

## Clinical Review Criteria

### Ultrafiltration for the Treatment of Congestive Heart Failure

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## Criteria

### For Medicare Members

Source	Policy
CMS Coverage Manuals	None
National Coverage Determinations (NCD)	<a href="#">Ultrafiltration, Hemoperfusion and Hemofiltration (110.15)</a>
Local Coverage Determinations (LCD)	None
Local Coverage Article	None

### For Non-Medicare Members

There is insufficient evidence in the published medical literature to show that this service/therapy is as safe as standard services/therapies and/or provides better long-term outcomes than current standard services/therapies.

#### If requesting this service, please send the following documentation to support medical necessity:

- Last 6 months of clinical notes from requesting provider &/or consulting specialist.

The following information was used in the development of this document and is provided as background only. It is provided for historical purposes and does not necessarily reflect the most current published literature. When significant new articles are published that impact treatment option, Kaiser Permanente will review as needed. This information is not to be used as coverage criteria. Please only refer to the criteria listed above for coverage determinations.

## Background

Heart failure (HF) is a major and growing health problem worldwide and is the leading cause of hospitalization in the Western world. In the United States more than 5 million patients suffer from HF, and more than one million are admitted annually to hospitals for acute decompensated heart failure (ADHF). The great majority of patients present with dyspnea and edema from the volume overload and pulmonary congestion driven by sodium and water retention, and many are discharged without clinical evidence of adequate decongestion. The prognosis of patients with ADHF is poor with an approximately 4% in-hospital mortality rate. 25% are readmitted within 30 days, and up to 23% die within 6 months. 25-33% of patients with ADHF develop acute cardiorenal syndrome which is defined as worsening renal function (often defined as an increase in creatinine  $\geq 0.3$  mg/dL from baseline). This results from a number of contributing factors and is usually associated with poor outcome (Chiong 2010, Giglioli 2011, Bart 2012, Felker 2012).

Standard therapy for decompensated HF consists predominantly of intravenous (IV) loop diuretics and vasodilators. Loop diuretics induce rapid diuresis that reduces lung congestion and edema. Intravenous administration of an effective dose of furosemide (a loop diuretic) typically results in a diuretic effect within 30 minutes and peaks at one hour. Heart failure patients require a higher dose to achieve this same effect. It was reported that in ADHF, renal responsiveness to loop diuretics may be decreased, and that patients with New York Heart Association (NYHA) class II or III HF have one third to one fourth the natriuretic response as compared with normal subjects. This response decreases further as the severity of HF increases, and higher doses are required. The effectiveness of the diuretics also declines with repeated exposure, and resistance to the therapy may

develop as heart failure progresses. In some patients fluid overload persists despite the higher doses. Investigators described two types of diuretic resistance; short-term resistance, which is a decrease in response to the first administration, and long-term resistance that develops after long-term administration of loop diuretics. Approximately 25%-30% of HF patients develop diuretic resistance which is usually associated with worsened outcomes and higher risk of death. In some cases, the intravenous administration of diuretics to patients with ADHF may directly contribute to worsening of renal function, and its continued use for treating persistent congestion after the onset of worsening renal function, may lead to additional kidney injury. Despite the concerns about these potential harms associated with higher doses of diuretic therapy and the lack of proven survival benefit, diuretics remain the standard therapy for removing the excess extracellular fluid in patients with heart failure. Other therapeutic alternatives include inotropic therapy, IV nitroglycerine and natriuretic peptides. When these pharmacological approaches fail, or are unsuitable, the alternative means for fluid removal are dialysis, phlebotomy, or ultrafiltration (Costanzo 2005, 2007, Chiong 2012, Bart 2012, Felker 2009, 2012)

