



Name of Policy:**Transcatheter Ablation of Arrhythmogenic Foci ~~in the Pulmonary Veins~~ as a Treatment of Atrial Fibrillation**

Policy #: 283
Category: Medical

Latest Review Date: June 2014
Policy Grade: A

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

- 1. The technology must have final approval from the appropriate government regulatory bodies;*
- 2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
- 3. The technology must improve the net health outcome;*
- 4. The technology must be as beneficial as any established alternatives;*
- 5. The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

- 1. In accordance with generally accepted standards of medical practice; and*
- 2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
- 3. Not primarily for the convenience of the patient, physician or other health care provider; and*
- 4. 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.*

Description of Procedure or Service:

Radiofrequency ablation using a percutaneous catheter-based approach is widely used to treat supraventricular arrhythmias. Atrial fibrillation frequently arises from an abnormal focus at or near the junction of the pulmonary veins and the left atrium, thus leading to the feasibility of more focused ablation techniques directed at these structures. Catheter-based ablation, using both radiofrequency ablation and cryoablation, is being studied in the treatment of various types of atrial fibrillation.

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and is associated with considerable morbidity and a decrease in the quality of life. The prevalence of AF is estimated at 0.4% of the general population and increases with age. At present, approximately 2.3 million adults in the U.S. have AF.

AF is primarily a disorder of the atrial pacemaker, which initiates the electrical activity leading to coordinated contractions of the atria and ventricles. The underlying mechanism of AF involves interplay between the electrical triggering events and the myocardial substrate that permits propagation and maintenance of the aberrant electrical circuit. The most common focal trigger of AF appears to be located within the cardiac muscle that extends into the pulmonary veins.

AF accounts for approximately one-third of hospitalizations for cardiac rhythm disturbances. Symptoms of AF, e.g., palpitations, decreased exercise tolerance, and dyspnea, are primarily related to poorly controlled or irregular heart rate. The loss of AV synchrony results in a decreased cardiac output, which can be significant in patients with compromised cardiac function. In addition, patients with AF are at higher risk for stroke and thromboembolic events, and anticoagulation is typically recommended. AF is also associated with other cardiac conditions, such as valvular heart disease, heart failure, hypertension and diabetes. Although episodes of AF can be converted to normal sinus rhythm using either pharmacologic or electroshock conversion, the natural history of AF is one of recurrence, thought to be related to fibrillation induced anatomic and electrical remodeling of the atria.

AF represents a relatively heterogeneous disorder. AF can be subdivided into paroxysmal (self-terminating), persistent (non-self terminating), or permanent. Treatment strategies can be broadly subdivided into rate control, in which only the ventricular rate is controlled and the atria are allowed to fibrillate, or rhythm control, in which there is an attempt to re-establish and maintain normal sinus rhythm. Rhythm control has long been considered an important treatment goal for AF management, although it should be noted that its primacy has recently been challenged by the results of two randomized trials, both of which reported that pharmacologically maintained rhythm control offered no improvement in mortality compared to rate control. In any event, in patients with persistent AF, rhythm control typically involves initial pharmacologic or electronic cardioversion, followed by pharmacologic maintenance of normal sinus rhythm. However, episodes of recurrent AF are typical, and patients may require multiple episodes of cardioversion. Implantable defibrillators, which are designed to detect and terminate an episode of AF, may be an alternative in patients otherwise requiring serial cardioversions. Patients with paroxysmal AF, by definition, do not require cardioversion, but may be treated pharmacologically to prevent further episodes of AF. Treatment of permanent AF, by definition,

focuses on rate control, using either pharmacologic therapy or ablation of the AV node followed by ventricular pacing. Although AV nodal ablation produces symptomatic improvement, it does entail lifelong anticoagulation (due to the ongoing fibrillation of the atria), loss of AV synchrony, and lifelong pacemaker dependency. Implantable defibrillators are contraindicated in patients with permanent AF.

The above treatment options are not considered curative. A variety of ablative procedures have been investigated as potentially curative approaches, or perhaps modifying the arrhythmia such that drug therapy becomes more effective. Ablative approaches focus on interruption of the electrical pathways that contribute to AF, through modifying the triggers of AF and/or the myocardial substrate that maintains the aberrant rhythm. The Maze procedure, an open surgical procedure often combined with other cardiac surgeries (e.g., valve repair) is an ablative procedure involving sequential atriotomy incisions designed to create electrical barriers that prevent the maintenance of AF. Since the inception of this technique in the early 1990s, there has been a progressive understanding of the underlying electrical pathways in the heart, such that catheter based radiofrequency procedures have become feasible. Radiofrequency ablation is a widely used technique for a variety of supraventricular arrhythmias where intracardiac mapping identifies a discrete arrhythmogenic focus that is the target of ablation. The situation is more complex for AF, since there is not a single arrhythmogenic focus. However, the recent recognition that triggering foci are commonly located within the myocytes extending into the pulmonary veins creates a potential target for ablation. Three basic strategies have emerged: focal ablation within the pulmonary veins, as identified by electrophysiologic mapping; segmental ostial ablation guided by pulmonary vein potential (electrical approach); or circumferential pulmonary vein ablation (anatomic approach). Circumferential pulmonary vein ablation using radiofrequency energy appears to be the preferred approach at the present time. The procedure also can be done using cryoablation technology. Use of currently available catheters for AF has a steep learning curve because they require extensive guiding to multiple ablation points. One of the potential advantages to cryoablation techniques is that cryoablation catheters have a circular or shaped end point, allowing a “one-shot” ablation. Other types of radiofrequency catheters, such as Medtronic’s radiofrequency-based Pulmonary Vein Ablation Catheter®, that incorporate circular or otherwise shaped end points are under investigation.

Repeat procedures following an initial radiofrequency ablation are commonly performed if atrial fibrillation recurs or if atrial flutter develops post-procedure. The need for repeat procedures may, in part, depend on clinical characteristics of the patient (age, persistent vs. paroxysmal atrial fibrillation, atrial dilatation, etc.), and the type of initial ablation performed. Repeat procedures are generally more limited than the initial procedure. For example, in cases where electrical reconnections occur as a result of incomplete ablation lines, a “touch up” procedure is done to correct gaps in the original ablation. In other cases where atrial flutter develops following ablation a “flutter ablation” is performed, which is more limited than the original atrial fibrillation ablation procedure. A number of clinical and demographic factors have been associated with the need for a second procedure, including age, length of atrial fibrillation, permanent atrial fibrillation, left atrial size, and left-ventricular ejection fraction.

