Prior Authorization Review
Panel MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review. Policies submitted without this form will not be considered for review.

Plan: Aetna Better Health

<table>
<thead>
<tr>
<th>Policy Number: 0395</th>
<th>Submission Date: 09/04/2018</th>
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</thead>
<tbody>
<tr>
<td>Policy Name: Ethanol Injection for Thyroid Lesions</td>
<td></td>
</tr>
</tbody>
</table>

Type of Submission – Check all that apply:
- [ ] New Policy
- [x] Revised Policy*
- [ ] Annual Review – No Revisions

*All revisions to the policy must be highlighted using track changes throughout the document. Please provide any clarifying information for the policy below:

CPB 395 Ethanol Injection for Thyroid Lesions

Clinical content was last revised on 07/20/2007. Additional non-clinical updates were made by Corporate since the last PARP submission, as documented below.

Revision and Update History since last PARP submission:
08/03/2018 - This CPB has been updated with additional references.
04/11/2019 – Tentative next scheduled review date by Corporate

Name of Authorized Individual (Please type or print):
Dr. Bernard Lewin, M.D.

Signature of Authorized Individual: [Signature]

www.aetnabetterhealth.com/pennsylvania
Updated 08/03/2018
Ethanol Injection for Thyroid Lesions

Policy

I. Aetna considers ethanol injection sclerotherapy medically necessary for the treatment of thyroglossal duct cysts when all of the following selection criteria are met:

   A. A monocystic lesion is present; and
   B. Cystographic studies indicate that there is no extravasation; and
   C. Cytologic studies show that the lesion is benign.

   Note: It may be medically necessary to repeat injections after 1 month in cases of recurrence of cyst.

II. Aetna considers ethanol injection sclerotherapy of thyroglossal duct cysts experimental and investigational when these criteria are not met.

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.
III. Aetna considers percutaneous ethanol injection experimental and investigational for the treatment of thyroid cancer because its effectiveness for this indication has not been established.

Background

The thyroglossal duct cyst (TGDC) is the commonest congenital neck mass and the second commonest of all childhood cervical masses. An anterior midline neck mass presenting before the age of 20 and displaying vertical movement with tongue protrusion and swallowing is the hallmark of this lesion. For recurrent or persistently infected TGDC, the traditional treatment is a Sistrunk operation -- excision of the cyst, the tract connecting it to the foramen cecum, and the central portion of the hyoid bone.

Another approach in treating TGDC is ethanol injection sclerotherapy. Injection is performed under sonographic guidance. Studies have shown that ethanol sclerotherapy is safe and effective in treating benign, monocystic TGDC.

Guidelines on thyroid nodules from the American Association of Clinical Endocrinologists and the Associazione Medici Endocrinologi (2006) stated that percutaneous ethanol injection is useful in the treatment of benign cystic thyroid lesions.

Surgery is the gold standard for the treatment of patients with recurrent well-differentiated thyroid cancer (WTC). Percutaneous ethanol injection is a new minimally invasive surgical option for the treatment of this disease. Monchik and colleagues (2006) evaluated the long-term effectiveness of radiofrequency ablation (RFA) and percutaneous ethanol injection in the treatment of patients with local recurrence or focal distant metastases of WTC. A total of 20 patients
Ethanol Injection for Thyroid Lesions

underwent treatment of biopsy-proven recurrent WTC in the neck: 16 of these patients had lesions treated by ultrasound (US)-guided RFA (mean size, 17.0 mm; range of 8 to 40 mm), while 6 had US-guided ethanol injection treatment (mean size, 11.4 mm; range of 6 to 15 mm). A total of 4 patients underwent RFA treatment of focal distant metastases from WTC: 3 of these patients had CT-guided RFA of bone metastases (mean size, 40.0 mm; range of 30 to 60 mm), and 1 patient underwent RFA for a solitary lung metastasis (size, 27 mm). Patients were then followed with routine US, whole body scan, and/or serum thyroglobulin levels for recurrence at the treatment site. No recurrent disease was detected at the treatment site in 14 of the 16 patients treated with RFA and in all 6 patients treated with ethanol injection at a mean follow-up of 40.7 and 18.7 months, respectively. Two of the 3 patients treated for bone metastases are free of disease at the treatment site at 44 and 53 months of follow-up, respectively. The patient who underwent RFA for a solitary lung metastasis is free of disease at the treatment site at 10 months of follow-up. No complications were experienced in the group treated by ethanol injection, while 1 minor skin burn and 1 permanent vocal cord paralysis occurred in the RFA treatment group. The authors concluded that RFA and ethanol ablation show promise as alternatives to surgical treatment of recurrent WTC in patients with difficult re-operations. They stated that further long-term follow-up studies are needed to ascertain the precise role these therapies should play in the treatment of recurrent WTC and if certain more invasive surgical procedures can be replaced.