The concept of extracorporeal removal of fluid with ultrafiltration has been used for decades to treat refractory edema. The pump-driven extracorporeal ultrafiltration (UF) was described in the 1970s and was used for patients with heart failure in the mid-1980s. Ultrafiltration is accomplished by mechanically drawing blood from the patient either through peripheral or central venous access. Plasma is then filtered by means of the negative hydrostatic pressure generated by a second pump, and re-infused back into the patient. The ultrafiltrate is composed of water with electrolytes in the same concentration as in the serum without the cells or proteins which are too large to pass through the filter pores. Unlike dialysis, ultrafiltration operates by convection in eliminating iso-osmolar extracellular fluid resulting in a decrease in ventricular filling pressure without significant changes in the renal function, creatinine, or urea concentration. It is reported that ultrafiltration can improve cardiac hemodynamics by reducing both right and left sided filling pressure, increasing the stroke volume and cardiac output. Researchers also found that it restores diuretic responsiveness and improves natriuresis without changes in the heart rate, systolic blood pressure, intravascular volume, or electrolytes. A potential advantage of UF over loop diuretics is that the ultrafiltrate is isotonic, whereas the urinary output with loop diuretics is hypotonic, thus UF removes more sodium (and less potassium) than diuretics for an equivalent volume loss. Ultrafiltration is not a substitute for dialysis and will not lead to removal of accumulated toxins or potassium in hyperkalemic patients (Bourge 2005, Boyle 2005, Costanzo 2005).

Earlier, ultrafiltration required physician placement of a double-lumen central venous catheter and monitoring by a dialysis technician. Recently a simpler, smaller, and portable ultrafiltration device was introduced (System 100, CHF Solutions, Minneapolis, Minnesota). The device is less invasive and does not require intensive care unit monitoring or central intravenous access. It allows a technician to place the blood withdrawal and infusion catheters in peripheral veins, usually the brachial-cephalic system, with subsequent monitoring by a clinical nurse. The device removes water and non-protein-bound small and medium molecular weight solutes through a semipermeable membrane when hydrostatic pressure generated by blood pressure or external blood pump exceeds oncotic pressure. The fluid removal rate can range from 100 to 500 ml/hour and is set by the treating physician. UF requires systemic anticoagulation with the possibility of excess bleeding. Other potential complications include air embolism, and overly aggressive volume removal (Bourge 2005, Bart 2012).

The ACC/AHA clinical practice guidelines do not recommend the use of UF as a class I therapeutic option but as a class II recommendation (level B evidence) for the relief of fluid overload in patients with refractory congestion not responding to medical therapy.

CHF Solutions received marketing clearance from the FDA for System 100 in June 2002 and for central venous access with the system in December 2003. System 100 is indicated for temporary (up to 8 hours) ultrafiltration treatment of patients with fluid overload. In 2005, System 100 was renamed Aquadex FlexFlow™ and launched with several new features (according to the manufacturer).

## Medical Technology Assessment Committee (MTAC)

### *Ultrafiltration in the Treatment of Congestive Heart Failure*

#### **08/07/2006: MTAC REVIEW**

**Evidence Conclusion:** The RAPID-CHF trial (Bart 2005) was a randomized, controlled, non-blinded trial that compared usual care vs. usual care plus ultrafiltration (UF) in 40 patients admitted to hospital with acute decompensated heart failure and fluid overload. Patients randomized to the usual care group received the conventional heart failure therapy. Those in the UF group received an 8 hour UF treatment with a maximum fluid removal rate of 500 cc/hour. Diuretics were administered after the 8 hours of UF, and additional courses of UF were allowed after 24 hours. The results of the trial show that the weight loss (primary endpoint of the trial) was not