Policy:**Effective for dates of service on or after May 1, 2014:**

Transcatheter ablation of arrhythmogenic foci ~~in the pulmonary veins (pulmonary vein isolation)~~ by means of radiofrequency energy or cryoballoon ablation, meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage as a treatment for atrial fibrillation when all the following criteria are met:

- ~~There is no **significant** structural heart disease. Individual case consideration will be given to patients with hypertrophic cardiomyopathy (both primary and secondary to hypertension), other forms of left ventricular hypertrophy (LVH), coronary artery disease (CSD), or mild forms of valvular heart disease.~~
- Patients have recurrent, symptomatic AF.
- Patients have failed treatment with two or more antiarrhythmic drugs (or have intolerance of or a contraindication to appropriate antiarrhythmic drug therapy).

OR

- Patients with Class II or III congestive heart failure and symptomatic AF in whom heart rate is poorly controlled by standard medications, as an alternative to atrioventricular nodal ablation and pacemaker insertion.

Transcatheter ablation of arrhythmogenic foci ~~in the pulmonary veins~~ does not meet Blue Cross and Blue Shield of Alabama's medical criteria for coverage and is considered investigational as a treatment for all indications except for specific cases of atrial fibrillation as noted above.

Effective for dates of service on or after June 1, 2013 and prior to May 1, 2014:

Transcatheter ablation of arrhythmogenic foci in the pulmonary veins (pulmonary vein isolation) by means of radiofrequency energy or cryoballoon ablation, meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage as a treatment for atrial fibrillation when all the following criteria are met:

1. There is no **significant** structural heart disease. Individual case consideration will be given to patients with hypertrophic cardiomyopathy (both primary and secondary to hypertension), other forms of left ventricular hypertrophy (LVH), coronary artery disease (CSD), or mild forms of valvular heart disease.
2. Patients have recurrent, symptomatic AF.
3. Patients have failed treatment with two or more antiarrhythmic drugs (or have intolerance of or a contraindication to appropriate antiarrhythmic drug therapy).

OR

4. Patients with Class II or III congestive heart failure and symptomatic AF in whom heart rate is poorly controlled by standard medications, as an alternative to atrioventricular nodal ablation and pacemaker insertion.

Transcatheter ablation of arrhythmogenic foci in the pulmonary veins does not meet Blue Cross and Blue Shield of Alabama's medical criteria for coverage and is considered investigational as a treatment for all indications except for specific cases of atrial fibrillation as noted above.

Effective for dates of service prior to June 1, 2013:

Transcatheter ablation of arrhythmogenic foci in the pulmonary veins as a treatment for atrial fibrillation (AF) meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage when the following criteria are met:

1. There is no **significant** structural heart disease. Individual case consideration will be given to patients with hypertrophic cardiomyopathy (both primary and secondary to hypertension), other forms of left ventricular hypertrophy (LVH), coronary artery disease (CAD), or mild forms of valvular heart disease.
2. Patients have recurrent, symptomatic AF.
3. Patients have failed treatment with two or more antiarrhythmic drugs (or have intolerance of or a contraindication to appropriate antiarrhythmic drug therapy).

OR

4. Patients with Class II or III congestive heart failure and symptomatic AF in whom heart rate is poorly controlled by standard medications, as an alternative to atrioventricular nodal ablation and pacemaker insertion.

Transcatheter ablation of arrhythmogenic foci in the pulmonary veins **does not meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage and is considered **investigational** as a treatment for all indications **except for specific cases of atrial fibrillation as noted above.**

Transcatheter **cryoablation** of arrhythmogenic foci in the pulmonary veins as a treatment for **atrial fibrillation does not meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage and is considered **investigational**.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the members' contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

This policy was originally created in 2004 and updated periodically with literature review since that time. The most recent literature search was performed through February 4, 2014. Following is a summary of the key literature to date.

In patients with paroxysmal or persistent atrial fibrillation (AF), catheter ablation may be considered an alternative to drug therapy. In patients with permanent AF, catheter ablation may be considered an alternative to drug therapy or to atrioventricular (AV) nodal ablation and pacing. For all types of AF, it is possible that catheter ablation may not be curative as a sole treatment but might alter the underlying myocardial triggers or substrate in such a way that subsequent pharmacologic therapy may become more effective.

There is ongoing controversy regarding the relative benefits of rhythm versus rate control in AF, which underlies the evaluation of evidence on catheter ablation. Randomized trials of pharmacologic therapies have not demonstrated the superiority of rhythm versus rate control. However, the apparent equivalency of these two strategies with pharmacologic therapy cannot be extrapolated to the rhythm control achieved with ablation. Antiarrhythmic medications used for rhythm control are only partially effective and have serious complications, including proarrhythmic properties, which can be lethal. Therefore, nonpharmacologic strategies for rhythm control have the potential to achieve superior outcomes than have been seen with pharmacologic strategies.

A variety of outcomes for treatment of AF may be considered. The mortality and morbidity related to AF, such as cardiovascular mortality, stroke, and heart failure, are the most important clinical outcomes. However, these are uncommon events, and currently available trials are not powered to detect differences in these outcomes. Quality of life (QOL) is also an important outcome, as these measures reflect important manifestations of AF, such as symptoms and reduced exercise tolerance. AF has been shown to be associated with lower QOL scores, and maintenance of sinus rhythm has been associated with higher QOL scores for patients with paroxysmal AF.

Recurrence of AF is a more problematic outcome measure, because the intermittent and often transient nature of recurrences makes accurate measurement difficult. This outcome measure has been reported in different ways. For example, the proportion of patients in sinus rhythm at the end of the study, the time to first recurrence, and the number of recurrences within a time period have been reported. A recent publication highlights the difficulties in measuring AF recurrence and recommends a measure of AF “burden,” defined as the percentage of time an individual is in AF, as the optimal measure of treatment efficacy. However, this parameter requires continuous monitoring over a relatively long period of time, which is inconvenient for patients, resource intensive, and usually not pragmatic in patients who do not already have an implanted pacemaker.

