This policy does not apply to patients with renal failure being treated using dialysis.

Name of Policy:
Ultrafiltration in Decompensated Heart Failure

Policy #: 435
Category: Medicine

Latest Review Date: May 2018
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:

Ultrafiltration is used to remove excess fluid from patients with volume overload and heart failure. It removes fluid from the blood by using pressure differentials with dialysis equipment or similar filtration devices.

Heart Failure

Heart failure is a relatively common condition that frequently results in hospitalizations and readmissions.

Treatment

Various treatment approaches are being explored, especially when the condition is refractory to conventional therapy. Ultrafiltration, also referred to as aquapheresis, is a technique being investigated for a possible role in hospitalized patients with marked volume overload from heart failure.

It has been suggested that ultrafiltration may offer greater and more expeditious volume and sodium removal than conventional therapies, particularly in patients with decompensated heart failure whose fluid overload is unresponsive to medical management.

Newer devices that allow continuous ultrafiltration in ambulatory patients are under investigation to reduce volume overload.

Outcome Measures

Heart failure is a condition with a variable natural history and multiple confounders of outcome. Clinical outcomes of interest in the treatment of heart failure include survival, hospitalization, complications, and quality of life; although removal of fluid and sodium, and weight loss, are important, they are surrogate outcomes that do not necessarily translate into clinical outcomes. Because ultrafiltration does not directly affect ventricular function, its effect on clinical outcomes is difficult to evaluate.

Policy:

The **use of ultrafiltration does not meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage in **patients with heart failure** and is considered **investigational**.

This policy does not apply to patients with renal failure being treated using dialysis.

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 member's 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:

The most recent literature review is through March 6, 2018.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, two domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Heart Failure

Systematic Reviews

A number of systematic reviews of RCTs have been published. None of the meta-analyses reporting all-cause mortality found significant differences in mortality between ultrafiltration and diuresis. Moreover, all but one of the meta-analyses that reported rehospitalizations found no evidence that ultrafiltration was significantly associated with a decrease in rates. All meta-analyses found that ultrafiltration resulted in significantly greater weight loss and fluid removal than diuretic therapy and none of the pooled analyses found significant differences between treatments in adverse events.

Most recently, Kwok et al (2017) published a systematic review and meta-analysis of 10 RCTs (total N=857 participants) evaluating ultrafiltration in patients with acute decompensated heart failure. A pooled analysis of 7 RCTs did not find a significant difference between groups in all-cause mortality (relative risk [RR], 1.08; 95% confidence interval [CI], 0.77 to 1.52; p=0.65). A pooled analysis of 7 RCTs did not find a significant difference in absolute change in creatinine (mean difference [MD], 0.01 mg/dL, 95% CI, -0.17 to 0.19 mg/dL; p=0.92). However, in a pooled analysis of 9 RCTs, there was significantly greater weight change in the ultrafiltration group than in the control group (MD = -1.86 kg; 95% CI, -4.68 to 0.97 kg; p<0.001). Pooled analyses of hospitalization rates did not find a statistically significant benefit of ultrafiltration. In a pooled analysis of 3 RCTs, the relative risk for all cause hospitalization was 0.89 (95% CI, 0.43 to 1.86) and in a pooled analysis of 5 RCTs, the relative risk was 0.71 (95% CI, 0.51 to 1.00; p=0.05).

Randomized, Controlled Trials

The UNLOAD trial was a non-blinded trial that involved 200 patients hospitalized for heart failure and hypervolemia randomized during the first 24 hours of hospitalization to ultrafiltration or usual care (diuretics). The trial was conducted 28 U.S. centers. Primary efficacy end points were 48-hour weight loss and dyspnea score (1–7 Likert scale). Primary safety end points were changes in blood urea nitrogen, creatinine, and electrolyte levels throughout hospitalization and 90-day follow-up, and episodes of hypotension requiring therapeutic intervention at 48 hours. The trial had at least 13 secondary efficacy end points, including length of index hospitalization, quality-of-life assessments throughout follow-up, and resource utilization (rehospitalization for heart failure, unscheduled office and emergency department visits) during follow-up. Results showed more weight loss in the ultrafiltration group (5.0 kg) than in the usual care group (3.1 kg) from baseline at 48 hours (p=0.001), with no difference in groups in dyspnea scores. There was no significant difference in the length of stay of the index hospitalization between groups, but the ultrafiltration group (18%) had a smaller percentage of patients rehospitalized for heart failure at 90 days than the diuretics group (32%, p=0.037) There were no significant differences between treatment groups for quality-of-life assessments or renal function, except for a greater likelihood of hypokalemia in the diuretics group (p=0.018). Additional subgroup analysis by Costanzo et al (2010) compared outcomes between ultrafiltration and standard intravenous diuretics by continuous infusion or bolus injection. Similar fluid loss was observed for ultrafiltration and continuous diuretic infusion, with outcomes similar to the original UNLOAD trial (i.e., fewer re-hospitalizations for heart failure at 90 days only in patients who underwent ultrafiltration).