significantly different between the two study groups. The average volume removal of fluid was significantly higher in the UF group at 24 and 48 hours. Patients in the two treatment groups experienced improvement in their symptoms during the treatment period. The improvement observed was significantly greater in the UF group compared to the usual care group at 48 hours but not at 24 hours. The significant difference may be due to the greater fluid removal or due to chance as the trial was small, un-blinded, and the outcome measure was subjective. Costanzo et al (2005) reported their experience with early initiation of UF in 20 selected HF patients admitted to hospital with manifest signs and symptoms of fluid overload. The patients underwent UF which was continued until the acute decompensation heart failure symptoms were resolved. The removal of fluid was aggressive (8,654 + 4,205 ml) and resulted in a mean decrease of 6 kg of weight at discharge, and improvement in the clinical signs of symptoms of fluid overload that seem to have lasted for the 90 days of follow-up. This was only an observational case series with no comparison or control group and subject to selection and observation bias. The results of the UNLOAD (or UltrafiltrationN versus IV diuretics for patients hospitalized for Acute Decompensated congestive heart failure) trial was presented at the 2006 ACC conference in Atlanta, but have not been published in a peer reviewed journal to date. The trial randomized 200 patients from 28 centers to receive the standard intravenous diuretic drug therapy or IV diuretics plus ultrafiltration to treat fluid overload. The study was not blinded, the primary outcomes were weight loss and dyspnea score at 48 hours, and the patients were followed up for 90 days. The unpublished results of the trial indicate that both treatments were associated with significant improvement in the dyspnea score at 48 hours, but with no significant difference between the two treatment groups. Patients in the UF group had significantly greater net fluid and weight loss at 48 hours, and a lower incidence of hypokalemia. The results also show that the hospital readmission rate, during the 3 months of follow-up, was significantly lower in the UF group, vs. the IV diuretic group. All three studies were funded or supported by the manufacturer of the device CHF Solutions, Brooklyn Park, Minnesota, which may introduce bias. In conclusion, there is insufficient evidence to date to determine the efficacy and long-term safety of ultrafiltration versus standard care in acute decompensated heart failure, or to determine who would benefit most from the intervention.

**Articles:** The search yielded around 280 articles most of which were review articles, opinion pieces, or dealt with the technical aspects of the procedures. There was one RCT, and several small case series, many of which dated back in the 1980s and 1990s. The RCT and the relevant case series using the new UF device (System 100, CHF Solutions, Minneapolis, Minnesota) were selected for critical appraisal: Bart BA, Boyle A, Bank AJ, et al. Ultrafiltration versus 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; 46:2043-2046. See [Evidence Table](#). MR, Saltzberg M, O'sollivan J, et al. Early ultrafiltration in patients with decompensated heart failure and diuretic resistance. *J Am Coll Cardiol* 2005;46:2047-2051. See [Evidence Table](#).

The use of ultrafiltration in the treatment of congestive heart failure does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

## 06/17/2013: MTAC REVIEW

### Ultrafiltration in the Treatment of Congestive Heart Failure

**Evidence Conclusion:** All published trials on the use of ultrafiltration in patients with acute decompensated heart failure with or without renal dysfunction compared UF with IV diuretic-based therapy. No published RCT, to date, examined the efficacy and safety of ultrafiltration in patients with ADHF who refractory to diuretics were. This latter indication of ultrafiltration was only evaluated in a one retrospective study with no control group. Ultrafiltration as a first line therapy The UNLOAD (ultrafiltration versus Intravenous Diuretics for Patients Hospitalized for Acute Decompensated Congestive Heart Failure) trial compared ultrafiltration to diuretic therapy in patients hospitalized for acute decompensated heart failure. The trial examined UF as a first-line early therapy not as a rescue therapy (i.e. patients did not have to fail an initial diuretic therapy to be included in the trial). 200 patients were randomized to receive early UF (within 24 hours of hospitalization) or intravenous diuretic drug therapy. The co-primary outcomes were weight loss and patient self-assessed dyspnea score at 48 hours. The results show that both the UF and IV diuretic therapies were associated with significant improvement in the dyspnea score at 48 hours, with no statistically significant difference between the two treatment groups. Patients in the UF group had significantly greater fluid and weight loss at 48 hours, and a lower incidence of hypokalemia. This however, did not have an impact on the length of the index hospital stay. The rates of rehospitalization and unscheduled visits during the 90 days of follow-up were significantly lower in the UF group, vs. the IV diuretic group. The results also show a higher rise in serum creatinine levels in the UF group vs. the IV diuretic group (twice as many patients in the UF arm experienced an increase in sCr level >0.3 ml/dL during the first 24 hours of therapy) but the difference did not reach a statistically significant level. The authors considered the lack of significant difference between the two groups for this as well as other outcomes, as similar effects when the trial was not designed as equivalent study, and the lack of significant differences could result from insufficient statistical power. The study was a multicenter RCT but had several limitations many of which were acknowledged by the authors. The trial had a relatively small size and short follow-up duration, excluded