Recommendations for outcome assessment in trials of AF treatment were included in the 2006 American College of Cardiology/American Heart Association practice guidelines for the treatment of AF. These guidelines pointed out that the appropriate end points for evaluation of treatment efficacy in patients with paroxysmal or persistent AF have little in common. For

example, in studies of persistent AF, the proportion of patients in sinus rhythm at the end of follow-up is a useful end point, but this is a less useful measure in studies of paroxysmal AF. Given all these variables, ideally, controlled clinical trials would report a range of outcomes (including QOL) and complications in homogeneous patient groups and compare with the most relevant treatment alternatives, such as pharmacologic therapy; defibrillator therapy; and AV nodal ablation, depending on the classification of AF (paroxysmal, persistent, permanent).

RFA for AF

The literature review for this policy was originally based on a 2008 TEC Assessment. Six randomized controlled trials (RCTs) met the inclusion criteria for this TEC Assessment. The trials differed in their patient populations, the specific catheter ablation techniques used, and the comparisons made. The trials addressed three distinct indications for catheter ablation: patients with paroxysmal AF, as a first-line treatment option (n=1 trial); patients with symptomatic paroxysmal or persistent AF who have failed treatment with antiarrhythmic drugs (n=4 trials); and patients with symptomatic AF and heart failure who have failed treatment with standard medications for rate control and who would otherwise be considered for AV nodal ablation and pacemaker insertion (n=1 trial).

All six trials reported that maintenance of sinus rhythm was improved for the catheter ablation group. Recurrence rates of AF at one year ranged from 11% to 44% for the catheter ablation groups in these trials, compared with 63% to 96% for the medication groups. Four of the six trials reported QOL outcomes. One of these only reported within-group comparisons, as opposed to between-group comparisons. The other three trials reported improvements in QOL associated with catheter ablation. These QOL measures were self-reported, and because both trials were unblinded, there is the possibility of reporting bias due to placebo effect.

None of the available trials reported meaningful data on cardiovascular morbidity and mortality associated with AF. The Assessment concluded that radiofrequency catheter ablation is more effective than medications in maintaining sinus rhythm across a wide spectrum of patients with AF and across different variations of catheter ablation. The evidence on QOL is suggestive, but not definitive, of a benefit for patients undergoing catheter ablation. For other outcomes, the evidence did not permit conclusions. It was not possible to estimate the rate of serious complications, such as pulmonary vein stenosis, cardiac tamponade, or atrioesophageal fistula with precision given the limited number of patients in the trials and the continued evolution of the technique. However, the rate of serious complications is expected to be low, likely in the 1% to 5% range.

Based on these findings, TEC criteria were met for two indications: patients with symptomatic paroxysmal or persistent AF who have failed treatment with antiarrhythmic drugs and patients with symptomatic AF and heart failure who have failed treatment with standard medications for rate control and who would otherwise be considered for AV nodal ablation and pacemaker insertion. For the first indication, the conclusion followed from the premise that reducing episodes of recurrent AF for this population will reduce or eliminate the symptoms associated with episodes of AF. For the other indication, the single multicenter RCT available was judged sufficient to conclude that catheter ablation improved outcomes compared with the alternative, AV nodal ablation and pacemaker insertion. While this trial was relatively small, it was judged

to be otherwise of high quality and reported improvements of a relatively large magnitude across a range of clinically important outcome measures, including QOL, exercise tolerance, left-ventricular ejection fraction (LVEF), and maintenance of sinus rhythm.

Since the publication of the 2008 TEC Assessment, several additional systematic reviews and meta-analyses of catheter ablation for AF have been published. A Cochrane Review on catheter ablation for paroxysmal and persistent AF was published in 2012. This review included seven RCTs of catheter ablation versus medical therapy. Main conclusions were that catheter ablation was superior at reducing the recurrence of AF (risk ratio [RR], 0.27; 95% confidence interval [CI], 0.18 to 0.41) but that there were no differences in mortality (RR=0.50; 95% CI, 0.04 to 5.65), embolic complications (RR=1.01; 95% CI, 0.18 to 5.68), or death from thromboembolism (RR=3.04; 95% CI, 0.13 to 73.4).

In 2013, Ganesan et al published results from a systematic review and meta-analysis of studies reporting long-term outcomes after percutaneous catheter ablation for paroxysmal and nonparoxysmal AF. The authors included 19 studies (RCTs, case-control and cohort studies, case series) that reported catheter ablation outcomes at three years or more after the index ablation procedures. Sample sizes in these studies ranged from 39 to 1404, with a total of 6167 patients included overall. For a single procedure, the pooled overall success rate at 12 months post-procedure was 64.2% (95% CI, 57.5% to 70.3%). At late follow-up, the overall single-procedure success, defined as freedom from atrial arrhythmia at latest follow-up, was 53.1% (95% CI, 46.2% to 60.0%). The pooled overall multiple-procedure long-term success rate was 79.8% (95% CI, 75.0% to 83.8%). The analysis was unable to identify any predictors of short- or long-term recurrence. Reporting of periprocedural complications was heterogeneous across the studies, but complication rates were generally low.