Lim et al (2007) evaluated the local therapeutic effect of percutaneous ethanol injection therapy (PEIT) in recurrent thyroid cancers. These researchers performed ultrasound-guided PEIT on 24 recurrent lesions (8 in thyroid beds and 16 in neck nodes) of 16 papillary thyroid carcinoma patients. Ethanol was injected at 3-month intervals under sonographic guidance. All patients tolerated PEIT well with only mild local pain, although 1 patient complained of transient hoarseness.
after the procedure. The median diameter of lesions was significantly reduced, from 9.9 mm (range of 5.5 to 25.0 mm) to 5.3 mm (range of 0.0 to 17.0 mm) by PEIT. Four recurrent lesions disappeared sonographically. The authors concluded that PEIT may be an alternative treatment option for locally recurrent thyroid carcinomas in properly selected patients. However, a prospective, long-term follow-up study is needed to determine the effect of PEIT on patient survival and tumor recurrence.

Verges et al (2011) described a new procedure of ethanol sclerotherapy without US guidance for the treatment of pure thyroid cysts. A total of 9 patients with recurrent large thyroid cysts following aspiration, and showing symptoms of compression and/or cosmetic complaints were treated by ethanol injection without US guidance and followed for up to 11 years. After ethanol injection, mean cyst volume was significantly reduced (9.9 +/- 13.6 versus 31.3 +/- 34.1 ml, p = 0.007) and the mean percentage volume reduction was 72.7%. A size reduction of the thyroid lesion more than 50 % was achieved in 8 of the 9 patients (89 %). Compressive symptoms and cosmetic complaints totally disappeared after sclerotherapy in all patients. During a mean follow-up of 48 months (ranging from 12 to 135 months), no recurrences were observed. The treatment was well-tolerated with no major side effects. The authors concluded that non-US-guided ethanol sclerotherapy is a safe and "easy-to-use" procedure to treat benign thyroid cysts effectively.

Guenette et al (2013) evaluated the clinical outcomes of US-guided percutaneous RF ablation and PEI as salvage therapy for loco-regional recurrence after resection of well-differentiated thyroid carcinoma. There were 42 loco-regional, biopsy-proven, papillary and follicular thyroid carcinoma lesions (0.5 to 3.7 cm) treated, 21 with RF ablation and 21 with PEI. Of treated lesions, 35 were located in the lateral compartments, and 7 were located in the central compartment. Data points in the retrospective analysis,
determined beforehand by the investigators, were progression at the ablation site, serum thyroglobulin levels before and after the procedure, and procedural complications. Average follow-up after RF ablation was 61.3 months and after PEI was 38.5 months. No progression was detected in the region of ablation for any of the lesions treated with RF ablation. Local progression was detected 4 to 11 months after ablation in 5 of the 21 lesions treated with PEI, 3 in the lateral compartment and 2 in the central compartment; all of the lesions were successfully re-treated with repeat PEI, RF ablation, or surgery. Permanent vocal cord paralysis occurred after 1 RF ablation procedure of a lateral compartment supraclavicular node. There were no complications after PEI. The authors concluded that this case series provided long-term follow-up evidence of the safety and effectiveness of US-guided RF ablation and PEI for control of loco-regional recurrence of well-differentiated thyroid carcinoma after surgery. The findings of this case-series study need to be validated by well-designed studies.

Papillary Thyroid Cancer:

Fontenot et al (2015) stated that re-operation for recurrent papillary thyroid cancer (PTC) can be associated with a high rate of complications and failure to provide lasting remission. Percutaneous ethanol injection may be an effective non-surgical management option for locally recurrent PTC. In a systematic analysis of the current literature, these investigators compared the effectiveness and complications related to PEI versus re-operative surgical intervention for treatment of locally recurrent PTC. Original studies were identified using the keywords "thyroid/ethanol" and "recurrent thyroid cancer/repeat surgery". Studies evaluating re-operation or PEI for lymph node metastases in patients with primary surgery of total thyroidectomy with appropriate lymph node dissection where indicated were included in the analysis for both re-operation and PEI. Animal studies, single-case reports, and studies with fewer than 10 lesions were excluded. Outcomes
included interval to detection of recurrence, success and failure rates, recurrence rates, complication rates, and follow-up duration. Between-group outcome differences were calculated using random-effects models, and pooled data cross-tabulation and logistic regression analysis were used. In all, 945 publications were identified, and 27 studies met the inclusion criteria. There were no studies that directly compared the 2 treatment techniques. A total of 1,617 patients were included in this analysis; 168 (11.4 %) were treated with PEI, and 1,449 (88.6 %) were treated with re-operation. Re-operation was successful in 94.8 % of cases compared with an 87.5 % success rate for PEI (odds ratio [OR], 2.58; 95 % confidence interval [CI]: 1.55 to 4.31; p < 0.001). The recurrence rates for PEI and re-operation at the site of the treated lesion or elsewhere in the neck were also similar (OR, 1.07; 95 % CI: 0.65 to 1.77; p = 0.78). Re-operation was associated with a 3.5 % pooled risk of complications, while PEI incurred a pooled risk of 1.2 % (OR, 2.9; 95 % CI: 0.72 to 12.3; p = 0.08). However, most studies did not report routine pre-operative and post-operative laryngoscopies, an evaluation needed for accurate neural complication analysis associated with each procedure. The authors concluded that high-quality, well-designed studies are needed to evaluate the feasibility of incorporating PEI into the treatment protocol of PTC. They noted that although presently inferior to re-operation, PEI has the potential to be a widely accepted and effective non-surgical treatment option for limited recurrent PTC in poor surgical candidates or patients seeking to avoid multiple re-operations.

