Aetna considers a Food and Drug Administration-approved metal-on-metal, metal-on-plastic, ceramic-on-plastic, or ceramic-on-ceramic total hip arthroplasty (THA) prosthesis medically necessary for adult members when the following criteria are met:

I. Member has advanced joint disease demonstrated by:

A. Pain and functional disability that interferes with activities of daily living (ADLs) from injury due to osteoarthritis, rheumatoid arthritis, avascular necrosis, or post-traumatic arthritis of the hip joint; and

B. Limited range of motion (ROM), antalgic gait, and pain in hip joint with passive ROM on physical examination; and

C. Radiographic evidence of severe osteoarthritis (as evidence by 2 or more of the following: subchondral cysts, subchondral sclerosis, periarticular osteophytes, joint subluxation, bone on bone articulation or joint space narrowing) of hip joint, or avascular necrosis (osteonecrosis) with stage III collapse of the femoral head, or rheumatoid arthritis (joint space narrowing); and

D. History of of unsuccessful conservative therapy (non-surgical medical management) that is clearly addressed in
A. the medical record (see Note). If conservative therapy is not appropriate, the medical record must clearly document why such approach is not reasonable; or

II. Fracture of the femoral neck by imaging with pain interfering with ADLs; or

III. Malunion of acetabular, femoral head or proximal femur fracture with pain interfering with ADLs; or

IV. Nonunion by imaging or failure of previous hip fracture surgery with pain interfering with ADLs; or

V. Malignancy of the joint involving the bones or soft tissues of the pelvis or proximal femur by imaging.

Note: Members with osteoarthritis, traumatic arthritis, rheumatoid arthritis, or avascular necrosis should have at least 12 weeks of non-surgical treatment documented in the medical record (at least 24 weeks for persons with a relative contraindication* -- see below), including all of the following, unless contraindicated:

A. Anti-inflammatory medications or analgesics; and
B. Flexibility and muscle strengthening exercises, and
C. Activity modification; and
D. Supervised physical therapy (ADLs diminished despite completing a plan of care); and
E. Assistive device use (required for persons with relative contraindications* to joint replacement, optional for others); and
F. Therapeutic injections into the hip (required for persons with relative contraindications* to joint replacement, optional for others).

* Relative contraindications to joint replacement include the following: morbid obesity (BMI greater than 40), age less than 50 years. Persons with relative contraindications should exhaust all non-surgical treatment options.

VI. Total joint replacement is considered not medically necessary in persons with any of the following absolute contraindications:
A. Active infection of the joint or active systemic bacteremia that has not been totally eradicated; or
B. Active skin infection (exception recurrent cutaneous staph infections) or open wound within the planned surgical site of the hip; or
C. Allergy to components of the implant (e.g., cobalt, chromium or alumina); or
D. Paraplegia or quadriplegia; or
E. Permanent or irreversible muscle weakness in the absence of pain that prevents ambulation; or
F. Rapidly progressive neurological disease except in the clinical situation of a concomitant displaced femoral neck fracture; or
G. Skeletal immaturity.

VII. For persons with significant conditions or co-morbidities, the risk/benefit of THA should be appropriately addressed in the medical record.

VIII. Aetna considers THA experimental and investigational for all other indications because of insufficient evidence of effectiveness.

Aetna considers a revision or replacement of a THA or hip resurfacing arthroplasty medically necessary for the following indications when accompanied by pain and functional disability (interference with ADLs):

I. Aseptic loosening of one or more prosthetic components confirmed by imaging, or
II. Fracture or mechanical failure of 1 or more components of the prosthesis confirmed by imaging, or
III. Confirmed periprosthetic infection confirmed by gram stain and culture, or
IV. Displaced periprosthetic fracture confirmed by imaging, or
V. Progressive or substantial periprosthetic bone loss confirmed by imaging, or
VI. Bearing surface wear leading to symptomatic synovitis or local bone or soft tissue reaction*, or
VII. Recurrent (2 or more) dislocations confirmed by imaging not
responsive to a reasonable course of conservative
management or irreducible dislocation confirmed by imaging;
or
VIII. Clinically significant leg length discrepancy; or
IX. Upon individual case review, persistent hip pain of unknown
etiology not responsive to a period of non-surgical care for six
(6) months.

And the member does not have any of the following
contraindications to total hip revision or replacement:

A. Loss of musculature (in particular hip abductor
   musculature), neuromuscular compromise or vascular
deficiency in the affected limb, rendering the procedure
   unjustifiable; or
B. Osteoporosis or other osseous abnormalities which would
   make the likelihood of a poor outcome more probable; or
C. Poor skin coverage; or
D. Severe instability due to anatomic causes that would make
   the likelihood of a poor surgical outcome more probable.

Aetna considers a revision or replacement of a THA or hip
resurfacing experimental and investigational when criteria are not met.

Aetna considers minimal incision or minimally invasive THA a
medically necessary acceptable alternative to conventional THA.

Aetna considers measurement of synovial C-reactive protein, and
the alpha-defensin test (Synovasure) experimental and
investigational as a marker for peri-prosthetic infection in THA
because the effectiveness of this approach has not been
established.

Aetna considers MAKOplasty/MAKO Tactile Guidance System for
total hip replacement experimental and investigational because
its effectiveness has not been established.

Aetna considers the prophylactic use of tranexamic acid medically
necessary in total hip arthroplasty to decrease blood loss.
* Aetna considers removal and revision surgery due to post total hip replacement (THR) metallosis alone, without evidence of loosening or malposition, experimental and investigational because there is insufficient clinical evidence in the published peer-reviewed medical literature.

See also CPB 0661 - Joint Resurfacing.