Three systematic reviews and meta-analyses comparing RFA with antiarrhythmic drug therapy for AF were published from 2008 to 2009. Nair et al included six RCTs comparing RFA with antiarrhythmic drug therapy for AF, five of which were included in the TEC Assessment. Two systematic reviews published in 2008 summarized and synthesized the RCT evidence on catheter ablation versus alternate therapy. These reviews included four of the six trials reviewed for the TEC Assessment. Noheria et al included three of these four RCTs, as well as an additional small RCT of 30 patients not included in the TEC Assessment. Gjesdal et al included five RCTs in their analysis, including the four trials in the Noheria et al systematic review, and one additional trial (included in the TEC Assessment) that compared catheter ablation plus antiarrhythmic drugs with antiarrhythmic drugs alone. All three systematic reviews concluded that catheter ablation was more effective than pharmacologic treatment in maintaining normal sinus rhythm. Nair et al demonstrated a pooled relative risk for AF at one year after procedure of 0.35 compared with antiarrhythmic drug therapy. In combined analysis, Noheria et al reported AF-free survival at one year to be 75.7% in the catheter ablation group compared with 18.8% in the comparison group. The relative risk for maintaining sinus rhythm was 3.73 (95% CI, 2.47 to 5.63) for the catheter-ablation group compared with alternative treatment. Gjesdal et al concluded that the available evidence was of moderate quality and consistent in reporting that AF-free survival was superior for the catheter ablation group. However, due to unexplained heterogeneity, these authors did not perform a combined analysis.

Since the TEC Assessment, six additional RCTs comparing radiofrequency ablation (RFA) versus pharmacologic treatment have been identified. Wilber et al enrolled 167 patients who had failed at least one antiarrhythmic medication and had at least three AF episodes in the prior six months. Patients were randomly assigned to either catheter ablation or continued drug therapy and followed for nine months. At the end of follow-up, 66% of patients in the ablation group were free of recurrent AF compared with 16% of patients in the medication group. Adverse events related to treatment occurred in 4.9% (5/103) of patients treated with ablation and in 8.8% (5/57) of patients treated with medications.

Forleo et al randomly assigned 70 patients with Type 2 diabetes and AF to either RFA or an antiarrhythmic medication. Follow-up was for one year, with the primary outcome being recurrence of AF. At the end of the trial, 42.9% of patients in the medication group were free of AF compared with 80% of patients in the ablation group. There was also a significant improvement in QOL for patients in the ablation group. Adverse events from medications occurred in 17.2% (6/35) patients, whereas complications from ablation occurred in 2.9% (1/35).

An RCT of RFA ablation as the initial therapy for paroxysmal AF was published in 2012. A total of 294 patients were randomized to initial treatment with catheter ablation or pharmacologic therapy. Patients were followed for up to 24 months for the primary outcomes of burden of AF (percent of time in AF on Holter monitor) at each time point and cumulative burden of AF over all time points. For the individual time points, the burden of AF was lower in the catheter ablation group at 24 months (9% vs 18%, $p=0.007$), but not at other time points. The cumulative burden did not differ significantly for the catheter ablation group compared with pharmacologic therapy (90th percentile of cumulative burden, 13% vs 19%, $p=0.10$). The secondary outcome of percent of patients free from AF at 24 months was greater for the catheter ablation group (85% vs 71%, $p=0.004$), as was the secondary outcome of freedom from symptomatic AF (93% vs 84%, $p=0.01$). There was one death in the ablation group due to a procedural-related stroke, and there were three patients in the ablation group who developed cardiac tamponade following the procedure.

Mont et al conducted an RCT comparing radiofrequency catheter ablation with antiarrhythmic drug therapy among 146 patients with symptomatic persistent AF. Patients were randomized in a 2:1 fashion to catheter ablation ($n=98$) or antiarrhythmic drug therapy ($N=48$). Although the study was terminated before the planned sample size of 208 was met due to lower than expected enrollment, at 12 months of follow up, the proportion of patients who were free of sustained episodes of AF was higher in the catheter ablation group than the antiarrhythmic drug therapy group (70.4% vs 43.7%, $p=0.002$). QOL scores did not significantly differ between the groups. Longer term outcomes were not reported.

Several studies have compared catheter ablation with medical therapy for AF in the setting of heart failure. Hunter et al conducted an RCT comparing catheter ablation with medical rate control for patients with persistent AF and symptomatic heart failure, with adequate rate control at the time of enrollment. The study's primary end point was difference between groups in LVEF at six months postprocedure. Fifty patients were randomized, 26 to catheter ablation and 24 to medical management. At six months, 81% of the catheter ablation group was free from

recurrent AF off antiarrhythmic drugs. LVEF at six months after procedure was 40% ($\pm 12\%$) in the catheter ablation group, compared with 31% ($\pm 13\%$, $p=0.015$). Catheter ablation was also associated with improvements in health-related QOL. Jones et al reported results from an RCT comparing catheter ablation with medical rate control for patients with symptomatic heart failure, LVEF 35% or less, and persistent AF. Fifty-two patients were randomized, 26 each to catheter ablation or medical rate control. At 12 months after procedure, sinus rhythm was maintained in 88% of the catheter ablation group, with a single-procedure success rate of 68%. For the study's primary outcome, peak oxygen consumption at 12 months after procedure, there was a significant increase in the catheter ablation group compared with the medical management group ($+3.07$ mL/kg/min; 95% CI, 0.56 to 5.59; $p=0.018$).

Longer-term outcomes

The available RCTs mainly report on short-term outcomes up to one year and, therefore, do not evaluate the rate of late recurrences after one year. Longer-term outcomes have been reported by several authors. These studies generally report rates of early recurrence in the range of 20% to 30%, requiring repeat ablations. Rates of longer-term recurrence are lower if early recurrence does not occur, in the range of 1% to 2% per year.

Hussein et al reported on 831 patients who were treated in 2005, with a median follow-up of 55 months. During the first year following ablation, 23.8% had a recurrence of AF. During the remaining follow-up, recurrences occurred in 8.9% additional patients. The overall rate of arrhythmia-free and off drugs was 79.4% at 55 months. An additional 10.5% of patients were arrhythmia-free on drugs, for a total rate of 89.9% clinical improvement.

In 2013, Bunch et al reported results from a prospective cohort study comparing risk of stroke between patients with AF who had undergone catheter ablation, patients with AF who did not undergo ablation, and patients without a history of AF. A total of 4212 patients with AF who had undergone catheter ablation were age and sex matched in a 1:4 ratio to 16,848 subjects in each of the other groups. The mean follow up time was 3.9 years. At one year postprocedure, significantly more patients with AF who did not undergo ablation had a stroke (3.5%) than those with AF who underwent ablation (1.4%) or had no history of AF (1.4%; $p<0.001$ for trend). During the follow up period, for all ages and CHADS2 profiles, patients with AF who had ablation had a lower stroke risk than those with AF without ablation.

