Chelation Therapy for Off-Label Uses

Policy Number: 8.01.02  Last Review: 02/2017
Origination: 02/2016  Next Review: 02/2018

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will not provide coverage for off-label uses of chelation therapy. This is considered investigational.

When Policy Topic is covered
A number of indications for chelation therapy have received Food and Drug Administration (FDA) approval and for which chelation therapy is considered standard of care treatment. They include:

- extreme conditions of metal toxicity;
- treatment of chronic iron overload due to blood transfusions (transfusional hemosiderosis) and due to non-transfusion-dependent thalassemia (NTDT);
- Wilson disease (hepatolenticular degeneration);
- lead poisoning
- control of ventricular arrhythmias or heart block associated with digitalis toxicity; and
- emergency treatment of hypercalcemia.

For the last 2 bullet points, most patients should be treated with other modalities. Digitalis toxicity is currently treated in most patients with Fab monoclonal antibodies. FDA removed the approval for NaEDTA as chelation therapy due to safety concerns and recommended that other chelators be used. This was the most common chelation agent used to treat digitalis toxicity and hypercalcemia.

When Policy Topic is not covered
Off-label applications of chelation therapy are considered investigational, including, but not limited to:

- Alzheimer disease;
- arthritis (includes rheumatoid arthritis);
- atherosclerosis (e.g., coronary artery disease, secondary prevention in patients with myocardial infarction, or peripheral vascular disease);
- autism;
- diabetes; and
- multiple sclerosis

Considerations
Prior authorization is recommended for coverage of chelation therapy.

This Blue Cross and Blue Shield of Kansas City policy Statement was developed using available resources such as, but not limited to: Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, Local medical policies of other health plans, Medicare (CMS), Local providers.

Description of Procedure or Service
Chelation therapy, an established treatment for heavy metal toxicities and transfusional hemosiderosis,
has been investigated for a variety of off-label applications, such as treatment of atherosclerosis, Alzheimer disease, and autism. This evidence review does not address indications for chelation therapy approved by the U.S. Food and Drug Administration. Off-label indications that will be addressed include the following conditions: Alzheimer disease, cardiovascular disease, autism, diabetes, multiple sclerosis, and arthritis.

The evidence for chelation therapy in individuals who have Alzheimer disease, cardiovascular disease, autism, diabetes, multiple sclerosis, or arthritis includes a small number of randomized controlled trials (RCTs) and case series. Relevant outcomes are symptoms, change in disease status, morbid events, functional outcomes, health status measures, quality of life, and treatment-related morbidity. One RCT, the Trial to Assess Chelation Therapy (TACT), reported that chelation therapy reduced cardiovascular events in patients with a previous myocardial infarction and that the benefit was greater in diabetic patients compared with nondiabetic patients. However, this trial had significant limitations, including high dropout rates, and therefore conclusions are not definitive. For other conditions, the available RCTs do not report improvements in health outcomes with chelation therapy and the case series are not adequate evidence to determine efficacy. The evidence is insufficient to determine the effect of the technology on health outcomes.

Chelation therapy is an established treatment for the removal of metal toxins by converting them to a chemically inert form that can be excreted in the urine. Chelation therapy comprises intravenous or oral administration of chelating agents that remove metal ions such as lead, aluminum, mercury, arsenic, zinc, iron, copper, and calcium from the body (see Appendix Table 1). Specific chelating agents are used for particular heavy metal toxicities. For example, desferrioxamine (not approved by the Food and Drug Administration [FDA]) is used for patients with iron toxicity, and calcium-ethylenediaminetetraacetic acid (EDTA) is used for patients with lead poisoning. (Disodium-EDTA is not recommended for acute lead poisoning due to the increased risk of death from hypocalcemia.)

Another class of chelating agents, called metal protein attenuating compounds (MPACs), is under investigation for the treatment of Alzheimer disease, which is associated with the disequilibrium of cerebral metals. Unlike traditional systemic chelators that bind and remove metals from tissues systemically, MPACs have subtle effects on metal homeostasis and abnormal metal interactions. In animal models of Alzheimer disease, they promote the solubilization and clearance of β-amyloid by binding its metal-ion complex, and also inhibit redox reactions that generate neurotoxic free radicals. MPACs therefore interrupt 2 putative pathogenic processes of Alzheimer disease. However, no MPACs have received FDA approval for the treatment of Alzheimer disease.