Background
Previously, most total hip prostheses utilize an acetabular cup either lined with polyethylene or composed entirely of polyethylene articulating against a cobalt-chromium-molybdenum (CoCr) or ceramic femoral head. Serious problems affecting the outcome of total joint replacement with these types of prostheses have been extensive and progressive peri-prosthetic osteolysis and aseptic loosening, which may result in revision, even though the components are still well fixed and functioning. Polyethylene particulate debris generated from metal-on-polyethylene bearing surfaces and the resulting biologic response to this debris are thought to be largely responsible.

In recent years, there has been renewed interest in metal-on-metal bearing surfaces for total joint arthroplasty. This is especially true in younger and more active patients who face the possibility of multiple revision procedures during their lifetime. In the long-term, the second-generation all-metal prostheses have demonstrated lower friction and wear rates than metal-on-polyethylene bearing surfaces. Recent studies reported that the second-generation metal-on-metal hip replacement prostheses exhibit a lower rate of acetabular revision and loosening than did those with previous metal-on-metal designs and that they had no more acetabular loosening or osteolysis than did those with metal-on-polyethylene articulations for follow-up periods of 5 to 10 years.

Another alternative to standard polyethylene is alumina-on-alumina ceramic. When comparing hard-on-hard bearings, the ceramic-on-ceramic coupling has several theoretical advantages over metal-on-metal. Because of the ceramic's extremely low coefficient of friction and its potential for superior wear
resistance, these couples promise both wear rates that are appreciably less than polyethylene-on-metal and metal-on-metal couples.

Available literature indicates that alumina-on-alumina ceramic couplings are a viable alternative to metal-on-polyethylene designs. The combination of new high quality ceramic acetabular and femoral bearing heads with hip systems that have achieved long-term stable fixation can result in a substantial increase in the longevity of fixation for implants especially in the younger and more active patients.

Available studies of metal-on-metal and ceramic-on-ceramic total hip implants primarily involve cohorts of younger, more active patients. The chief advantage of these hip implants over standard metal-on-polyethylene hip implants is their greater longevity. There is no adequate evidence that metal-on-metal or ceramic-on-ceramic total hip implants offer clinically significant benefits over standard metal-on-polyethylene hip implants for older patients.

Bhandari et al (2005) reported a meta-analysis of 6 randomized controlled studies suggested that bisphosphonates have a beneficial effect with regard to maintaining more peri-prosthetic bone mineral density than that in controls. However, the limitations of the available studies and the lack of analyses of clinically relevant outcomes (e.g., functional outcomes, revision rates, and quality of life) necessitate the planning and conduct of a sufficiently sized, methodologically sound trial with clinically relevant end points. Until this has been done, the current evidence regarding the beneficial effects of bisphosphonates on peri-prosthetic bone following total joint (e.g., knee and hip) arthroplasty should be interpreted with caution.

A technology assessment of hip implants by the Institute for Clinical Effectiveness and Health Policy (Augustovsky et al, 2006) found that the clinical trials comparing ceramic against conventional prostheses found no significant differences in the revision rate among the different types of prostheses. In case series of patients with the ceramic prosthesis, reported revision
rates at 10 years were less than 10%, which is considered within acceptable limits and comparable to those reported for conventional prostheses. Similar results have been reported for metal-on-metal hip prostheses, where randomized controlled trials with follow-up up to 5 years found no differences between metal-on-metal and conventional prostheses in effectiveness and complication rates (Augustovsky et al., 2006). The assessment noted that, although there are some reports of an increase in cancer in persons with metal-on-metal hip prostheses, there are other reports evaluating metal-on-metal prostheses with follow-up up to 28 years that have found no increase in the incidence of any cancer. The assessment stated that no study comparing ceramic prosthesis with metal-on-metal prosthesis was found. The assessment concluded that, although interim results with both the ceramic and metal-on-metal prostheses are promising, available studies have found no significant differences in revision rates during follow-up periods of 10 to 15 years. The assessment stated that, because the advantages of these materials may be observed at longer terms, their potential benefits would be greatest for younger patients (under 50 years of age) (Augustovsky et al., 2006).

In a meta-analysis, Smith and colleagues (2010) compared the clinical and radiological outcomes and complication rates of hip resurfacing (HRS) and total hip arthroplasty (THA). A systematic review was undertaken of all published (Medline, CINAHL, AMED, EMBASE) and unpublished or gray literature research databases up to January 2010. Clinical and radiological outcomes as well as complications of HRS were compared to those of THA using risk ratio, mean difference, and standardized mean difference statistics. Studies were critically appraised using the CASP appraisal tool. A total of 46 studies were identified from 1,124 citations. These included 3,799 HRSs and 3,282 THAs. On meta-analysis, functional outcomes for subjects following HRS were better than or the same as for subjects with a THA, but there were statistically significantly greater incidences of heterotopic ossification, aseptic loosening, and revision surgery with HRS compared to THA. The evidence base showed a number of methodological inadequacies such as the limited use of power calculations and poor or absent blinding of both patients and
assessors, possibly giving rise to assessor bias. The authors concluded that on the basis of the current evidence base, HRS may have better functional outcomes than THA, but the increased risks of heterotopic ossification, aseptic loosening, and revision surgery following HRS indicate that THA is superior in terms of implant survival.