Several smaller studies have also reported longer-term follow-up after radiofrequency catheter ablation. Weerasooriya et al reported five-year follow-up in 100 patients treated with catheter ablation. Recurrences were most common within the first six months, with repeat procedures being common during that period. At one, two, and five years after ablation, arrhythmia-free survival was 87%, 81%, and 63%, respectively. Tzou et al reported long-term follow-up for 123 patients who had a previous successful ablation, defined as free of AF at one year. At three years of follow-up, 85% of patients were still free of AF and off of all medications, and at five years, 71% remained free of AF. The authors estimated a late recurrence rate of approximately 7% per year for patients with an initial successful procedure. In a similar study, Bertaglia et al reported outcomes after six years of follow-up for 229 patients who had a single, successful ablation. At one-year follow-up, 77% of patients (177/229) were free of AF and off of all medications. After a mean additional follow-up of 49.7 ± 13.3 months for these 177 patients,

58% remained free of AF. Sawhney et al reported five-year success rates in 71 patients who underwent ablation in 2002 or 2003. Freedom from symptomatic AF off medications was achieved in 86% of patients at one year, 79% at two years, and 56% at five years. A substantial minority of patients (22.5%) had recurrence at times greater than two years after ablation. A 2013 study by Anselmino et al followed 196 patients who underwent radiofrequency catheter ablation for paroxysmal or persistent AF and had LVEF 50% or less for a mean of 46.2 months. During follow-up, 29.6% of patients required repeat ablation procedures. At the end of follow up, 37.8% had at least one episode of AF, atrial flutter, or ectopic atrial tachycardia.

Numerous RCTs of RFA of the pulmonary veins versus medical management report that freedom from AF at one year is higher with RFA compared with medical management. The trials mainly include patients who have failed antiarrhythmic medications, although two trials treat patients with paroxysmal AF as initial treatment. These studies report that most patients undergoing RFA are free of AF at one year. QOL is also improved in these trials for patients undergoing catheter ablation. A smaller number of studies evaluate outcomes longer than one year and report that late recurrences occur up to five years but are uncommon after the first year. Complications from RFA are reported at low rates in the RCTs, but the numbers of patients in these trials are too low to accurately estimate rates of uncommon events. There is a lack of data on clinical outcomes other than freedom from AF. Larger RCTs are underway to evaluate long-term clinical outcomes such as stroke and mortality.

Cryoablation of the pulmonary veins

A number of studies reported outcomes of ablation using cryoablation. These were mainly case series reporting success rates in the range of that reported for RFA. One small matched analysis compared 20 patients undergoing cryoablation with 20 patients undergoing RFA, matched for age, gender, LVEF, and AF history. Freedom from AF at six months was 55% for the cryoablation group, compared with 45% for the RFA group, a difference that was not significantly different.

In 2013, Packer et al reported results of the STOP-AF trial, an RCT of cryoablation versus antiarrhythmic medications. This study enrolled 245 patients with paroxysmal AF who had failed at least one (median, 1.2) membrane-active antiarrhythmic medications. Patients were randomized in 2:1 fashion to either cryoballoon ablation (n=163) or drug therapy (n=82). At one-year follow-up, 69.9% of patients in the ablation group were free of AF versus 7.3% in the medication group. The single-procedure success rate was 57.7%. There was also a significantly greater reduction in symptoms for the ablation group. Seventy-nine percent of the drug treatment group crossed over to cryoablation during 12 months of study follow-up because of recurrent, persistent AF. Cryoablation procedure-related adverse events occurred in five patients (3.1%); major AF events occurred in 3.1% of the cryoablation group compared with 8.5% of the drug-treatment group (non-inferiority $p<0.001$). Phrenic nerve injury occurred at a rate of 13.5%, with 86% resolved at 12 months.

The Mesh Ablator versus Cryoballoon Pulmonary Vein Ablation of Symptomatic Paroxysmal AF (MACPAF) study was a single-center RCT comparing cryoablation with RFA with the HD Mesh Ablator Catheter (Bard®, purchased by Boston Scientific in 2013) for AF. The HD Mesh Ablator Catheter, which is not cleared for use in the U.S., is a multielectrode RF catheter that

involves a mesh electrode that is designed to delivery RF energy to multiple points of contact. Primary short-term results for MACPAF were reported by Koch et al in 2013. The study randomized symptomatic paroxysmal AF to catheter ablation with the Arctic Front® cryoablation catheter or the HD Mesh Ablator. The study's primary end point was complete isolation of the pulmonary veins at the end of the procedure. Enrollment was initially planned for 108 with symptomatic paroxysmal AF that was inadequately controlled with antiarrhythmic drug treatment. However, at interim analysis, the HD Mesh Ablator demonstrated a lack of efficacy for the primary end point, and the study's data safety monitoring board prematurely terminated the subject. Forty-four patients with drug-resistant paroxysmal AF were randomized at the time the study was terminated and comprise the intention-to-treat analysis cohort. The per-protocol analysis cohort included 32 patients. Three patients withdrew before the catheter procedure; nine additional patents were excluded from analysis due to use of a study noncompliant catheter (n=2), identification of a trigger arrhythmia, which was subsequently ablated (n=1), failure of transseptal puncture (n=1), or ablation occurring after the interim analysis (n=5). For the primary end point, by intention-to-treat analysis, complete pulmonary vein isolation was achieved in 13/23 (56.5%) of patients in the cryoablation group, compared with 2/21 (9.5%) of patients in the mesh ablator group (p=0.001). In the per-protocol cryoablation group, 76.5% of subjects had complete pulmonary vein isolation. Major complications included one case of retroperitoneal hematoma in the cryoablation group and one case of pericardial tamponade requiring drainage in the mesh ablator group.