Chelation therapy also has been discussed as a treatment for other indications including atherosclerosis and autism. For example, EDTA chelation therapy has been proposed in patients with atherosclerosis as a method of decreasing obstruction in the arteries.

The U.S. Food and Drug Administration (FDA) approved calcium-EDTA (Versenate) for lowering blood lead levels among both pediatric and adult patients with lead poisoning. Succimer is approved for the treatment of lead poisoning in pediatric patients only. FDA approved disodium-EDTA for use in selected patients with hypercalcemia and for use in patients with heart rhythm problems due to intoxication with digitalis. In 2008, FDA withdrew approval of disodium-EDTA due to safety concerns, and recommended that other forms of chelation therapy be used.

Several iron chelating agents are FDA-approved:

- **Deferoxamine for subcutaneous, intramuscular, or intravenous injections** was approved to treat acute iron intoxication and chronic iron overload due to transfusion-dependent anemia.
- **Deferasirox**, approved in 2005, is available as a tablet for oral suspension and is indicated for the treatment of chronic iron overload due to blood transfusions in patients age 2 years and older.

Under the accelerated approval program, FDA expanded the indications for deferasirox in 2013 to
include treatment of patients age 10 years and older with chronic iron overload due to nontransfusion-dependent thalassemia.

In 2011, FDA approved the iron chelator, deferiprone (Ferriprox®), for treatment of patients with transfusional overload due to thalassemia syndromes when other chelation therapy is inadequate. Deferiprone is available in tablet form for oral use.

In a June 2014 warning to consumers, FDA advised that FDA-approved chelating agents are available by prescription only. There are no FDA-approved over-the-counter chelation products.

Rationale
Chelation therapy is an established treatment for metal toxicity and transfusional hemosiderosis. These uses are not covered in this evidence review. Literature searches have focused on the use of chelation therapy for off-label conditions including, but not limited to, Alzheimer disease, atherosclerosis, autism, diabetes, and other conditions (eg, multiple sclerosis, arthritis).

Alzheimer Disease
A 2008 Cochrane review evaluated metal protein attenuating compounds (MPACs) for treating Alzheimer disease.4 The review identified 1 placebo-controlled randomized trial. This study, by Richie et al, was published in 2003. Patients were treated with PBT1, an MPAC also known as clioquinol, which is an antifungal medication that crosses the blood-brain barrier.5 The Food and Drug Administration withdrew clioquinol for oral use in 1970 because of its association with subacute myelo-optic neuropathy. Richie administered oral clioquinol to 16 Alzheimer disease patients in doses increasing to 375 mg twice daily and compared this group with 16 matched controls who received placebo. At 36 weeks, there was no statistically significant between-group difference in cognition measured by the Alzheimer Disease Assessment Scale–Cognitive (ADAS-Cog). One patient in the treatment group developed impairments in visual acuity and color vision during weeks 31 to 36 of treatment with clioquinol 375 mg twice daily. Her symptoms resolved on treatment cessation. A 2012 update of this review included trials through December 2011.6 Only the Lannfelt et al trial, discussed next, was identified.

Further studies of PBT1 have been abandoned in favor of a successor compound, PBT2. Lannfelt et al (2008) completed a double-blind, placebo-controlled randomized trial of 78 Alzheimer disease patients who were treated for 12 weeks with PBT2 50 mg (n=20), PBT2 250 mg (n=29), or placebo (n=29).7 There was no statistically significant difference in ADAS-Cog or Mini-Mental Status Examination scores among groups in this short-term study. The most common adverse event was headache. Two serious adverse events (urosepsis, transient ischemic event) were reported in the placebo arm.