Garbuz and associates (2010) conducted a prospective randomized clinical trial to compare clinical outcomes of resurfacing versus large-head metal-on-metal THA. These researchers randomized 107 patients deemed eligible for resurfacing arthroplasty to have either resurfacing or standard THA. Patients were assessed for quality-of-life outcomes using the PAT-5D index, WOMAC, SF-36, and UCLA activity score. The minimum follow-up was 0.8 years (mean of 1.1 years; range of 0.8 to 2.2 years). Of the 73 patients followed at least 1 year, both groups reported improvement in quality of life on all outcome measures. There was no difference in quality of life between the 2 arms in the study. Serum levels of cobalt and chromium were measured in a subset of 30 patients. In both groups cobalt and chromium was elevated compared to baseline. Patients receiving a large-head metal-on-metal total hip had elevated ion levels compared to the resurfacing arm of the study. At 1 year, the median serum cobalt increased 46-fold from baseline in patients in the large-head total hip group, while the median serum chromium increased 10-fold. At 1 year, serum cobalt was 10-fold higher and serum chromium 2.6-fold higher than in the resurfacing arm. Due to these excessively high metal ion levels, the authors recommended against further use of this particular large-head THA.

Kim and colleagues (2013) stated that the timing of total hip replacement (THR) in patients with active tuberculosis (TB) of the hip is controversial, because of the potential risk of re-activation of infection. There is little information about the outcome of THR in these patients. These investigators performed a systematic review of published studies that evaluated the outcome of THR in patients with active TB of the hip. A review of multiple databases referenced articles published between 1950 and 2012 was carried out. A total of 6 articles were identified, comprising 65 patients.
Tuberculosis was confirmed histologically in all patients. The mean follow-up was 53.2 months (range of 24 to 108). Anti-TB treatment continued post-operatively for between 6 and 15 months, after debridement and THR. One non-compliant patient had re-activation of infection. At the final follow-up the mean Harris hip score was 91.7 (range of 56 to 98). The authors concluded that THR in patients with active TB of the hip is a safe procedure, providing symptomatic relief and functional improvement if undertaken in association with extensive debridement and appropriate anti-TB treatment.

In a multi-center randomized, controlled trial with a non-inferiority design based on a minimal clinically important difference of 2.0 %, Anderson et al (2013) compared extended prophylaxis with aspirin and dalteparin for prevention of symptomatic venous thrombo-embolism (VTE) after THA. Randomization was electronically generated; patients were assigned to a treatment group through a Web-based program. Patients, physicians, study coordinators, health care team members, outcome adjudicators, and data analysts were blinded to interventions. The setting of this study was 12 tertiary care orthopedic referral centers in Canada; and a total of 778 patients who had elective unilateral THA between 2007 and 2010 were enrolled. After an initial 10 days of dalteparin prophylaxis after elective THA, patients were randomly assigned to 28 days of dalteparin (n = 400) or aspirin (n = 386). Main outcome measures were symptomatic VTE confirmed by objective testing (primary efficacy outcome) and bleeding. Five of 398 patients (1.3 %) randomly assigned to dalteparin and 1 of 380 (0.3 %) randomly assigned to aspirin had VTE (absolute difference, 1.0 percentage point [95 % confidence interval [CI]: -0.5 to 2.5 percentage points]). Aspirin was non-inferior (p < 0.001) but not superior (p = 0.22) to dalteparin. Clinically significant bleeding occurred in 5 patients (1.3 %) receiving dalteparin and 2 (0.5 %) receiving aspirin. The absolute between-group difference in a composite of all VTE and clinically significant bleeding events was 1.7 percentage points (CI: -0.3 to 3.8 percentage points; p = 0.091) in favor of aspirin. The authors concluded that extended prophylaxis for 28 days with aspirin was non-inferior to and as safe as dalteparin for the prevention of VTE after THA in patients.
who initially received dalteparin for 10 days. Given its low cost and greater convenience, aspirin may be considered a reasonable alternative for extended thrombo-prophylaxis following THA.

An UpToDate review on “Total hip arthroplasty” (Erens et al, 2014) states that: “Contraindications -- Total hip arthroplasty (THA) should not be undertaken in a number of clinical settings, including:

- Active infection (local or systemic)
- Preexisting significant medical problems (e.g., recent myocardial infarction, unstable angina, heart failure, or severe anemia)
- Skeletal immaturity
- Paraplegia or quadriplegia
- Permanent or irreversible muscle weakness in the absence of pain

Relative contraindications include a neuropathic (Charcot) joint, inability to ambulate that is not related to the hip disorder per se, absence of hip abductor muscle mass, progressive neurologic loss, and morbid obesity. However, the effects of obesity on outcome remain uncertain. Most studies do show an increased risk of infection, particularly in the highly obese. This must be weighed against the fact that some morbidly obese patients can have significant improvement postoperatively. A 2011 study from Canada noted that patients with morbid obesity can experience substantial benefit, despite a very small but statistically significant increase in the need for revision due to septic complications. Other studies have emphasized the increased risk of both superficial and deep infections and have described an increased risk of dislocation in such patients”.

Omar et al (2015) examined the role of synovial C-reactive protein (CRP) in the diagnosis of chronic peri-prosthetic hip infection. These researchers prospectively collected synovial fluid from 89 patients undergoing revision hip arthroplasty and measured synovial CRP, serum CRP, erythrocyte sedimentation rate (ESR), synovial white blood cell (WBC) count and synovial percentages of polymorphonuclear neutrophils (PMN). Patients
were classified as septic or aseptic by means of clinical, microbiological, serum and synovial fluid findings. The high viscosity of the synovial fluid precluded the analyses in 9 patients permitting the results in 80 patients to be studied. There was a significant difference in synovial CRP levels between the septic (n = 21) and the aseptic (n = 59) cohort. According to the receiver operating characteristic curve, a synovial CRP threshold of 2.5 mg/L had a sensitivity of 95.5 % and specificity of 93.3 %. The area under the curve was 0.96. Compared with serum CRP and ESR, synovial CRP showed a high diagnostic value. The authors concluded that according to these preliminary results, synovial CRP may be a useful parameter in diagnosing chronic periprosthetic hip infection.