Detailed analysis of the UNLOAD study identified methodologic concerns that could influence trial results. The publication provided insufficient detail of patient status during the trial. The authors reported that 20 patients died during the trial (nine in the ultrafiltration group and 11 in the usual care group), but the timing of deaths was not reported. The study results, as reported, also raise concerns about dropout rates and patient follow-up for various outcome measures. For example, although 100 patients were randomly assigned to each group, at 48 hours, only 83, 80, and 69 patients in the ultrafiltration group and 84, 83, and 75 patients in the standard care group were reported in the assessment of the three primary outcomes (weight loss, dyspnea score, and change in serum creatinine level, respectively). For readmission at 90 days, while the denominators are reported as 89 for the treatment group and 87 for the usual care group, information from the report lists 45 and 41 patients at risk, respectively, at 90 days. In addition, it is not clear from the methods that intention-to-treat analyses were performed; and, despite the number of outcomes assessed, there appears to be no statistical correction for multiple comparisons. Finally, neither participants nor investigators were blinded to treatment, which is a potential source of bias in outcomes such as re-hospitalizations, which are clinically based decisions.

The CARRESS Trial, published by Bart et al in (2012), compared fixed-rate ultrafiltration with diuretic-based stepped pharmacologic therapy in 188 patients hospitalized with acute decompensated heart failure and decreased renal function. Unlike the UNLOAD trial, outcomes in CARRESS were better in the diuretic group. Primary outcomes were changes in serum creatinine and body weight, as measured 96 hours after randomization. The ultrafiltration group

experienced a significant increase in serum creatinine levels (0.23±0.70 mg/dL) compared with the pharmacologic therapy group (0.04±0.53 mg/dL), which had a decrease (p=0.003). Mean weight loss did not differ significantly between groups (5.7±3.9 kg in the ultrafiltration group vs 5.5±5.1 kg in the pharmacologic therapy group; p=0.58). Serious adverse events occurred more frequently in the ultrafiltration group (72%) during the 60-day follow-up period than in the pharmacologic therapy group (57%; p=0.03). Those events included kidney failure, bleeding complications, and complications related to intravenous catheters.

Marenzi et al published findings of the CUORE trial in 2014. The randomized controlled trial included 56 hospitalized heart failure patients without severe renal insufficiency who were treated with ultrafiltration (n=27) or standard medical therapy (n=29). All patients had left ventricular ejection fraction of 40% or less and fluid overload of 4kg or more of recent weight gain and were partially responsive to diuretic therapy. The primary end point was the incidence of heart failure related re-hospitalizations during the year after treatment. Four re-hospitalizations occurred in the ultrafiltration group, which was significantly fewer instances than the 30 re-hospitalizations in the control group (hazard ratio, 0.14; 95% confidence interval, 0.04 to 0.48; p=0.002). At the one-year follow-up, 7 (26%) deaths were reported in the ultrafiltration group versus 11 (38%) in the control group (p=0.33). Weight loss at discharge was similar in both groups (p=0.75).

The most recently published RCT was the AVOID-HF (Aquapheresis versus Intravenous Diuretics and Hospitalization for Heart Failure) trial published by Costanzo et al in 2016. This unblinded multicenter RCT tested a strategy of adjustable ultrafiltration and compared it to adjustable intravenous loop diuretic treatment. Eligibility included hospitalization with a primary diagnosis of acute decompensated heart failure, and participants were randomized within 24 hours of hospital admission. The trial originally aimed to include 810 patients and the sample size calculation determined that this number of participants was needed to have sufficient power for the primary end point. However, after enrolling 224 (27.5%) patients, the study sponsor terminated the study due to slow enrollment. The analysis reports on 221 (110 patients in the ultrafiltration group, 111 in the diuretic group) enrolled at the time of study termination. The primary end point, a composite variable comprised of heart failure re-hospitalization or unscheduled or outpatient or emergency department treatment for heart failure, occurred in 25% of the ultrafiltration group and 35% of the diuretic group (exact numbers not reported). The difference in event rates between groups was not statistically significant (p=0.106). By 90 days, death occurred in 17 (15%) ultrafiltration patients and 14 (13%) diuretic patients, p=0.827). The proportion of patients who experienced any adverse event or any serious adverse event did not differ significantly between groups, but the ultrafiltration group (15%) experienced significantly more serious adverse events determined to be related to study therapy than the diuretic group (5%; p=0.026).