Malmborg et al reported results from an RCT comparing cryoablation with the Arctic Front® cryoballoon catheter to RFA with the Pulmonary Vein Ablation Catheter®. One hundred ten patients with paroxysmal or persistent AF were randomized, 54 to the cryoablation group and 56 to the RFA group. Complete pulmonary vein isolation was achieved in 98% of the cryoablation group, compared with 93% of the RFA group (p=0.37). At six-month follow-up, freedom from AF (absence of symptoms and no AF episodes on seven-day Holter monitoring or 12-lead electrocardiogram) without antiarrhythmic drug treatment was achieved in 52% of the cryoablation group and 38% of the RFA group (p=0.13).

Schmidt et al used data from a prospective German registry of catheter ablation procedures to compare RF with cryoablation for paroxysmal AF. The cohort included 905 patients who underwent cryoablation and 2870 patients who underwent RFA who were enrolled from January 2007 to August 2011. The two groups were generally similar, with the exception that patients who underwent RFA were significantly more likely to have valve disease (8.1% vs 3.0%, p<0.001) and an ejection fraction 40% or less (2.4% vs 1.2%, p<0.05). Rates of acute success were similar for the two groups (97.5% for cryoablation vs 97.6% for RFA, p=0.92), as were rates of major procedure-related adverse cardiac and cerebrovascular events (0.4% for cryoablation vs 0.2% for RFA, p=0.15). The overall procedural complication rates were similar for the two groups (4.6% for each group, p=1.0); the rate of postprocedural phrenic nerve palsy was significantly higher for the cryoablation group (2.1% for cryoablation vs 0% for RFA, p=0.15). Long-term follow rates are not reported.

A meta-analysis of studies of cryoablation was published in 2011. This analysis included the STOP-AF results in abstract form and a total of 22 other nonrandomized studies, primarily case series. Procedural success was reported in over 98% of cases. At one year, the rates of success,

as defined by no recurrent AF, were 73% (95% CI, 69% to 77%) for paroxysmal AF and 60% (95% CI, 54% to 66%) for persistent AF. Complications were inconsistently reported among the available studies. The most common complication reported was phrenic nerve palsy, which occurred in 6.4% of patients. Other rates of reported complications were pericardial effusion or tamponade (1.5%), groin complications at insertion site (1.8%), stroke (0.3%), and pulmonic stenosis (0.9%).

Vogt et al reported longer-term follow up for 605 patients who underwent cryoablation for symptomatic, paroxysmal or persistent AF. Follow-up data beyond 12 months were available for 451 patients (median follow-up, 30 months). Of those with follow up available, 278 (61.6%) were free of AF recurrence with no need for repeat procedures after a three-month blanking period. After one, two, and three repeat procedures, rates of freedom from AF were 74.9%, 76.2%, and 76.9%, respectively. Phrenic nerve palsy was the most common adverse event, occurring in 2% of patients, all of which resolved within three to nine months. There were two periprocedural strokes, and one case each of periprocedural pericardial tamponade and pericardial effusion.

Neumann et al reported five-year outcomes after a single cryoablation procedure among 163 patients with symptomatic, drug-refractory paroxysmal AF. Fifty-three percent of subjects were free from recurrent AF, atrial tachycardia, or atrial flutter at five years of follow-up with no additional procedures (after a three-month blanking period).

There are ongoing trials of cryoablation versus RFA for AF. The FreezeAF trial is a non-inferiority RCT comparing cryoablation with RFA for patients with paroxysmal AF. Enrollment of 244 patients is planned, and patients will be followed for at least one year. The primary outcome is freedom from AF off all drugs. Secondary outcomes include longer-term success rates, procedural data, and cost-effectiveness.

The evidence related to cryoablation for AF includes three RCTs and numerous uncontrolled case series. The STOP AF trial, which compared cryoablation with antiarrhythmic medication therapy, reported that cryoablation is superior to medical management, and that rates of freedom from arrhythmia at one year in the cryoablation group are in the range reported with RFA. Nonrandomized studies also report that cryoablation has efficacy in the same range as RFA. However, data from randomized trials directly comparing cryoablation with RFA are limited. Interpretation of the MACPAF study is limited by early termination due to unexpectedly low efficacy of the RFA method used. While the Malmberg et al study is suggestive that cryoablation is comparable with RFA, success in the RFA group was also unusually low. This study is also limited by relatively short-term follow-up (six months) and use of a catheter that is not cleared for use in the U.S.

Therefore, the evidence is not sufficient to determine the comparative efficacy of cryoablation compared with RFA. Ongoing RCTs, particularly the FreezeAF trial, are currently addressing this question.

Repeat procedures

Repeated procedures for recurrent AF or atrial flutter were commonly performed in most of the clinical trials included in this policy statement. Of the 10 RCTs reviewed that compared RFA with medical management, only two did not include repeated procedures. In the other five studies, one or more repeated procedures were allowed, and success rates reported generally incorporated the results of up to three procedures. In four studies that reported these data, repeated procedures were performed in 8.2%, 9%, 20%, and 32% of patients randomized to ablation. In their RCT of catheter ablation of AF in patients with heart failure, Hunter et al report that repeat procedures were required in 65.4% of the catheter ablation group. Stabile et al did not report specifics on how many patients actually underwent repeated procedures, but limited data in the publication indicated that up to 30% of treated patients were eligible for repeated procedures. In the Jais et al study, patients underwent a mean of 1.8 procedures per patient and a median of two procedures per patient, indicating that approximately 50% of patients in the ablation group underwent at least one repeated procedure.

Because of this high rate of repeated procedures, the results reported in these studies do not reflect the success of a single procedure. Rather, they more accurately estimate the success of an ablation strategy that includes repeated procedures for recurrences that occur within the first year of treatment. Nonrandomized evidence suggests that early reablation increases the success of the procedure, when defined as maintenance of sinus rhythm at one year. There is variability in the protocol for when repeated procedures should be performed. There is also uncertainty concerning other details on repeated procedures, such as how soon after the initial procedure it should be done, the threshold of AF recurrence that should prompt a repeat, and whether medications should be tried before a repeated procedure.