Furthermore, an UpToDate review on “Total hip arthroplasty” (Erens et al, 2014) does not mention the use of synovial CRP as a post-operative management tool.

**MAKOplasty/MAKO Tactile Guidance System:**

Werner and colleagues (2014) stated that in comparison with standard surgical techniques robotic-assisted surgery has the advantages of increased surgical accuracy, reproducibility, optimization of component position, and improved patient outcomes in unicompartmental knee arthroplasty (UKA) and THA procedures. The MAKO Tactile Guidance System (TGS; MAKO Surgical Corp, Fort Lauderdale, FL) facilitates robotic-assisted arthroplasty procedures currently implemented in many operating rooms. The benefits of this technology are evident, but have not been shown to improve patient outcomes and justify the added financial burden imposed. The authors concluded that further research is needed to determine if this technological advancement will translate into improvements in longevity and clinical outcomes.

Domb et al (2014) compared THA with a robotic-assisted posterior approach with manual alignment techniques through a posterior approach, using a matched-pair controlled study design, to assess whether the use of the robot made it more likely for the acetabular cup to be positioned in the safe zones described by
Lewinnek et al and Callanan et al. Between September 2008 and September 2012, a total of 160 THAs were performed by the senior surgeon; 62 patients (38.8 %) underwent THA using a conventional posterior approach, 69 (43.1 %) underwent robotic-assisted THA using the posterior approach, and 29 (18.1 %) underwent radiographic-guided anterior-approach THAs. From September 2008 to June 2011, all patients were offered anterior or posterior approaches regardless of bone mass index (BMI) and anatomy. Since introduction of the robot in June 2011, all THAs were performed using the robotic technique through the posterior approach, unless a patient specifically requested otherwise. The radiographic cup positioning of the robotic-assisted THAs was compared with a matched-pair control group of conventional THAs performed by the same surgeon through the same posterior approach. The safe zone (inclination, 30° to 50°; ante-version, 5° to 25°) described by Lewinnek et al and the modified safe zone (inclination, 30° to 45°; ante-version, 5° to 25°) of Callanan et al were used for cup placement assessment. Matching criteria were gender, age ± 5 years, and (BMI) ± 7 units. After exclusions, a total of 50 THAs were included in each group. Strong inter-observer and intra-observer correlations were found for all radiographic measurements (r > 0.82; p < 0.001). One hundred percent (50/50) of the robotic-assisted THAs were within the safe zone described by Lewinnek et al compared with 80 % (40/50) of the conventional THAs (p = 0.001); 92 % (46/50) of robotic-assisted THAs were within the modified safe zone described by Callanan et al compared with 62 % (31/50) of conventional THAs (p = 0.001). The odds ratios for an implanted cup out of the safe zones of Lewinnek et al and Callanan et al were zero and 0.142, respectively (95 % CI: 0.044 to 0.457). The authors concluded that use of the robot allowed for improvement in placement of the cup in both safe zones, an important parameter that plays a significant role in long-term success of THA. However, whether the radiographic improvements that were observed would translate into clinical benefits for patients (e.g., acetabular wear, prosthetic dislocations, reductions in component impingement, and improved longevity) remains unproven.

Elmallah and associates (2015) stated that complications
following THA (e.g., dislocation, component loosening and wear) continue to be common indications for revision surgery. Multiple studies have attributed some of these problems to poor acetabular cup alignment and placement outside of the purported radiographic safe zone. In addition, it has been shown that conventional manually performed acetabular cup placement may not lead to optimal alignment, regardless of surgical experience. Additionally, incorrect leg length and offset can lead to dissatisfaction and instability. Therefore, robotic-arm assisted surgery has been introduced to improve accuracy of cup placement and leg length, and to offset with the aim of reducing the risk of hip instability and improving satisfaction after primary THA. These investigators reviewed the use of robotic-arm assisted surgery in 224 patients and examined if pre-operatively determined radiographic targets were achieved post-operatively and the proportion of acetabular cups outside of the safe zone. Pre-determined ante-version and inclination were 15 and 40 degrees, respectively. Results have shown that the use of robotic-arm assisted surgery resulted in a post-operative mean inclination of 40 degrees (range of 34 to 51 degrees) and a mean ante-version of 16 degrees (range of 9 to 25 degrees); 99% of the patients remained within the pre-designated safe zone. Evidence has shown that robotic-arm assisted surgery may have improved accuracy in cup placement when compared to conventional surgery and possibly to computer-assisted surgery. The authors concluded that when compared to the literature on robotic-arm assisted surgery, the findings were comparable. They believed that this surgical technique may aid in reducing post-operative THA complications (e.g., aseptic loosening and dislocations); but further prospective studies are needed to evaluate clinical outcomes and long-term results.

Banerjee et al (2016) stated that precise and accurate biomechanical reconstruction during THA is essential for durable long-term survivorship. Accurate fit of cementless hip implants is also crucial to reduce micro-motion between the bone-implant interfaces to allow for stable osseointegration. Robotic technology aims to minimize potential human errors and improve implant alignment and fit, and address persisting concerns with modern-day cementless THA. Although robotic THA dated back
to the early 1990s, concerns with increased operating times, costs, and complications led to its withdrawal. However, semi-active systems have renewed interest in robot-assisted joint arthroplasty. These researchers reviewed the current technology, its potential benefits, and the reported clinical and radiographic outcomes. Early evidence suggested that robotic use may lead to more accurate reconstruction of radiographic parameters (e.g., implant positioning, fit, center-of-rotation, and leg-length discrepancy). The authors concluded that further research is needed to determine if these will translate into better outcomes and improved implant longevity to justify increased costs. (Keywords of this article included MAKO).