Summary of Evidence

For individuals who have decompensated heart failure who receive ultrafiltration, the evidence includes randomized controlled trials (RCTs) and systematic reviews. Relevant outcomes are overall survival, quality of life, hospitalizations, and treatment-related morbidity. A number of RCTs and meta-analyses of RCTs have been published. Meta-analyses did not find significant differences in all-cause mortality in patients receiving ultrafiltration or diuretics, and nearly all

meta-analyses did not find significant between-group differences in rehospitalization rates. RCTs and meta-analysis found that patients undergoing ultrafiltration had significantly greater weight loss and more fluid removal than diuretic therapy. Although pooled analyses of RCTs have not find significant differences in adverse events in groups receiving ultrafiltration or diuretics, some RCTs (e.g., CARESS and, AVOID-HR) have reported higher rates of adverse events after ultrafiltration including significant worsening of renal function and treatment-related serious adverse events. The available trials have several methodologic limitations (e.g., unblinded outcome assessment, incomplete information on patient status). Moreover, long-term outcomes (i.e., >1 year) have not been reported. The evidence is insufficient to determine the effects of the technology on health outcomes.

Practice Guidelines and Position Statements

American College of Cardiology Foundation and American Heart Association

The 2013 American College of Cardiology Foundation and American Heart Association published joint guidelines on the diagnosis and management of heart failure in adults (under Recommendations for Hospitalized Patient) lists ultrafiltration as a Class IIb recommendation (benefit greater than or equal to risk, additional studies needed). The recommendations stated ultrafiltration "may be considered for patients with obvious volume overload to alleviate congestive symptoms and fluid weight" (level of evidence B: conflicting evidence) and "for patients with refractory congestion not responding to medical therapy" (level of evidence C: recommendation less well established).

European Society of Cardiology and Heart Failure Association

The European Society of Cardiology Heart Failure Association released joint guidelines in 2012 on the diagnosis and treatment of acute heart failure stated that "ultrafiltration is sometimes used to remove fluid in patients with HF [heart failure], although is usually reserved for those unresponsive or resistant to diuretics." The guidelines noted, however, the efficacy and safety of ultrafiltration is unknown.

Heart Failure Society of America

The Heart Failure Society of America's (HFSA) 2010 Comprehensive Heart Failure Practice Guidelines indicate ultrafiltration may be considered for the treatment of acute decompensated heart failure fluid overload in lieu of diuretics. (Level B evidence- cohort or smaller studies) The HFSA guidelines also indicate ultrafiltration may be considered when congestion continues despite diuretic therapy. (Level C evidence - opinion)

U.S. Preventive Services Task Force

Not applicable

Key Words:

Ultrafiltration, Aquapheresis, Aquadex, FlexFlow, CHF Solutions, Congestive Heart Failure, CHF

Approved by Governing Bodies:

In June 2002, the Aquadex FlexFlow™ System (Baxter, Deefield, IL) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. An amended 510(k) approval (classified as a high permeability dialysis system) was given in September 2007 following modifications. The FDA determined that this device was substantially equivalent to existing devices for use in temporary (up to eight hours) ultrafiltration treatment of patients with fluid overload who have failed diuretic therapy, and for extended (longer than eight hours) ultrafiltration treatment of patients with fluid overload who have failed diuretic therapy and require hospitalization.

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: Special benefit consideration may apply. Refer to member's benefit plan. FEP does not consider investigational if FDA approved and will be reviewed for medical necessity.