Pokushalov et al reported results of an RCT comparing repeat catheter ablation with antiarrhythmic drug therapy for patients with paroxysmal AF who had failed an initial pulmonary vein isolation procedure. After an initial postablation blanking period, 154 patients with symptomatic AF recurrence were randomized to drug therapy (n=77) or repeat ablation (n=77). Patients were followed for three years with an implanted cardiac monitor. At the three-year follow up, 58% (45/77) of the repeat ablation group were free from AF or atrial tachycardia on no antiarrhythmic drugs, compared with 12% (9/77) of the antiarrhythmic therapy group ($p<0.01$). In the antiarrhythmic drug group, 43 patients (56%) crossed over to receive repeat ablation; in the repeat ablation group, 21 patients (27%) required antiarrhythmic drug therapy. By intention-to-treat analysis, 65% (50/77) of the repeat ablation group and 45% (35/77) of the drug therapy group were free from AF or atrial tachycardia ($p=0.02$).

Complications

Individual clinical trials and case series report relatively low rates of complications, but may be limited in their ability to detect uncommon outcomes due to their small size. In 2013, Gupta et al reported results from a systematic review and meta-analysis of periprocedural complications following catheter ablation for AF. The authors included 192 studies that included at least 100 participants undergoing catheter ablation for symptomatic AF and that reported complications. The total sample size was 83,236 patients. The overall acute complication rate was 2.9% (95% CI, 2.6 to 3.2), with significant heterogeneity across studies. The most common complications

were vascular complications (1.4%), cardiac tamponade (1.0%), pericardial effusion (0.7%), stroke/transient ischemic attack (TIA) (0.6%), and pulmonary vein stenosis (0.5%).

In addition to the complication rates reported in available clinical trials and case series, there have been a number of database studies and postmarketing surveillance that report complications in larger numbers of patients than are in the clinical trials. A representative sample of these studies is discussed next, some of which were included in the Gupta et al review (Shah et al, Dagres et al).

Waldo et al reported the results of a U.S. Food and Drug Administration (FDA) –directed postmarketing safety study involving 1275 patients from six prospective, multicenter studies of RFA ablation using an open-irrigated catheter. A total of 4.9% (63/1275) of patients experienced any acute serious complication within seven days of the procedure. Vascular access complications were most common, ranging from 0.5% to 4.7% across the six studies. Exacerbations of heart failure occurred in 1.5% of patients, and two patients experienced cardiac tamponade. There were no strokes or TIAs reported after the procedure.

Shah et al used data from a California hospital database to evaluate complications in 4156 patients who underwent catheter ablation for AF. Major complications occurred in 5.1% (211/4156) of patients, with approximately half of these (2.6%, 110/4156) consisting of hemorrhage or hematoma at the vascular entry site. The most common cardiac complication was cardiac perforation and/or tamponade, which occurred in 2.5% (104/4156) of patients. Less common rates of serious adverse events included death (0.02%), stroke/TIA (0.31%), and pneumothorax/hemothorax (0.1%). Factors that were predictive of complications were female gender, older age, prior hospitalizations for AF, and less hospital experience with ablation.

In a study of Medicare beneficiaries, Ellis et al identified 6065 admissions from 168 hospitals in which RFA for AF was performed. The total rate of in-hospital complications was 9.1%, with vascular complications accounting for over half of the total complications at a rate of 5.7%. The mortality rate was 0.4%, and 0.6% of patients suffered a stroke or TIA. Perforation or tamponade occurred in 3.1% of patients and pneumothorax occurred in 0.4% of patients. The presence of chronic obstructive pulmonary disease or unstable angina was associated with a higher risk of complications, while obesity and hyperlipidemia were associated with a lower risk. Age and hospital volume were not significant predictors of risk, but low hospital volume was a significant predictor of in-hospital death.

Complications of catheter ablation were reported in a large cohort of 1000 patients undergoing ablation at a high-volume center in Europe. There were no deaths definitely attributable to the procedure, but there were two deaths of uncertain cause within the first 30 days following ablation. Overall, 3.9% of patients had a major complication resulting from the procedure. Tamponade was the most serious life-threatening complication, occurring in 1.3% of patients. Major vascular complications occurred in 1.1%. Thromboembolism, cerebrovascular accident/TIA, atriopharyngeal fistula, and endocarditis were all reported complications that occurred at a rate of less than 1%.

Cappato et al performed a multicenter, retrospective case series to estimate the overall mortality rate following ablation. Data were collected on 32,569 patients from 162 clinical centers worldwide. There were 32 deaths reported, for a mortality rate of 0.98 per 1000 patients. The most common causes of death were tamponade (n=8), stroke (n=5), atrioesophageal fistula (n=5), and pneumonia (n=2).

In the MACPAF study, one goal was to identify adverse events, particularly cerebral thromboembolism through the use of serial magnetic resonance imaging (MRIs) and neuropsychologic testing. While there is some evidence that RFA for patients with AF improves stroke risk, a clinically significant stroke or TIA attack occurs in 0.1% to 0.8% of patients undergoing catheter ablation, and several case series have demonstrated peridural brain lesions on diffusion weighted MRI imaging in up to 18% of patients undergoing catheter ablation of the left atrium. Thus, the MACPAF investigators evaluated patients' pre- and post-catheter ablation with brain MRI at three Tesla and neurologic and neuropsychologic testing. Short-term outcomes from these evaluations were reported by Haeusler et al in 2013 and demonstrated that new ischemic lesions occurred in 41% of all patients. However, these brain lesions were not associated with cognitive dysfunction immediately after procedure. Longer-term follow-up was reported by Herm et al in 2013. At follow-up MRI at six months after procedure, 31.3% of the acute brain lesions had formed a persistent glial scar. Similar to the short-term findings, there was no significant effect of either the ablation procedure or the presence of persistent brain lesions on attention or executive functions, short-term memory, or learning after six months.

Several large, database studies estimate the rate of adverse events from catheter ablation in the clinical care setting. The range of major adverse events in these studies is from 4% to 9%. Deaths have been reported and occur at rates less than 1%. Vascular complications at the groin site are the most common adverse events, occurring at rates of up to 5%. Serious cardiovascular adverse events such as tamponade and stroke occur uncommonly, at rates of approximately 1% or lower. There is some evidence that new ischemic lesions are commonly found on MRI after procedure, but the clinical significance of these defects is unclear.