Ultrasound-Guided Percutaneous Ethanol Injection for the Treatment of Thyroid Nodules:

Felicio and colleagues (2016) noted that US-guided PEI has been proposed for treatment of benign thyroid nodules (TNs). However, there is no consensus for the optimal amount of ethanol injection, number of applications, and time to re-evaluation in order to achieve maximum volume reduction with
minimum adverse effects (AEs). These investigators analyzed the effectiveness of an US-guided PEI protocol to treat solid and mixed TNs based on a new target outcome. They performed a prospective study evaluating the results of PEI in 52 patients with benign solid and mixed TNs. The ethanol dose was fixed in 30% of the nodular volume per session. Patients returned 1 month after each session for US re-evaluation. Therapeutic success was defined as volume reduction of at least 30% associated with disappearance of clinical symptoms and a complete esthetic satisfaction reported by the patient. These researchers performed a mean of 2.8 ± 1.9 PEI sessions, with an average total volume of ethanol injected of 9.1 ± 10.3 ml, and a follow-up time of 10.0 ± 8.7 months. There was a reduction of at least 50% of the initial nodular volume in 33 patients (63.5%). In 11 patients (21.2%), the reduction did not reach 50% (mean reduction of 31 ± 11%), but 6 of them reported esthetically satisfactory results and treatment was stopped. The therapeutic success rate considering the patients with esthetic improvement was 75%. There were no severe complications. The authors concluded that their protocol was safe and effective in treating solid and mixed benign TNs.

An UpToDate review on “Diagnostic approach to and treatment of thyroid nodules” (Ross, 2017) states that “Ablation techniques -- Benign, autonomous, and cystic thyroid nodules can be treated by ultrasound-guided injection of ethanol or sclerosing agents and by ultrasound-directed physical energy. These approaches have not gained widespread acceptance in the United States because of potential complications, including occasional reports of prolonged pain after the procedure”.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by “+”: 
<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
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<tbody>
<tr>
<td></td>
<td>Ethanol injection sclerotherapy for thyroglossal duct cyst:</td>
</tr>
<tr>
<td></td>
<td>No specific code</td>
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<tr>
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<td>CPT codes covered if selection criteria are met:</td>
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<tr>
<td>49185</td>
<td>Sclerotherapy of a fluid collection (eg, lymphocele, cyst, or seroma), percutaneous, including contrast injection(s), sclerosant injection(s), diagnostic study, imaging guidance (eg, ultrasound, fluoroscopy) and radiological supervision and interpretation when performed</td>
</tr>
<tr>
<td></td>
<td>Other CPT codes related to the CPB:</td>
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<tr>
<td>60300</td>
<td>Aspiration and/or injection, thyroid cyst</td>
</tr>
<tr>
<td>76942</td>
<td>Ultrasonic guidance for needle placement (e.g., biopsy, aspiration, injection, localization device), imaging supervision and interpretation</td>
</tr>
<tr>
<td>77012</td>
<td>Computed tomography guidance for needle placement (e.g., biopsy, aspiration, injection, localization device), radiological supervision and interpretation</td>
</tr>
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<td>ICD-10 codes covered if selection criteria are met:</td>
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<tr>
<td>Q89.2</td>
<td>Congenital malformations of other endocrine glands [thyroglossal duct cyst]</td>
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<tr>
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<td>ICD-10 codes not covered for indications listed in the CPB:</td>
</tr>
<tr>
<td>C73</td>
<td>Malignant neoplasm of thyroid gland</td>
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</tbody>
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The above policy is based on the following references:


quality of life of percutaneous ethanol injection as first-line treatment in symptomatic thyroid cysts. BMC Endocr Disord. 2015;15:73.


Amendment to
Aetna Clinical Policy Bulletin Number:
0395 Ethanol Injection for Thyroid Lesions

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania Updated 08/03/2018