

Corporate Medical Policy

Vesicoureteral Reflux, Treatment with Periureteral Bulking Agents

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Description of Procedure or Service

Vesicoureteral reflux (VUR) is the retrograde flow of urine from the bladder upward toward the kidney, most commonly seen in children. Severe reflux may damage the kidney through mechanical or immunological mechanisms. VUR also predisposes an individual to renal infection (pyelonephritis) by facilitating the transport of bacteria from the bladder to the upper urinary tract. Pyelonephritis causes renal scarring in as many as 40% of children, and extensive scarring may lead to renal insufficiency and hypertension. The central management strategy of children with VUR has been the reduction of reflux and prevention of renal damage induced by urinary tract infection (UTI).

In most cases, VUR is diagnosed during evaluation of UTI. About one third of children with UTIs are found to have VUR. The average age for the onset of UTI is 2 to 3 years, corresponding to the age when toilet training occurs. There also appears to be a genetic predisposition to VUR, and siblings may also be examined. The gold standard for diagnosis is voiding cystourethrography, a procedure which involves catheterization of the bladder. The severity of reflux is described by a grade, typically with the International Reflux Study Group grading system, which grades severity from I (reflux partway up the ureter) to V (massive reflux of urine up the ureter with marked tortuosity and dilation of the ureter and calyces). Determination of VUR grade is not exact, however, due to factors such as bladder pressure, which may vary at the time of measurement. In general, more severe reflux is associated with higher rates of renal injury. Spontaneous resolution and treatment success also varies with reflux grade.

Treatment strategies include bladder training, antibiotic prophylaxis, and surgical modification of the ureters to correct the underlying reflux. VUR is likely to resolve spontaneously over a period of 1 to 5 years; lower grades of reflux (i.e., grades I and II) are associated with a higher probability of spontaneous resolution. The decision to administer prophylactic antibiotic treatment depends both on the probability of spontaneous resolution and the level of parental concern for potential adverse effects of long-term antibiotic treatment, which can include allergic reactions and development of treatment-resistant bacteria resulting in breakthrough UTIs.

Open surgical treatment is typically reserved for patients with high-grade reflux (grades III and IV) or as salvage therapy for those who are noncompliant with antibiotic therapy or have breakthrough UTIs while receiving prophylactic therapy. Surgical management involves lengthening the intramural ureter by modification of the ureterovesical attachment with surgical transplantation of the ureters to a different site in the bladder. Success rates for open surgery are reported to be above 98% for reflux Grades I–V. In addition to surgery-associated morbidity, obstruction and reoperation rates have been reported to be as high as 9%.

The use of bulking agents in the treatment of VUR has been reported for over 20 years and has been suggested as an alternative to either antibiotic or surgical therapy. Bulking agents can be injected

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into tissue around the ureteral orifices to minimize reflux. The STING procedure (subureteral trans-urethral injection) involves the endoscopic injection of a bulking agent into the submucosal bladder wall just below the ureteral opening. In the more recently used modified STING procedure, the needle is placed in the ureteral tunnel and the bulking agent is injected into the submucosal intraureteral space. When successfully injected the compound tracks along the length of the detrusor tunnel and establishes a coapted ureteral tunnel. This endoscopic procedure can be performed in an outpatient setting.

A variety of bulking agents have been tested for biocompatibility and absence of migration. Some of the compounds used in clinical studies are collagen (Contigen, Zyderm, Zyplast), polytetrafluoroethylene paste (Teflon), polydimethylsiloxane (Macroplastique®), calcium hydroxyapatite (Coaptite®), and dextranomer/hyaluronic acid copolymer (Deflux® or Dx/HA). In 2001, Deflux® received pre-market approval from the U.S. Food and Drug Administration (FDA) for the “treatment of children with vesicoureteral reflux (VUR) grades II-IV.” Contraindications include patients with non-functioning kidney(s), duplicated ureters, active voiding dysfunction, and ongoing urinary tract infection.

*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Policy

BCBSNC will provide coverage for periureteral bulking agents as a treatment of vesicoureteral reflux when it is determined to be medically necessary and when medical criteria and guidelines shown below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Treatment of Vesicoureteral Reflux with Periureteral Bulking Agents is covered

Periureteral bulking agents may be considered medically necessary as a treatment of vesicoureteral reflux grades II–IV when open surgical intervention is otherwise indicated.

When Treatment of Vesicoureteral Reflux with Periureteral Bulking Agents is not covered

The use of bulking agents as a treatment of vesicoureteral reflux in clinical situations other than listed above is considered investigational.