Practice Guidelines and Position Statements

In 2006, the American College of Cardiology published an update to their practice guidelines for the treatment of atrial fibrillation. These guidelines reflect the results of the rate versus rhythm controlled randomized studies. Explicit recommendations are classed as I, IIa, IIb, or III. Class IIa is defined as: "the weight of evidence or opinion is in favor of the procedure or treatment." The recommendations are further classified according to the type of data available. Class C data are defined as "expert consensus."

The guidelines describe the use of ablation of the pulmonary vein (PV) and note that the "...technique of ablation has continued to evolve from early attempts to target individual ectopic foci within the PV to circumferential electrical isolation of the entire PV musculature." Two specific recommendations regarding the use of catheter ablation were judged Class IIa. These are 1) "It is reasonable to use ablation of the AV node or accessory pathway to control heart rate when pharmacological therapy is insufficient or associated with side effects. (*Level of Evidence: B*)"; and 2) "Catheter ablation is a reasonable alternative to pharmacological therapy

to prevent recurrent [atrial fibrillation] in symptomatic patients with little or no [left atrial] enlargement. (*Level of Evidence: C*)."

The guidelines also encourage further research in this area given uncertainties in patient populations, technique, and outcome assessment. The authors state that "despite these advances, the long-term efficacy of catheter ablation to prevent recurrent [atrial fibrillation] requires further study."

The American College of Physicians and American Academy of Family Physicians issued clinical practice guidelines in 2003 for patients with new-onset atrial fibrillation. These guidelines state the majority of patients with new-onset atrial fibrillation should be treated with a pharmacologic rate control strategy and long-term anticoagulation. Similar to the American College of Cardiology/American Heart Association guidelines, this document does not include specific recommendations for catheter-based ablation techniques in their treatment algorithms.

Key Words:

Atrial fibrillation, circumferential pulmonary vein ablation (PVA), pulmonary vein isolation, arrhythmogenic, cryoablation, cryoballoon therapy, cryoballoon intervention, cryoballoon technique, cryoballoon isolation, cryoballoon ablation

Approved by Governing Bodies:

In February 2009, the NAVISTAR® THERMOCOOL® Irrigated Deflectable Diagnostic/Ablation Catheter and EZ Steer ThermoCool NAV Catheter (Biosense Webster Inc.) were approved by the U.S. Food and Drug Administration (FDA) through the pre-market approval (PMA) process for "catheter-based cardiac electrophysiological mapping (stimulating and recording), and when used with the Stockert 70 generator, for the treatment of a) Type I atrial flutter in patients age 18 or older; b) recurrent drug/device refractory sustained monomorphic ventricular tachycardia (VT) due to prior myocardial infarction (MI) in adults; c) drug refractory recurrent symptomatic paroxysmal atrial fibrillation, when used with compatible three-dimensional electroanatomic mapping systems." (For radiofrequency ablation)

In December 2010, Medtronic's Arctic Front® Cardiac CryoAblation Catheter and CryoConsole were approved by the FDA for the "treatment of drug refractory recurrent symptomatic paroxysmal atrial fibrillation." In addition, Medtronic's Freezor® MAX Cardiac CryoAblation Catheter was approved as an adjunctive device to be used in conjunction with the Arctic Front system for "gap cryoablation to complete electrical isolation of the pulmonary veins, cryoablation of focal trigger sites, and creation of ablation line between the inferior vena cava and the tricuspid valve." (For cryoablation)

Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Home Policy provisions apply.

FEP contracts: Special benefit consideration may apply. Refer to member's benefit plan.

Pre-certification requirements: Not applicable

Current Coding:

CPT Codes:	93656	Comprehensive electrophysiologic evaluation including transseptal catheterizations, insertion and repositioning of multiple electrode catheters with induction or attempted induction of an arrhythmia including left or right atrial pacing/recording when necessary, right ventricle pacing/recording when necessary, and HIS bundle recording when necessary with intracardiac catheter ablation of atrial fibrillation by pulmonary vein isolation.
	93657	; additional linear or focal intracardiac catheter ablation of the left or right atrium for treatment of atrial fibrillation remaining after completion of pulmonary vein isolation.
	93799	Unlisted cardiovascular service or procedure

Previous Coding

Prior to 2013, there was no specific CPT code for pulmonary vein ablation. CPT code 93651 included ablation of intra-atrial arrhythmogenic foci as treatment of a supraventricular tachycardia. Circumferential ablation of the pulmonary vein might be considered basically intra-arterial in location due to its close proximity of the pulmonary os and atria. Supraventricular tachycardias typically describe arrhythmias due to accessory pathways within the atria, such as Wolff Parkinson White or AV nodal re-entry arrhythmias. Although not consistently associated with tachycardia, strictly speaking, AF could be considered a type of supraventricular tachycardias.

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Policy History:

Medical Policy Group, May 2006 (2)

Medical Policy Group, August 2006 (2)

Medical Policy Group, January 2007 (2)

Medical Policy Administration Committee, February 2007

Available for comment February 9-March 26, 2007

Medical Policy Group, September 2009 (3)

Medical Policy Administration Committee, September 2009

Available for comment September 18-November 2, 2009

Medical Policy Group, October 2012 (2): Cryoablation of pulmonary veins as a treatment for atrial fibrillation added as a non covered indication. Updates to Description, Policy, Key Points, Approved by Governing Bodies, and References

Medical Policy Administration Committee, November 2012

Medical Policy Group, May 2013 (2): Added policy statement for coverage of cryoablation of pulmonary veins. Key Points, Key Words, and References updated to support coverage statement.

Medical Policy Administration Committee, June 2013

Available for comment May 30 through July 13, 2013

Medical Policy Panel March 2014

Medical Policy Group March 2014 (4): Changed title by removing “in the Pulmonary Veins”; Removed “in the Pulmonary Veins” from the policy; Updated Description, Key Points, and References.

Medical Policy Administration Committee, May 2014

Available for comment May 5 through June 18, 2014

Medical Policy Group June 2014(4): Updated 2013 CPT Codes. Removed section of the policy related to structural heart disease.

Medical Policy Administration Committee, July 2014

Available for comment June 30 through August 13, 2014

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plan contracts.