Furthermore, an UpToDate review on “Total hip arthroplasty” (Erens et al, 2016) does not mention “robotic-assisted arthroplasty/MAKOplasty” as a therapeutic option.

The Alpha-Defensin Test (Synovasure):

Patel and colleagues (2016) noted that synovial fluid biomarkers can be considerably helpful in the diagnosis of peri-prosthetic joint infection (PJI) and improve the accuracy of other tests such as serum biomarkers. Synovial fluid white blood cell (WBC) count and differential are currently minor criteria in the definition of PJI as proposed by the International Consensus Group. In recent years, however, numerous biomarkers have been investigated for patients with PJI, including inflammatory cytokines (e.g., interleukins 1, 6, 8,10, and 17, tumor necrosis factor-alpha [TNF-α], interferon-γ, resistin, and thrombospondin), inflammatory reactive proteins (such as CRP), bactericidal leukocyte enzymes (e.g., esterase, elastase, and bactericidal/permeability-increasing protein, gelatinase-associated lipocalin, and lactoferrin, all of which are present in polymorphonuclear leukocytes), markers of angiogenesis (e.g., vascular endothelial growth factor) and antimicrobial proteins (e.g., as alpha-defensing [α-defensin], β-defensin, and cathelicidin LL-37). Many of these synovial fluid biomarkers did not have any correlation with synovial WBC count, so these synovial fluid markers are not simply surrogate markers for an increase in local inflammation in the joint as a result of a PJI. Additionally, it was found that the markers that had the
highest specificity and sensitivity were proteins that have antimicrobial properties, which is likely the reason for their increased concentration in synovial fluid during PJI. Since the mechanism of action for these biomarkers is different than that of currently used tests, these biomarkers hold great promise for a novel approach in diagnosing PJI. The authors stated that the main disadvantage of synovial biomarkers is that these tests depend on the availability of synovial fluid, and synovial fluid cannot be aspirated from a joint in all PJI cases. Moreover, some of the inflammatory biomarkers may represent any type of inflammatory process in the prosthetic joint (e.g., an adverse reaction to foreign material); thus, these tests may not be specific enough for PJI.

Kasparek and co-workers (2016) investigated the novel Synovasure PJI lateral flow test device for detection of alpha-defensin and determined its diagnostic accuracy for the intra-operative diagnosis of PJI and compared it to frozen section. A total of 40 consecutive patients, who underwent revision surgery, between September 2014 and September 2015 were included. Patients underwent 29 revision total knee arthroplasties (TKAs) and 11 revision THAs; 12 patients had a confirmed PJI based on Musculo-Skeletal Infection Society (MSIS) criteria, and 28 patients were considered aseptic. The overall accuracy to detect PJI using the lateral flow assay was 85 % (95 % CI: 70 % to 93 %). The device has a positive predictive value (PPV) of 80 % (95 % CI: 44 % to 96 %) and a negative predictive value (NPV) of 87 % (95 % CI: 68 % to 96 %) and showed a sensitivity of 67 % (95 % CI: 35 % to 89 %) and specificity of 93 % (95 % CI: 75 % to 99 %). Frozen section had a lower sensitivity (58 % [95 % CI: 29 % to 84 %]) but a higher specificity (96 % [95 % CI: 80 % to 100 %]). Receiver operator curve analysis demonstrated an area under the curve of the Synovasure PJI Lateral Flow Test Kit and frozen section of 0.80 and 0.77, respectively. The authors concluded that the findings of the present study suggested that the intra-operative lateral flow test was at least equivalent to intra-operative frozen section and was a useful tool to confirm the absence of PJI. Moreover, they stated that although the clinical results are promising, they are not as good as previous studies using alpha-defensin levels measured in a laboratory.
Pupaibool and colleagues (2016) reviewed the current evidence on the utility of serum and synovial fluid biomarkers to help aid in the diagnosis of PJI with focusing on synovial fluid alpha-defensin. Articles and data for this review were identified by searches of PubMed and Ovid Medline up to June 1, 2016. In addition, these investigators manually reviewed the bibliographies of the retrieved articles for additional citations for references from relevant articles on the diagnosis of PJI. Serum biomarkers can be elevated in various inflammatory conditions. Synovial fluid biomarkers are more accurate for the diagnosis of PJI compared to serum biomarkers. Based on current available data, alpha-defensin is the most promising synovial fluid biomarker for the diagnosis of PJI and is commercially available. The authors concluded that synovial fluid alpha-defensin could enhance the ability to identify PJI and incorporate into the diagnostic algorithm in the future. Moreover, they stated that large-scale studies are needed to provide more data for its significance for the diagnosis of PJI.

Sigmund and associates (2017) stated that the diagnosis of PJI remains demanding due to limitations of all the available diagnostic tests. The synovial fluid marker, α-defensin, is a promising adjunct for the assessment of potential PJI. These investigators examined the qualitative assessment of α-defensin, using Synovasure to detect or exclude peri-prosthetic infection in total joint arthroplasty. In a prospective diagnostic study, these researchers studied 50 patients (28 women, 22 men, mean age of 65 years; range of 20 to 89) with a clinical indication for revision arthroplasty who met the inclusion criteria. The presence of α-defensin was determined using the qualitative Synovasure test and compared with standard diagnostic methods for PJI. Based on modified MSIS criteria, 13 cases were categorized as septic and 36 as aseptic revisions; 1 test was inconclusive. The Synovasure test achieved a sensitivity of 69 % and a specificity of 94 %. The positive and negative likelihood ratios were 12.46 and 0.33, respectively. A good diagnostic accuracy for PJI, with an area under the curve of 0.82, was demonstrated. Adjusted p-values using the method of Hochberg showed that Synovasure was as good at diagnosing PJI as histology (p = 0.0042) and bacteriology with 1 positive culture (p = 0.0327). The authors
concluded that with its ease of use and rapid results after approximately 10 minutes, Synovasure may be a useful adjunct in the diagnosis of PJI.