Ongoing investigations in chelation therapy for the treatment of Alzheimer disease and other neurodegenerative diseases include linking a carbohydrate moiety to drug molecules to enhance drug delivery across the blood-brain barrier; this strategy may solve the potential problem of premature and indiscriminate metal binding. In addition, multifunction drugs that not only bind metal but also have significant antioxidant capacity are in development.8

Section Summary: Alzheimer Disease
There is insufficient evidence on the safety and efficacy of chelation therapy for treating patients with Alzheimer disease. The few published randomized controlled trials (RCTs) did not find that the treatment was superior to placebo for improving health outcomes.

Cardiovascular Disease
Atherosclerosis
In 2002, Villarruz et al published a Cochrane review that evaluated ethylenediaminetetraacetic acid (EDTA) chelation therapy for treating patients with atherosclerotic cardiovascular disease.9 Five placebocontrolled randomized trials were identified, none of which reported mortality, nonfatal events, or cerebrovascular events. Four (n=250 patients) of the 5 studies found no significant benefit of EDTA
chelation therapy on reported outcomes, including direct or indirect measurement of disease severity and subjective measures of improvement. The fifth study (n=10 patients) was stopped early due to benefit, but relevant outcome data were unavailable. The Cochrane reviewers concluded that evidence was insufficient to draw conclusions about the efficacy of chelation therapy for treating atherosclerosis; additional RCTs that report health outcomes including mortality and cerebrovascular events were needed.

Among published RCTs, Knudtson et al (2002) randomized 84 patients with coronary artery disease and a positive treadmill test to receive EDTA chelation therapy or placebo. Treatment was administered for 3 hours twice weekly for 15 weeks and then monthly for 3 months. Outcome measures included change in time to ischemia, functional reserve for exercise, and quality of life. There was no significant difference between the 2 groups. Another double-blind, placebo-controlled randomized trial of EDTA chelation showed no difference between groups in short- or long-term improvement in vasomotor response. Two small RCTs from the 1990s also reported no benefit of chelation therapy as a treatment for peripheral arterial disease.

Section Summary: Atherosclerosis
Several RCTs of chelation therapy for treating atherosclerosis generally have reported intermediate outcomes and have not found EDTA chelation therapy to be more effective than placebo. Additional RCTs that report health outcomes are needed to establish treatment efficacy.

Myocardial Infarction
In 2013, Lamas et al published results of the multicenter, 2 factorial, randomized, double-blind Trial to Assess Chelation Therapy (TACT). TACT included 1708 patients, ages 50 years or older, who had a history of myocardial infarction (MI) at least 6 weeks before enrollment and a serum creatinine level of 2.0 mg/dL or less. Patients were randomized to receive 40 intravenous infusions of disodium EDTA (n=839) or placebo (n=869). Patients also received oral high-dose vitamin plus mineral therapy or placebo. The first 30 infusions were given weekly, and the remaining 10 infusions were given 2 to 8 weeks apart. Primary end point was a composite outcome that included death from any cause, reinfarction, stroke, coronary revascularization, or hospitalization for angina at 5 years. The threshold for statistical significance was adjusted for multiple interim analyses to a p value of 0.036. A total of 361 (43%) patients in the chelation group and 464 (57%) patients in the placebo group discontinued treatment, withdrew consent, or were lost to follow-up. Kaplan-Meier 5-year estimates for the primary end point were 33% (95% confidence interval [CI], 29% to 37%) in the chelation group and 39% (95% CI, 35% to 42%) in the control group, a statistically significant difference (log-rank test, p=0.035). The most common individual clinical end point was coronary revascularization, which occurred in 130 (16%) of 839 patients in the chelation group and 157 (18%) of 869 patients in the control group (p=0.08). The next most frequent end point was death, which occurred in 87 (10%) patients in the chelation group and 93 (11%) patients in the placebo group (p=0.64). No individual component of the primary outcome differed statistically between groups; however, the study was not powered to detect differences in individual components. Four severe adverse events definitely or possibly related to study therapy occurred, 2 each in the treatment and control groups, including 1 death in each group. Quality-of-life outcomes (reported in 2014) did not differ between groups at 2-year follow-up.

