoms of HAE can present at any age, but there appears to be an increased occurrence of HAE after puberty and a reduction after menopause, suggesting a hormone-influenced mechanism. Attacks are commonly triggered by stress, hormonal changes, medical procedures, trauma, or medications that impact bradykinin or hormone levels, such as angiotensin-converting enzyme (ACE) inhibitors and estrogen-containing medications. In some cases, attacks occur without an apparent trigger. Attacks are usually preceded by a prodrome (usually a tingling sensation or painless, nonpruritic rash, skin tightness, and fatigue), which can occur 30 minutes to several hours before an HAE attack. As vascular permeability increases, swelling worsens gradually for the first 24 hours and subsides 48–72 hours after swelling reaches its peak. Unlike histamine-mediated allergic angioedema, HAE swelling attacks are not symmetrical and often extend locally. Edema may begin, worsen, and end in one anatomical location, or begin in one location and emerge in another location, or occur simultaneously in many locations. Abdominal attacks are thought to be the most debilitating attacks experienced by HAE patients. Severe attacks may cause obstruction of the gastrointestinal tract. Repeated attacks may lead to inadequate biliary/pancreatic drainage causing gallbladder disease or pancreatitis. Swelling involving the airway is less common but is potentially life-threatening. The time from symptom onset to asphyxiation ranges from 20 minutes to 14 hours. It has been reported that at least 50% of HAE patients will have a laryngeal attack at some point in their lives and many have these attacks repeatedly. Mortality rates are estimated at 15–30%, largely due to laryngeal edema.

HAE is diagnosed by clinical history, diagnostic tests and exclusion of other causes of angioedema. The specific tests required to make the diagnosis include C4, C1q, and C1-INH (antigenic or functional level). Genetic testing is not necessary to confirm the diagnosis of HAE.

©2021 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

C1 Esterase Inhibitor (Cinryze[®], Haegarda[®])

Policy # 00277

Original Effective Date: 02/16/2011

Current Effective Date: 02/08/2021

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Cinryze was FDA approved for routine prophylaxis against angioedema attacks in adolescent, adult, and pediatric patients with HAE, also known as C1 inhibitor deficiency.

Haegarda is FDA approved for routine prophylaxis to prevent HAE attacks in adolescent, adult, and pediatric patients. It carries the same warnings (hypersensitivity, thromboembolic events, and transmissible infectious agents) as Cinryze.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Cinryze

In the Phase 3 prophylactic treatment trial, Cinryze significantly decreased the number of HAE attacks compared to placebo. The trial had a crossover design with 22 subjects in the efficacy data set. The difference between the number of angioedema attacks during treatment with Cinryze and the number during treatment with placebo was statistically significant ($p < 0.0001$). During 12 weeks of prophylactic treatment with Cinryze, the number of attacks per patient ranged from 0 to 17 with a mean of 6.1 and a median of 6 attacks. During 12 weeks of treatment with placebo, the number of attacks per patient ranged from 6 to 22 with a mean of 12.7 and a median of 13.5 attacks. The clinically and statistically significant results for the primary endpoint demonstrating the efficacy of Cinryze were supported by statistically significant and clinically meaningful differences in all of the secondary endpoints, with Cinryze demonstrating reductions in the severity and duration of attacks and the number of days of swelling.

The safety and efficacy of Cinryze in pediatric patients aged 7 to 11 years of age was assessed in a randomized single-blind, dose-ranging cross-over study of 12 patients. During the 12-week study period, a greater reduction in the normalized number of angioedema attacks per month was observed

©2021 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

C1 Esterase Inhibitor (Cinryze[®], Haegarda[®])

Policy # 00277

Original Effective Date: 02/16/2011

Current Effective Date: 02/08/2021

with 1,000 units of Cinryze compared to 500 units of Cinryze ($p=0.03$). When compared to the baseline observational period, a reduction in the normalized number of angioedema attacks was observed for both Cinryze 500 units and Cinryze 1,000 units (mean absolute reduction in number of HAE attacks: 2.6, 3.0 respectively; mean percent reduction in HAE attacks: 71.1% and 84.5% =, respectively). In addition, both doses lessened the severity of attacks and reduced the use of acute treatment compared with baseline.

Cinryze has been well tolerated with an adverse event profile no different from placebo. The most common adverse reactions observed have been upper respiratory infection, sinusitis, rash and headache. No drug-related serious adverse events (SAEs), no immunogenicity and no decrease in efficacy have been observed in clinical trials. Severe hypersensitivity reactions may occur. Thrombotic events have occurred in patients receiving high dose off-label C1 inhibitor therapy well above the approved treatment dosage regimen. With any blood or plasma derived product, there may be a risk of transmission of infectious agents, e.g. viruses and, theoretically, the CJD agent. The risk has been reduced by screening patients for prior exposure to certain virus infections and by manufacturing steps to reduce the risk of viral transmission including pasteurization and nanofiltration.

Haegarda

Haegarda efficacy and safety were assessed in a multicenter, randomized, double-blind, placebo-controlled crossover study of 90 adult and adolescent subjects with symptomatic HAE type I or II. Subjects were randomized to receive either 60 IU/kg or 40 IU/kg Haegarda in one 16-week treatment period and placebo in the other 16-week treatment period. Patients self-administered Haegarda or placebo subcutaneously 2 times per week. Both studied doses provided a statistically significant decrease in the time-normalized number of HAE attacks relative to placebo. The time normalized number of HAE attacks in subjects dosed with 60 IU/kg was 0.52 attacks per month compared to 4.03 attacks per month while receiving placebo ($p<0.001$). In those dosed with 40 IU/kg, the time normalized number of HAE attacks was 1.19 attacks per month compared to 3.61 attacks per month while receiving placebo ($p<0.001$).