Suda and colleagues (2017) noted that diagnosing peri-prosthetic infection remains a challenge. Multiplex-PCR and biomarkers such as alpha-defensin are potentially useful and fast methods for detecting peri-prosthetic infection. These researchers compared these new methods with clinical assessment, conventional microbiological methods and histo-pathological examination. A total of 28 consecutive patients with 30 joints and a mean age of 67.7 years (range of 39 to 88) with removal of THA or TKA were included in this study. Patients were classified according to the modified MSIS for infected joints. Punction fluid and tissue specimens were taken for conventional microbiological examination, the alpha defensin test was performed, a synovial membrane specimen was used for multiplex-PCR and histopathological examination was carried out. The alpha-defensin test and multiplex-PCR showed a sensitivity of 76.9 versus 30.8 % and a specificity of 82.4 versus 100 %, respectively. These investigators found a significant difference between the positive and negative results (p = 0.0023). The conventional microbiological methods were not significantly different from the alpha-defensin test (p = 0.244) with a sensitivity of 84.6 % and a specificity of 100 % but did differ significantly from the multiplex PCR (p = 0.0030). There was a significant difference between modified MSIS classification and multiplex PCR (p = 0.0007). The authors concluded that neither the alpha-defensin test nor multiplex-PCR could detect peri-prosthetic infection immediately and reliably. They stated that the multiplex-PCR was suitable for detecting the non-infected but not the truly infected; and the alpha-defensin test was helpful but showed no satisfactory results. These researchers stated that the conventional microbiological methods remain the most reliable for peri-prosthetic infection diagnosis.

*Tranexamic Acid in Total Hip Replacement:*

Zhang and colleagues (2016) stated that as the prevalence of THA is increasing, it is usually associated with considerable blood loss.
Tranexamic acid (TXA) has been reported to reduce perioperative blood loss in hip joint arthroplasty. However, the best route of TXA administration continues to be controversial. In a meta-analysis, these investigators integrated all data from the 7 included trials to compare the safety and effectiveness of topical and intravenous TXA administration in primary THA. The endpoints assessed in this meta-analysis included the comparisons of total blood loss, post-operative hemoglobin (Hb) decline, transfusion rates, the incidence rate of deep vein thrombosis (DVT), pulmonary embolisms (PE), and wound infection.

Literature searches of PubMed, Embase, the Cochrane Library, the Chinese Biomedical Literature database, the CNKI database, and Wan Fang Data were performed up to August 30, 2016. Randomized controlled trials (RCTs) were included in this meta-analysis if they compared the safety and effectiveness of intravenous versus topical administration of TXA in patients who underwent primary THA. The meta-analysis was performed following the guidelines of the Cochrane Reviewer's Handbook and the PRISMA statement. The pooling of data was carried out by using RevMan 5.3, Denmark. A total of 7 RCTs involving 964 patients met the inclusion criteria. The meta-analysis indicated that there were no significant differences in the 2 groups in terms of total blood loss ([mean difference (MD) = -14.74, 95 % CI: -89.21 to 59.74, p = 0.7], transfusion rates [RD = -0.02, 95 % CI: -0.05 to 0.02, p = 0.39]; no significant differences were found regarding the incidence of adverse effects (AEs) such as DVT [RD = 0.00, 95 % CI: -0.01 to 0.01, p = 1.00], PE [RD = 0.00, 95 % CI: -0.01 to 0.01, p = 0.71], or wound infection [RD = -0.01, 95 % CI: -0.06 to 0.04, p = 0.66]). The pooled results showed that the intravenous groups had a lower post-operative Hb decline (MD = -0.47, 95 % CI: -0.74 to -0.20, p = 0.0006). It was probably due to insufficient data and the varied reporting of outcomes. There was some inherent heterogeneity due to the small sample size of each primary study. The authors concluded that topical and intravenous administrations of TXA had a similar effect on the decrease of blood loss without an increased risk of complications (e.g., DVT, PE, and wound infection). They noted that intravenous TXA administration may have a maximum efficacy; while topical TXA administration may be preferred in patients who with high risk of thrombo-embolic events. However, they stated that larger,
high-quality RCTs are needed to examine the optimal regimen, dosage, timing before recommending the widespread use of TXA in total joint arthroplasty.

Moskal and Capps (2016) stated that previous meta-analyses established that TXA confers benefits when used during THA. However, 2 of these meta-analyses included a variety of routes of administration of TXA in THA (topical, intravenous, oral, and intra-articular), another meta-analysis included a variety of anti-fibrinolytic drugs (not restricted to a single drug), and the final meta-analysis included non-RCTs. This meta-analysis focused on a single medication, TXA, administered in a specific way, intravenously in patients undergoing primary THA, using data reported only in RCTs. Outcomes were restricted to blood loss, allogeneic transfusion rates, and complications. Other outcomes, such as return to function or clinical scores, could not be evaluated because of lack of consistent reporting. The authors stated that to better understand the effects of intravenous TXA in THA on clinical outcomes, such as recovery, return to function, and patient-reported outcome measures, it would be helpful to have more RCTs examining these measures in a standardized manner. They noted that intravenous TXA was beneficial for blood loss intra-operatively, blood loss through drains, and total blood loss during hospitalization, in addition to reducing allogeneic transfusion rates. However, no difference between intravenous TXA and placebo was found for most complications, except DVT, which showed favorable results with placebo.