The use of bulking agents is contraindicated in patients with non-functioning kidney(s), hutch diverticuli, duplicated ureters, active voiding dysfunction, and ongoing urinary tract infection.

Policy Guidelines

The International Reflux Grading system classifies VUR into 5 grades, depending on the degree of

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retrograde filling and dilation of the renal collecting system. This system is based on the radiographic appearance of the renal pelvis and calyces on a voiding cystogram, as follows:

- Grade I: Urine backs up into the ureter only, and the renal pelvis appears healthy, with sharp calyces.
- Grade II: Urine backs up into the ureter, renal pelvis, and calyces. The renal pelvis appears healthy and has sharp calyces.
- Grade III: Urine backs up into the ureter and collecting system. The ureter and pelvis appear mildly dilated, and the calyces are mildly blunted.
- Grade IV: Urine backs up into the ureter and collecting system. The ureter and pelvis appear moderately dilated, and the calyces are moderately blunted.
- Grade V: Urine backs up into the ureter and collecting system. The pelvis severely dilates, the ureter appears tortuous, and the calyces are severely blunted.

Overall, the literature indicates that one or more periureteral injections of Deflux® can effectively resolve reflux in as many as 90%–96% of cases, depending on technical experience and patient selection. These resolution rates approach those of open surgical intervention. Procedural morbidity is lower with the endoscopic procedure compared with open surgical intervention. Injection of a bulking agent is less invasive than open surgical techniques and can be performed as an outpatient procedure with use of general anesthesia. Temporary postoperative ureteral obstruction may occur in less than 0.7% of patients following injection of bulking agents; this can be treated with ureteral stenting until the problem resolves. In comparison, an average 2% (range of 0% to 9%) ureteral obstruction and reoperation rate has been reported following ureteral reimplantation. Because of the differing benefits and risks of treatment with bulking agents in comparison with surgical reimplantation of the ureters, parents should make an informed choice between the procedures.

In 2010, the American Urological Association (AUA) published an updated guideline on management of primary VUR in children. They recommend that patients older than one year who have a febrile breakthrough UTI while receiving continuous antibiotic prophylaxis be considered for either open surgery or endoscopic injection of bulking agents. Specific bulking agents mentioned were Deflux and Macroplastique. The guideline was based on a review of the evidence, but the authors acknowledged the lack of robust randomized controlled trials.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 52327, L8603, L8604, L8606

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.102, 2/15/07.

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Specialty Matched Consultant Advisory Panel - 5/8/2007

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.102, 4/17/07.

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.102, 4/9/08.

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.102, 12/11/08.

Specialty Matched Consultant Advisory Panel - 9/2009

Routh JC, Inman BA, Reinberg Y. Dextranomer/hyaluronic acid for pediatric vesicoureteral reflux: Systematic review. *Pediatrics* 2010; 125(5):1010-9.

Peters CA, Skoog SJ, Arant BS et al. Summary of the AUA guidelines on the management of primary vesicoureteral reflux in children. Retrieved on November 18, 2010 from <http://www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines/main-reports/vur2010/AuthorsAndSummaryReport.pdf>

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.102, 10/8/10.

Specialty Matched Consultant Advisory Panel review 12/2010

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.102, 10/4/11

Specialty Matched Consultant Advisory Panel review 11/2011

Policy Implementation/Update Information

- 6/4/07 Notification of new policy. Periureteral bulking agents may be considered medically necessary as a treatment of vesicoureteral reflux grades II–IV when open surgical intervention is otherwise indicated. The use of bulking agents as a treatment of vesicoureteral reflux in clinical situations other than those listed is considered investigational. The use of bulking agents is contraindicated in patients with non-functioning kidney(s), hutch diverticuli, duplicated ureters, active voiding dysfunction, and ongoing urinary tract infection. Notification given 6/4/07. Effective date 8/13/07. (pmo)
- 01/05/09 HCPCS code L8604 effective January 1, 2009 added to Billing/Coding section. (pmo)
- 9/28/09 Reference sources added. (pmo)
- 6/22/10 Policy Number(s) removed (amw)
- 1/18/11 Specialty Matched Consultant Advisory Panel review 12/2010. References updated. Policy Guidelines updated. (mco)
- 12/20/11 Specialty Matched Consultant Advisory Panel review 11/2011. References updated. No changes to Policy Statements. (mco)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its

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medical policies periodically.