A second study evaluated Haegarda efficacy and safety in 120 adult and pediatric patients with symptomatic HAE type I or II. The median (range) age of subjects was 41 (8-72) years. Patients with a monthly attack rate of 4.3 in 3 months before entry in the study were enrolled and treated for a mean of 1.4 years. Mean steady-state C1-INH functional activity increased to 52% with 40 IU/kg

©2021 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

C1 Esterase Inhibitor (Cinryze[®], Haegarda[®])

Policy # 00277

Original Effective Date: 02/16/2011

Current Effective Date: 02/08/2021

and 66.6% with 60 IU/kg. Incidence of adverse events was similar in both groups. The percentages of subjects with $\geq 50\%$ reductions in the time-normalized number of HAE attacks on Haegarda relative to the time-normalized number of HAE attacks at baseline were 93.1% and 93.1% in the 40 IU/kg and 60 IU/kg treatment arms, respectively. The percentages of subjects with time normalized HAE attack frequency of < 1 HAE attack per 4-week period were 79.7% on 40 IU/kg and 86.9% on 60 IU/kg. The proportion of HAE attack-free subjects throughout the study duration with a maximum exposure of > 2.5 years was 35.6% and 44.3% in the 40 IU/kg and 60 IU/kg treatment arms, respectively.

References

1. Cinryze [C1 Esterase Inhibitor (Human)] US Package Insert. Lev Pharmaceuticals, Inc., New York, NY: October 2020.
2. Blue Cross and Blue Shield Association TEC-Specialty Pharmacy Combined Capacity (SPCC) Report #4. (05/2010). Hereditary *Angioedema (HAE)*.
3. Zuraw, B. 2005. Current and future therapy for hereditary angioedema. *Clinical Immunology*. 114: 10– 16.
4. Agostoni A, Aygoren-Pursun E, Binkley KE, et al. 2004. Hereditary and acquired angioedema: problems and progress: proceedings of the third C1 esterase inhibitor deficiency workshop and beyond. *J Allergy Clin Immunol*. 114(3 Suppl):S51-131.
5. Zwaan, C., Kleine, A., J. H. C. Diris, J., et al., 2002. Continuous 48-h C1-inhibitor treatment, following reperfusion therapy, in patients with acute myocardial infarction. *European Heart Journal*. 23:1670–1677.
6. Caliezi C, Wuillemin WA, Zeerleder S, Redondo M, Eisele B, Hack CE. C1-Esterase Inhibitor: An Anti-Inflammatory Agent and Its Potential Use in the Treatment of Diseases Other Than Hereditary Angioedema. *Pharmacol Rev*. 2000; 52:91-112
7. Davis AE, The pathophysiology of hereditary angioedema. *Clin Immunol*. 2005; 114:3-9.
8. Arzneimittelkommission der Deutschen Aertzeschaft. Schwerwiegende Thrombenbildung nach Berinert HS. *Dtsch Aertztebl*. 2000; 97:B-864
9. Horstick, G et al, 2002. *Circulation* 104:3125-3131.
10. <http://www.medicalnewstoday.com/articles/125247.php>
11. Haegarda [Package Insert]. CSL Behring LLC. Kankakee, IL. Updated October 2020.

©2021 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

C1 Esterase Inhibitor (Cinryze[®], Haegarda[®])

Policy # 00277

Original Effective Date: 02/16/2011

Current Effective Date: 02/08/2021

Policy History

Original Effective Date: 02/16/2011

Current Effective Date: 02/08/2021

02/16/2011 Medical Policy Committee review

02/11/2011 Medical Policy Implementation Committee approval. Format revision; including, addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.

02/02/2012 Medical Policy Committee review

02/15/2012 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

02/07/2013 Medical Policy Committee review

02/20/2013 Medical Policy Implementation Committee approval. Not medically necessary denial section added to policy.

02/06/2014 Medical Policy Committee review

02/19/2014 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

04/02/2015 Medical Policy Committee review

04/20/2015 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

04/07/2016 Medical Policy Committee review

04/20/2016 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes

04/06/2017 Medical Policy Committee review

04/19/2017 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

01/04/2018 Medical Policy Committee review

01/17/2018 Medical Policy Implementation Committee approval. Subcutaneous C1 esterase inhibitor, Haegarda, added to the title and the body of the policy with relevant background information.

02/06/2018 Coding update

01/10/2019 Medical Policy Committee review

©2021 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

C1 Esterase Inhibitor (Cinryze[®], Haegarda[®])

Policy # 00277

Original Effective Date: 02/16/2011

Current Effective Date: 02/08/2021

- 01/23/2019 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
- 01/03/2020 Medical Policy Committee review
- 01/08/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
- 09/14/2020 Coding update
- 01/07/2021 Medical Policy Committee review
- 01/13/2021 Medical Policy Implementation Committee approval. Updated background information to reflect approval for these drugs in pediatric patients 6 years of age and older.

Next Scheduled Review Date: 01/2022

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT[®])[‡], copyright 2020 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

©2021 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

C1 Esterase Inhibitor (Cinryze[®], Haegarda[®])

Policy # 00277

Original Effective Date: 02/16/2011

Current Effective Date: 02/08/2021

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J0598, J0599, J3490, J3590
ICD-10 Diagnosis	D81.810, D84.1 Added codes eff 10/1/2020: D84.81, D84.821, D84.822, D84.89

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 - 1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
 - 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 - 3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;

©2021 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

C1 Esterase Inhibitor (Cinryze[®], Haegarda[®])

Policy # 00277

Original Effective Date: 02/16/2011

Current Effective Date: 02/08/2021

- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

©2021 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.