Another 2014 follow-up publication reported results of the 4 treatment groups in the 2 factorial design (double-active group [disodium EDTA infusions with oral high-dose vitamins; n=421 patients], active infusions with placebo vitamins [n=418 patients], placebo infusions with active vitamins [n=432 patients], double placebo [n=437 patients]). The proportion of patients who discontinued treatment, withdrew consent, or were lost to follow-up per treatment group was not reported. Five-year Kaplan-Meier estimates for the primary composite end point were 32%, 34%, 37%, and 40%, respectively. The reduction in primary end point by double-active treatment compared with double placebo was statistically significant (hazard ratio [HR], 0.74; 95% CI, 0.57 to 0.95). In 633 patients with diabetes (36% of each treatment group), the primary end point reduction in the double-active group compared with the double placebo group was more pronounced (HR=0.49; 95% CI, 0.33 to 0.75).
The study is limited by the high number of withdrawals, with differential withdrawals between groups. The primary end point included components of varying clinical significance, and the largest difference between groups was for revascularization events. The primary end point barely met the significance threshold; if more patients had remained in the study and experienced events, results could have differed. Moreover, as noted in an editorial accompanying the original (2013) publication, 60% of patients were enrolled at centers described as complementary and alternative medicine sites, and this may have resulted in a population that was not generalizable to that seen in general clinical care. Editorialists commenting on the subsequent (2014) publication suggested that further research is warranted to replicate the findings.

This substudy has the same limitations as the parent study previously described, namely, high and differential withdrawal and heterogeneous composite end point. Additionally, because diabetes was not a stratification factor in TACT, results of this subgroup analysis are preliminary and require replication.

Section Summary: Myocardial Infarction
One RCT with limitations, including high dropout with differential dropout between groups, reported that cardiovascular events were reduced in patients treated with chelation therapy. This effect was greater among patients with diabetes mellitus. However, this trial was not of high quality and, therefore, results may be biased. More high-quality trials are needed to corroborate whether chelation therapy improves outcomes in patients with prior MI.

Section Summary: Autism
There is a lack of controlled studies on how chelation therapy effects health outcomes in patients with autism.

Diabetes
Cardiovascular Disease in Patients With Diabetes
A 2009 trial by Cooper et al in New Zealand evaluated the effect of copper chelation using oral trientine on left ventricular hypertrophy in 30 patients with type 2 diabetes. Twenty-one (70%) of 30 participants completed 12 months of follow-up. At 12 months, there was a significantly greater reduction in left ventricular mass indexed to body surface area in the active treatment group than in the placebo group (-10.6 g/m2 vs -0.1 g/m2, p=0.01). The study was limited by small sample size and high dropout rate.

Escolar et al (2014) published results of a prespecified subgroup analysis of diabetic patients in TACT. In TACT, there was a statistically significant interaction between treatment (EDTA or placebo) and presence of diabetes: Among 538 (31% of the trial sample) self-reported diabetic patients, those randomized to EDTA had a 39% reduced risk of the primary composite outcome compared with placebo (HR=0.61; 95% CI, 0.45 to 0.83; log rank test, p=0.02); among 1170 nondiabetic patients, risk of the primary outcome did not differ statistically between treatment groups (HR=0.96; 95% CI, 0.77 to 1.20; log rank test, p=0.73). The definition of diabetes mellitus was broadened to include self-reported diabetes, use of oral or insulin treatment for diabetes, or fasting blood glucose of 126 mg/dL or more at trial entry. Of 1708 patients in TACT, 633 (37%) had diabetes.
mellitus by this definition: 322 were randomized to EDTA and 311 to placebo. Compared with all other trial participants, this subgroup of diabetic patients had higher body mass index, fasting blood glucose, and prevalence of heart failure, stroke, hypertension, peripheral artery disease, and hypercholesterolemia. Within this subgroup, baseline characteristics were similar between treatment groups. With approximately 5 years of follow-up, the primary composite end point occurred in 25% of the EDTA group and 38% of the placebo group (HR=0.59; 99.4% CI, 0.39 to 0.88 [adjusted for multiple subgroups]: log-rank test, p=0.002). In adjusted analysis of the individual components of the primary end point, there were no statistically significant differences between treatment groups. Thirty-six adverse events attributable to study drug that led to trial withdrawal, 16 in the EDTA group and 20 in the placebo group.