In a meta-analysis, Shang and colleagues (2016) compared the safety and effectiveness of combined intravenous and topical TXA versus intravenous use alone in primary TKA and THA. PubMed, Embase, Cochrane library and OVID were searched. Eligible RCTs evaluating combined intravenous and topical TXA versus intravenous alone in primary TKA and THA were included. The relative risk (RR) or the mean difference (MD) for dichotomous or continuous data was calculated respectively, and heterogeneity was analyzed by Chi-square and I2 tests. A total of 5 RCTs met the inclusion criteria and were included in the study. The meta-analysis indicated that there was statistically significant difference favoring the combined group in total blood loss (MD = -160.90, 95
% CI: -201.26 to -120.54, p < 0.00001), Hb drop (MD = -0.41, 95 %
CI: -0.73 to 0.08], p = 0.01), transfusion requirements(RR = 0.29,
95 % CI: 0.12 to 0.70], p = 0.006) and length of hospital stays (MD
= -0.21, 95 % CI: -0.40 to -0.02], p = 0.03). Both groups showed
similar outcomes regarding thrombo-embolic complications(RR =
0.84, 95 % CI: 0.26 to 2.70], p = 0.76). The authors concluded
that based on the findings of this study, combined use of
intravenous and topical TXA was more effective than intravenous
TXA alone in primary TKA or THA without increasing the risk of
thrombo-embolic complications. Moreover, they stated that
further high quality studies with more patients are needed in
future studies.

In a meta-analysis, Li and associates (2017) evaluated the safety
and effectiveness of combined intravenous and topical methods
of application versus single intravenous of TXA in primary TKA and
THA. These researchers performed a systematic search in
Medline(from 1966 to September 25, 2016), PubMed (from 1966
to September 25, 2016), Embase (from 1980 to September 25,
2016), ScienceDirect (from 1985 to September 25, 2016) and the
Cochrane Library. Only high-quality RCT were identified; 2
authors independently performed data extraction and quality
assessment of included studies. Meta-analysis was conducted
using Review Manager 5.1 software. A total of 6 RCTs that
included 687 patients met the inclusion criteria. The present
meta-analysis indicated that there were significant differences in
terms of total blood loss (MD = -193.59, 95 % CI -338.06 to
-49.13, p = 0.009), transfusion rate (RD = -0.07, 95 % CI -0.12 to
-0.03, p = 0.001), Hb decline (MD = -0.51, 95 % CI -0.83 to -0.18, p
= 0.01) and length of stay (MD = -0.20, 95 % CI -0.38 to -0.02, p =
0.03) between groups. The authors concluded that combined
administration of TXA in patients with TKA and THA was
associated with significantly reduced total blood loss, transfusion
requirements, post-operative Hb decline and length of stay
compared to single application alone, but was not associated with
prolonged operation time. Moreover, no AEs, such as superficial
infection, DVT or PE, were associated with TXA. These
researchers suggested that combined administration of TXA
demonstrated excellent clinical safety and effectiveness in
patients with TKA and THA. Moreover, they stated that well-
designed studies with larger sample size are needed to provide further reliable evidence for the combined use of TXA.

A Veteran's Health Administration assessment (VHA, 2014) found evidence for use of TXA in patients undergoing total knee arthroplasty and total hip arthroplasty. They found, however, that "[e]vidence is lacking for the safe and effective use of TXA in joint revision surgery or use in hip fracture surgery, therefore the risk/benefit of TXA in these settings is unknown."

An assessment by the Canadian Agency for Drugs and Technologies in Health (CADTH, 2015) found that, overall, the conclusions of published reviews supported the use of TXA to decrease intraoperative and postoperative blood loss in primary hip and knee arthroplasty. An evidence-based guideline from Health Quality Ontario (2014) recommends the use of TXA for knee and hip replacement.

Guidelines on perioperative blood loss from the American Society of Anesthesiologists (2015) found: "Meta-analysis of placebo-controlled RCTs indicate that tranexamic acid for prophylaxis of excessive bleeding administered before and/or during a procedure is effective in reducing perioperative blood loss, the number of patients transfused, and the volume of blood products transfused (CategoryA1-B evidence). Randomized trials comparing tranexamic acid with placebo or no tranexamic acid controls report no differences for stroke, myocardial infarction, renal failure, reoperation for bleeding, or mortality (Category A2-B evidence). Meta-analysis of placebo-controlled RCTs indicate that tranexamic acid for prophylaxis of excessive bleeding initiated after a knee and hip arthroplasty and before tourniquet deflation compared with placebo also reported lower blood loss volumes (Category A1-B evidence). . . . The literature is insufficient to evaluate the postoperative administration of tranexamic acid for treatment of excessive blood loss."

<table>
<thead>
<tr>
<th>CPT Codes / HCPCS Codes / ICD-10 Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by &quot;+&quot;:</td>
</tr>
</tbody>
</table>
Total hip replacement (THA):

CPT codes covered if selection criteria are met:

27130  Arthroplasty, acetabular and proximal femoral prosthetic replacement (total hip arthroplasty), with or without autograft or allograft [minimally invasive or conventional approach]

27132  Conversion of previous hip surgery to total hip arthroplasty, with or without autograft or allograft [minimally invasive or conventional approach]

CPT codes not covered for indications listed in the CPB:

0055T  Computer-assisted musculoskeletal surgical navigational orthopedic procedure, with image-guidance based on CT/MRI images (List separately in addition to code for primary procedure) [MAKOplasty/MAKO Tactile Guidance System]

86140  C-reactive protein [as a marker for peri-prosthetic infection]

86141  [as a marker for peri-prosthetic infection]