patients with hypotension or hemodynamic instability, and used suboptimal dose and mode of administration of loop diuretics. The dose of the diuretic, duration, and rate of UF were all based on the discretion of the attending physician who was not blinded to the randomization groups and could be a source of bias. In addition, the authors did not present any data on low-salt diet compliance, or criteria for hospitalization. The study was supported by CHF Solution Inc., and the primary author as well as a number of other authors had financial ties to the manufacturer of the device CHF Solutions, Brooklyn Park, Minnesota. The Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARRESS-HF, sponsored by the NHLBI) investigated the role of UF as a treatment for patients with persistent congestion and worsening of kidney function (increase in serum creatinine  $\geq 0.3$  mg/dL within 12 weeks before or 10 days after index admission). 188 patients were randomized to undergo ultrafiltration (fluid removal at a rate of 200 ml/hour using Aquadex System 100; CHF Solutions), or to receive stepped pharmacological therapy involving increasing the doses of loop diuretics (with or without metolazone), vasodilators and inotropes (based on an algorithm that aimed at achieving urine output of 3-5 liters/ day). The assigned treatment was continued in the two groups until signs and symptoms of congestion were improved as possible. The primary endpoint was bivariate (simultaneous) change in serum creatinine level and body weight in 96 hours after randomization. The trial was not blinded, and the patients were followed-up for 60 days. Recruitment for the trial was stopped early before reaching the planned size of 200 subjects based on the advice of the data and safety monitoring board due to lack of benefit and excess adverse events with ultrafiltration. The results of CARRESS-HF show that stepped pharmacological therapy was superior to UF when the primary end point was assessed at 96 hours after randomization. There was a statistically significant reduction the serum creatinine (sCr) in the pharmacologic therapy group compared to the UF group. There was no significant difference between the groups in weight loss at 96 hours. At the 60 days of follow-up, there were no statistically significant differences in weight loss, or rate of hospitalization due to heart failure. There was a nonsignificant increase in the all-cause readmission rate in the UF group. UF, was also associated with a significantly higher rate of serious adverse events including kidney failure, bleeding complications, and catheter-related complications. The sixty-day mortality was 17% for the UF group and 13% for the pharmacological therapy group with no significant difference between the groups, however, as indicated earlier, a lack of significant difference does not indicate equivalence due to the study design. These results should be interpreted with caution and cannot be generalized to patients with ADHF with better renal function than those included in the trial.