Diabetic Nephropathy
Chen et al (2012) conducted a single-blind RCT of chelation therapy effects on the progression of diabetic nephropathy in Chinese patients with high-normal lead levels. Twenty-five patients with diabetes, high-normal body lead burden (80-6000 μg), and serum creatinine 3.8 mg/dL or lower were included. Baseline mean blood lead levels were 6.3 μg/dL in the treatment group and 7.1 μg/dL in the control group; baseline mean body lead burden was 151 g in the treatment group and 142 g in the control group. According to the U.S. Occupational and Health Safety Administration, maximum acceptable blood lead level in adults is 40 μg/dL. Patients were randomized to 3 months of calcium disodium EDTA or placebo. During 24 months of treatment follow-up, patients in the chelation group received additional chelation treatments as needed (ie, for serum creatinine level above pretreatment levels or body lead burden >60 μg), and patients in the placebo group continued to receive placebo medication. All patients completed the 27-month trial. The primary outcome was change in estimated glomerular filtration rate (eGFR). Mean (SD) yearly rate of decrease in eGFR was 5.6 (5.0) mL/min/173 m2 in the chelation group and 9.2 (3.6) mL/min/173 m2 in the control group, a statistically significant difference (p=0.04). Secondary end point was the number of patients in whom the baseline serum creatinine doubled or who required renal replacement therapy. Nine (36%) patients in the treatment group and 17 (68%) in the control group attained the secondary end point, a statistically significant difference (p=0.02). There were no reported adverse effects of chelation therapy during the 27-month trial period.

Section Summary: Diabetes
Two small RCTs with limitations represent insufficient evidence that chelation therapy is effective for treating cardiovascular disease in patients with diabetes. One small, single-blind RCT is insufficient evidence that chelation therapy is effective for treating diabetic nephropathy in patients with high-normal lead levels. Additional RCTs with larger numbers of patients that report health outcomes, such as cardiovascular events, end-stage renal disease, and mortality, are needed.

Other Potential Indications
No RCTs or other controlled trials that evaluated safety and efficacy of chelation therapy for other conditions, such as multiple sclerosis or arthritis, were identified. Iron chelation therapy is being investigated for Parkinson disease and endotoxemia.

REFERENCES:
18. Moron DJ, Hlatky MA. Trial to Assess Chelation Therapy (TACT) and equipoise: When evidence conflicts with beliefs. Am Heart J. Jul 2014;168(1):4-5. PMID 24952853


APPENDIX

Suggested toxic or normal levels of select heavy metals are listed in Appendix Table 1. Reference standards for bismuth, chromium, and manganese were not identified and are not included in the table.

**Appendix Table 1. Toxic or Normal Concentrations of Heavy Metals**

<table>
<thead>
<tr>
<th>Metal</th>
<th>Toxic Levels (Normal Levels Where Indicated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsenic</td>
<td>24-h urine: ≥50 μg/L urine or 100 μg/g creatinine</td>
</tr>
<tr>
<td>Cadmium</td>
<td>Proteinuria and/or ≥15 μg/g creatinine</td>
</tr>
<tr>
<td>Cobalt</td>
<td>Normative excretion: 0.1-1.2 μg/L (serum), 0.1-2.2 μg/L (urine)</td>
</tr>
<tr>
<td>Copper</td>
<td>Normative excretion: 25 μg/24 h (urine)</td>
</tr>
<tr>
<td>Iron</td>
<td>Nontoxic: &lt;300 μg/dL, Severe: &gt;500 μg/dL</td>
</tr>
<tr>
<td><strong>Lead</strong></td>
<td><strong>Pediatric</strong> Symptoms or blood lead level ≥45 μg/dL (blood)</td>
</tr>
<tr>
<td></td>
<td>CDC level of concern: 5 μg/dL</td>
</tr>
<tr>
<td></td>
<td><strong>Adult</strong> Symptoms or blood lead level ≥40 μg/dL</td>
</tr>
<tr>
<td></td>
<td>CDC level of concern: 10 μg/dL</td>
</tr>
<tr>
<td>Mercury</td>
<td>Background exposure normative limits: 1-8 μg/L (whole blood); 4-5 μg/L (urine), a</td>
</tr>
</tbody>
</table>
Nickel  
Excessive exposure: ≥8 μg/L (blood)
Severe poisoning: ≥500 μg/L (8-h urine)