HCPCS codes covered if selection criteria are met:

C1776  Joint device (implantable)

ICD-10 codes covered if selection criteria are met:

C40.20  Malignant neoplasm of long bones of lower limb [proximal femur]

C40.22  Malignant neoplasm of long bones of lower limb [proximal femur]

C79.51  Secondary malignant neoplasm of bone [proximal femur]

M05.00  Rheumatoid arthritis

M14.89  Traumatic arthropathy, hip

M12.551  Traumatic arthropathy, hip

M12.559  Traumatic arthropathy, hip

M16.0  Osteoarthritis of hip

M16.9  Osteoarthritis of hip unspecified

M16.2  Osteoarthritis, secondary, hip

M16.7  Osteoarthritis, secondary, hip

M16.9  Osteoarthritis of hip unspecified
Pathologic fracture of neck of femur (hip)
M80.051+, M80.059+, M80.851+, M80.859+, M84.451+, M84.453+, M84.459+, M84.551+, M84.559+, M84.651+, M84.659+, M84.750+, M84.759+

Atypical femoral fracture
M84.750+, M84.759+

Osteonecrosis of bone, site unspecified
M87.00, M87.10, M87.20, M87.30, M87.80, M87.9, M90.50

Osteonecrosis of femur
M87.051, M87.059, M87.151, M87.159, M87.251, M87.255, M87.351, M87.353, M87.851, M87.859, M90.551, M90.559

Periprosthetic fracture around internal prosthetic hip joint
M97.01x+, M97.02x+

Fracture of acetabulum, closed and open
S32.411+, S32.9xx+

Fracture of head and neck of femur
S72.001+, S72.26x+
Mechanical complication of internal orthopedic device, implant, and graft

Presence of artificial hip joint

ICD-10 codes contraindicated for this CPB:

- **T84.010 - T84.011, T84.020 - T84.021, T84.030 - T84.031, T84.050 - T84.051, T84.060 - T84.061, T84.090 - T84.091**
- **Z96.641 - Z96.649**

**ICD-10 codes contraindicated for this CPB:**

- **A00.0 - B99** Infectious and parasitic diseases [active infection of the joint, active systemic bacteremia or active skin infection]
- **G82.20** Paraplegia (paraparesis) and quadriplegia
- **G82.54** (quadripareasis)
- **M00.051 - M00.059, M00.151 - M00.159, M00.251 - M00.259, M00.851 - M00.859, M00.9** Pyogenic arthritis involving pelvic region and thigh
- **M01.X51 - M01.X59** Direct infection of hip in infection and parasitic diseases classified elsewhere
- **M62.81** Muscle weakness (generalized) [permanent or irreversible muscle weakness preventing ambulation in the absence of pain]
- **R62.50, R62.59** Lack of expected normal physiological development in childhood [skeletal immaturity]
S71.001+ - Open wound of hip and thigh
S71.159
T56.2x1+ - Toxic effect of chromium and its compounds [not covered for metallosis alone without evidence of loosening or malposition]
T56.2x4+ - Toxic effect of other metals [not covered for metallosis alone without evidence of loosening or malposition]
T56.811+ - Toxic effect of other metals [not covered for metallosis alone without evidence of loosening or malposition]
T78.40x+ - Allergy, unspecified

Revision, replacement of total hip arthroplasty, or revision hip resurfacing arthroplasty:

No specific code

CPT codes covered if selection criteria are met:

27125 - Hemiarthroplasty, hip, partial (eg, femoral stem prosthesis, bipolar arthroplasty) [Revision of resurfacing arthroplasty]
27130 - Arthroplasty, acetabular and proximal femoral prosthetic replacement (total hip arthroplasty), with or without autograft or allograft [revision of resurfacing arthroplasty]
27134 - Revision of total hip arthroplasty; with or without autograft or allograft

HCPCS codes covered if selection criteria are met:

C1776 - Joint device (implantable)
S2118 - Metal-on-metal total hip resurfacing, including acetabular and femoral components

ICD-10 codes covered if selection criteria are met:

T84.010+ - Mechanical complication of internal joint prosthesis
T84.099
T84.50x+ - Infection and inflammatory reaction due to internal joint prosthesis
T84.59x+

**Synovasure:**

CPT codes not covered for indications listed in the CPB:

*Alpha-defensin test (Synovasure)* - no specific code: ICD-10 codes not covered for indications listed in the CPB:
The above policy is based on the following references:


of ceramic or metal on metal prostheses in total hip replacement [summary]. Report IRR No. 84. Buenos Aires, Argentina: Institute for Clinical Effectiveness and Health Policy (IECS); 2006.


46. Walsh J. Metal-on-metal hip resurfacing as an alternative to


57. Wang J, Jiang B, Marshall RJ, Zhang P. Arthroplasty or internal fixation for displaced femoral neck fractures:


72. Erens GA, Thornhill TS, Katz JN. Total hip arthroplasty. UpToDate [online serial], Waltham, MA: UpToDate; reviewed December 2014.


80. Moskal JT, Capps SG. Meta-analysis of intravenous tranexamic acid in primary total hip arthroplasty.


89. Canadian Agency for Drugs and Technologies in Health (CADTH). Prophylactic Tranexamic Acid Administration for Patients Undergoing Hip and Knee Replacement: Clinical Effectiveness, Cost-Effectiveness, and Guidelines. Rapid
90. Health Quality Ontario; Ministry of Health and Long-Term Care. Quality-based procedures: Clinical handbook for primary hip and knee replacement [Internet]. Toronto, ON: Health Quality Ontario; February 2014.

AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0287 Total Hip Replacement

There are no amendments for Medicaid.