*Other published trials* Two other very small published RCTs (ULTRADISCO (Giglioli et al 2011), and Hanna and colleagues' trial (2012) also compared ultrafiltration versus intravenous diuretics inpatients hospitalized for ADHF. The trials had intermediate outcomes (hemodynamic variables in the ULTRADISCO trials, and time for pulmonary wedge pressure to be maintained at  $>18$  mmHg for  $\geq 4$  consecutive hours in Hanna and colleagues' study). Their overall results showed greater fluid loss with UF vs. diuretic therapy with no significant difference between the groups in the serum creatinine levels. Ultrafiltration as a rescue therapy for patients with ADHF who are refractory to IV diuretic therapy The literature search did not identify any published RCT to date, that examined the efficacy and safety of ultrafiltration in patients with ADHF who were refractory to diuretics. In a retrospective observational study with no comparison group, Patarroyo and colleagues (2012) analyzed data from hospital records for adult patients with ADHF admitted to one heart failure intensive care unit in Cleveland Ohio ((2004-2009) and who required slow continuous ultrafiltration therapy (SCUF). The study population was a highly selected group of 63 adult patients with advanced HF, worsening renal function, and congestion refractory to hemodynamically guided intensive medical therapy. Their median age was 58 years, mean LV ejection fraction  $26 \pm 15\%$ , baseline serum creatinine (sCr)  $1.9 \pm 0.8$  mg/dL and hemodynamics consistent with cardiogenic shock. SCUF was initiated after a mean of 8 days from admission, was performed at a rate of 200ml/hr. and for a mean duration of 8 days. At the initiation of SCUF therapy the sCr level was  $2.2 \pm 0.9$  mg/dL. The mean duration of the UF therapy was  $3 \pm 2$  days, and the primary endpoint of the study was all-cause mortality and the secondary endpoint included number of readmissions for ADHF and dialysis-dependent status at time of discharge. The results of the analysis showed that after 48 hours of SCUF the overall cohort lost weight significantly compared to baseline (mean 4.4 kg). This was associated with significant improvement in hemodynamic variables but with no improvements in sCr levels or blood urea. 37 patients (59%) required conversion to continuous hemodialysis during their hospital stay and 9 (14%) were dependent on hemodialysis at hospital discharge. 34/37 (93%) of these patients were readmitted to the hospital within 60 days form discharge. 19/63 patients (30%) died during the index hospitalization, and 4 were discharged to terminal care in hospice. The overall 1-year all-cause mortality was 70% and 2 of the surviving patients underwent heart transplantation. The results of the study should be interpreted with caution due to the study design and its inclusion of severely ill patients. Conclusion: There is insufficient evidence to support the use of ultrafiltration as a first-line treatment in hospitalized ADHF with volume overload. There is insufficient evidence to determine the safety and efficacy of ultrafiltration in patients with ADHF who are refractory to diuretic therapy. Results from UNLOAD trial, suggest, but do not provide good evidence, that ultrafiltration may provide better correction of volume overload than IV diuretics (given at the dose used in the trial) in patients hospitalized ADHF who are not resistant to diuretic therapy. The trial had its limitations and does not provide any evidence on the safest and most effective rates of fluid removal, duration of treatment, or the conditions for termination of ultrafiltration. There is evidence from the CARRESS-HF that IV loop diuretic-based therapy adding distal-acting

diuretics, IV vasodilator and inotropic agents as needed is superior to ultrafiltration in patients with acute decompensated heart failure and worsening renal function. CARESS-HF results show increased incidence of worsening kidney function in the ultrafiltration group versus the stepped pharmacologic therapy group. A large ongoing trial (AVOID-HF) (NCT01474200) involving 810 patients in 40 US centers is examining the effect of UF vs. intravenous diuretics in reducing hospitalization in patients with ADHF before worsening renal function. **Articles:** UNLOAD trial (Costanzo et al 2007, evidence table 1) [See Evidence Table](#). CARRESS-HF (Bart yet al 2012, evidence table 2) [See Evidence Table](#)

The use of ultrafiltration in the treatment of congestive heart failure does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

## Applicable Codes

**Medicare - Considered Medically Necessary when criteria in the applicable policy statements listed above are met**

**Non-Medicare - Considered Not Medically Necessary**

CPT® or HCPC Codes	Description
0692T	Therapeutic ultrafiltration

**\*Note:** Codes may not be all-inclusive. Deleted codes and codes not in effect at the time of service may not be covered.

\*\*To verify authorization requirements for a specific code by plan type, please use the [Pre-authorization Code Check](#).

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Date Created	Date Reviewed	Date Last Revised
08/29/2006	04/04/2011 <sup>MDCRPC</sup> , 02/07/2012 <sup>MDCRPC</sup> , 12/04/2012 <sup>MDCRPC</sup> , 08/06/2013 <sup>MPC</sup> , 06/03/2014 <sup>MPC</sup> , 02/03/2015 <sup>MPC</sup> , 12/01/2015 <sup>MPC</sup> , 10/04/2016 <sup>MPC</sup> , 08/01/2017 <sup>MPC</sup> , 07/10/2018 <sup>MPC</sup> , 07/09/2019 <sup>MPC</sup> , 07/07/2020 <sup>MPC</sup> , 07/06/2021 <sup>MPC</sup> , 07/05/2022 <sup>MPC</sup> , 07/11/2023 <sup>MPC</sup>	12/08/2022

<sup>MPC</sup> Medical Policy Committee

Revision History	Description
12/08/2022	Added new applicable CPT code to criteria