Coding:

CPT Codes:

There are no specific CPT codes for this procedure

References:

1. Badawy SS, Fahmy A. Efficacy and cardiovascular tolerability of continuous veno-venous hemodiafiltration in acute decompensated heart failure: a randomized comparative study. J Crit Care 2012; 27(1):106 e7-13.
2. Bart BA, Boyle A, Bank AJ et al. Ultrafiltration vs. usual care for hospitalized patients with heart failure: the Relief for Acutely Fluid-Overloaded Patients with Decompensated Congestive Heart Failure (RAPID-CHF) trial. J Am Coll Cardiol 2005; 46(11):2043-6.
3. Bart BA, Goldsmith SR, Lee KL et al. Ultrafiltration in decompensated heart failure with cardiorenal syndrome. N Engl J Med 2012; 367(24): 2296-304.
4. Cheng Z, Wang L, Gu Y, et al. Efficacy and safety of ultrafiltration in decompensated heart failure patients with renal insufficiency. Int Heart J. May 13 2015; 56(3):319-323.
5. Costanzo MR, Guglin ME, Saltzberg MT et al. Ultrafiltration versus intravenous diuretics for patients hospitalized for acute decompensated heart failure. J Am Coll Cardiol 2007; 49(6):675-683.
6. Costanzo MR, Negoianu D, Jaski BE, et al. Aquapheresis versus intravenous diuretics and hospitalizations for heart failure. JACC Heart Fail. Feb 2016; 4(2):95-105.
7. Costanzo MR, Saltzberg J, O'Sullivan J et al. Early ultrafiltration in patients with decompensated heart failure and diuretic resistance. J Am Coll Cardiol 2005; 46(11):2052-3.

8. Costanzo MR, Saltzberg MT, Jessup M, et al. Ultrafiltration is associated with fewer rehospitalizations than continuous diuretic infusion in patients with decompensated heart failure: results from UNLOAD. J Card Fail. Apr 2010; 16(4):277-284.
9. Costanzo MR, Saltzberg MT, Jessup M et al. Ultrafiltration versus intravenous diuretics for patients hospitalized for acute decompensated heart failure (UNLOAD) investigators. Ultrafiltration is associated with fewer rehospitalizations than continuous diuretic infusion in patients with decompensated heart failure: results from UNLOAD. J Card Fail 2010; 16(4):277-284.
10. Dahle TG, Blake D, Ali SS et al. Large volume ultrafiltration for acute decompensated heart failure using standard peripheral intravenous catheters. J Card Fail 2006; 12(5):349-52.
11. De Vecchis R, Esposito C, Ariano C. Efficacy and safety assessment of isolated ultrafiltration compared to intravenous diuretics for acutely decompensated heart failure: a systematic review with meta-analysis. Minerva Cardioangiol 2014; 62(2):131-46.
12. Dev S, Shirolkar SC, Stevens SR et al. Reduction in body weight but worsening renal function with late ultrafiltration for treatment of acute decompensated heart failure. Cardiology 2012; 123(3):145-53.
13. Dickstein K, Cohen-Solal A, Filippatos G et al. Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008. Eur J Heart Fail 2008; 10(10):933-89.
14. Ebrahim B, Sindhura K, Okoroh J, et al. Meta-Analysis of Ultrafiltration versus Diuretics Treatment Option for Overload Volume Reduction in Patients with Acute Decompensated Heart Failure. Arq Bras Cardiol. Jan 27 2015; 0.
15. Ebrahim B, Sindhura K, Okoroh J, et al. Meta-Analysis of Ultrafiltration versus Diuretics Treatment Option for Overload Volume Reduction in Patients with Acute Decompensated Heart Failure. Arq Bras Cardiol. May 2015; 104(5):417-425.
16. Giglioli C, Landi D, Cecchi E, et al. Effects of ULTRAfiltration vs. DIureticS on clinical, biohumoral and haemodynamic variables in patients with deCOmpensated heart failure: the ULTRADISCO study. Eur J Heart Fail. Mar 2011; 13(3):337-346.
17. Giglioli C, Landi D, Gensini GF et al. Cardiac efficiency improvement after slow continuous ultrafiltration is assessed by beat-to-beat minimally invasive monitoring in congestive heart failure patients: a preliminary report. Blood Purif 2010; 29(1):44-51.
18. Gura V, Beizai M, EzonC, et al. Continuous renal replacement therapy for congestive heart failure: the wearable continuous ultrafiltration system. ASAIO J 2006; 52(1):59-61.
19. Gura V, Ronco C, Nalesso F, et al. A wearable hemofilter for continuous ambulatory ultrafiltration. Kidney Int. Feb 2008; 73(4):497-502.
20. Hanna MA, Tang WH, Teo BW et al. Extracorporeal ultrafiltration vs. conventional diuretic therapy in advanced decompensated heart failure. Congest Heart Fail 2012; 18(1):54-63.
21. Heart Failure Society of America, Lindenfeld J, Albert NM et al. HFSA 2010 Comprehensive Heart Failure Practice Guideline. J Card Fail 2010; 16(6):e1-194.
22. Jain A, Agrawal N, Kazory A. Defining the role of ultrafiltration therapy in acute heart failure: a systematic review and meta-analysis. Heart Fail Rev. Sep 2016; 21(5):611-619.
23. Jaski BE, Romeo A, Ortiz B et al. Outcomes of volume-overloaded cardiovascular patients treated with ultrafiltration. J Card Fail 2008; 14(6):515-20.