Selenium  
Mild toxicity: >1 mg/L (serum)
Serious toxicity: >2 mg/L (spot urine)

Silver  
Asymptomatic workers have mean levels of 11 μg/L (serum) and 2.6 μg/L (spot urine)

Thallium  
24-hour urine thallium >5 g/L

Zinc  
Normative range: 0.6-1.1 mg/L (plasma), 10-14 mg/L (red cells)

CDC: Centers for Disease Control and Prevention.

* Hair analysis is useful to assess mercury exposure in epidemiologic studies. However, hair analysis in individual patients must be interpreted with consideration of the patient's history, signs, and symptoms, and possible alternative explanations. Measurement of blood and urine mercury levels can exclude exogenous contamination; therefore, blood or urine mercury levels may be more robust measures of exposure in individual patients.45

**Billing Coding/Physician Documentation Information**

<table>
<thead>
<tr>
<th>CPT</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>96365</td>
<td>Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour</td>
</tr>
<tr>
<td>96366</td>
<td>each additional hour (list separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>96374</td>
<td>Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); intravenous push, single or initial substance/drug</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HCPCS</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0300</td>
<td>IV chelation therapy (chemical endarterectomy)</td>
</tr>
<tr>
<td>J0470</td>
<td>Injection, dimercaprol, per 100 mg</td>
</tr>
<tr>
<td>J0600</td>
<td>Injection, edetate calcium disodium, up to 1000 mg</td>
</tr>
<tr>
<td>J0895</td>
<td>Injection, deferoxamine mesylate, 500 mg</td>
</tr>
<tr>
<td>J3520</td>
<td>Edetate disodium, per 150 mg</td>
</tr>
<tr>
<td>S9355</td>
<td>Home infusion therapy, chelation therapy; administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10-CM</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>E08.00-E13.9</td>
<td>Diabetes mellitus code range</td>
</tr>
<tr>
<td>F84.0</td>
<td>Autism disorder</td>
</tr>
<tr>
<td>G30.0-G30.9</td>
<td>Alzheimer's disease code range</td>
</tr>
<tr>
<td>G35</td>
<td>Multiple sclerosis</td>
</tr>
<tr>
<td>I25.10-I25.9</td>
<td>Atherosclerosis code range</td>
</tr>
<tr>
<td>M05.00-M06.09</td>
<td>Rheumatoid arthritis code range</td>
</tr>
<tr>
<td>M15.0-M19.93</td>
<td>Osteoarthritis code range</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10-PCS</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>3E030GC, 3E033GC</td>
<td>Introduction, therapeutic substance, peripheral vein, code by approach (open or percutaneous)</td>
</tr>
<tr>
<td>3E040GC, 3E043GC</td>
<td>Introduction, therapeutic substance, central vein, code by approach (open or percutaneous)</td>
</tr>
<tr>
<td>3E050GC, 3E053GC</td>
<td>Introduction, therapeutic substance, peripheral artery, code by approach (open or percutaneous)</td>
</tr>
<tr>
<td>3E060GC, 3E063GC</td>
<td>Introduction, therapeutic substance, central artery, code by approach (open or percutaneous)</td>
</tr>
</tbody>
</table>

**Additional Policy Key Words**

8.01.02
State and Federal mandates and health plan contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The medical policies contained herein are for informational purposes. The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents Blue KC and are solely responsible for diagnosis, treatment and medical advice. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, photocopying, or otherwise, without permission from Blue KC.