24. Jessup M, Abraham W, Casey D et al. 2009 focused update: ACCF/AHA Guidelines for the Diagnosis and Management of Heart Failure in Adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: developed in collaboration with the International Society for Heart and Lung Transplantation. Circulation 2009; 119(14):1977-2016.
25. Kwok CS, Wong CW, Rushton CA, et al. Ultrafiltration for acute decompensated cardiac failure: a systematic review and meta-analysis. Int J Cardiol. Feb 01 2017; 228:122-128.
26. Kwong JS, Yu CM. Ultrafiltration for acute decompensated heart failure: a systematic review and meta-analysis of randomized controlled trials. Int J Cardiol 2014; 172(2):395-402.
27. Marenzi G, Muratori M, Cosentino ER et al. Continuous ultrafiltration for congestive heart failure: the CUORE trial. J Card Fail 2014; 20(1):9-17.
28. McMurray JJ, Adamopoulos S, Anker SD et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J 2012; 33(14):1787-1847.
29. Nakayama M. Nonuremic indication for peritoneal dialysis for refractory heart failure in cardiorenal syndrome type II: review and perspective. Peritoneal Dialysis International 2012; 33: 8-14.
30. Patarroyo M, Wehbe E, Hanna M et al. Cardiorenal outcomes after slow continuous ultrafiltration therapy in refractory patients with advanced decompensated heart failure. J Am Coll Cardiol 2012; 60(19):1906-12.
31. Rogers HL, Marshall J, Bock J et al. A randomized, controlled trial of the renal effects of ultrafiltration as compared to furosemide in patients with acute decompensated heart failure. J Card Fail 2008; 14(1):1-5.
32. Ronco C, Nalesso F, Brendolan A et al. A wearable hemofilter for continuous ambulatory ultrafiltration. Kidney Int 2008; 73(4):497-502.
33. Wankowicz Z, Prochnicka A et al. Extracorporeal versus peritoneal ultrafiltration in diuretic-resistant congestive heart failure – a review. Med Sci Monit 2011; 17(12): RA271-281.
34. Wen H, Zhang Y, Zhu J et al. Ultrafiltration versus intravenous diuretic therapy to treat acute heart failure: a systematic review. Am J Cardiovasc Drugs 2013; 13(5):365-73.
35. www.clinicaltrials.govUH.
36. Yancy CW, Jessup M, Bozkurt B et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013; 62(16):e147-239.
37. Zhi Q, Liang JC. Diuretics and ultrafiltration in acute heart failure syndrome. Int Heart J 2013; 54(6):390-4

Policy History:

Medical Policy Group, December 2006 **(2)**
Medical Policy Panel, June 2008
Medical Policy Panel, June 2010
Medical Policy Group, June 2010 **(2)**

Medical Policy Administration Committee, June 2010
Available for comment June 18-August 2, 2010
Medical Policy Group, January 2012 **(3)**: Updated Key Points and References-added
Medical Policy Panel, June 2012
Medical Policy Group, July 2012 **(4)**: Updated Key Points and References
Medical Policy Group, September 2013 **(4)**: 2013 Update to Key Points and References
Medical Policy Group, October 2013 **(4)**: Removed ICD-9 Procedure codes; no change to policy statement.
Medical Policy Panel, June 2014
Medical Policy Group, June 2014 **(4):** Updated Key Points and References. No change to the policy statement.
Medical Policy Group, January 2015 **(3)**: Ad hoc request for literature review; References updated. No change in policy statement.
Medical Policy Panel, June 2015
Medical Policy Group, June 2015 **(4):** Updates to Key Points and References. No change in policy statement.
Medical Policy Group, May 2016 **(4)**: Updates to Description, Key Points, Key Words and References. No change in policy statement.
Medical Policy Panel, May 2017
Medical Policy Group, May 2017 **(4)**: Updates to Description, Key Points, Approved by Governing Bodies, and References. No change in policy statement.
Medical Policy Panel, May 2018
Medical Policy Group, May 2018 **(4)**: Updates to Description and Key Points. No change to policy statement.
