Aetna considers transjugular intrahepatic portosystemic shunt (TIPSS) medically necessary in members with bleeding gastric, esophageal or ectopic (including anorectal, intestinal, and stomal) varices, moderate Budd-Chiari syndrome and who have failed to respond to anticoagulation, portal hypertensive gastropathy with recurrent bleeding despite the use of beta-blockers, severe refractory ascites, and refractory hepatic hydrothorax (see background section for selection criteria).

Aetna considers polyfluorotetraethylene (PTFE)-coated stents medically necessary for TIPSS.

Aetna considers TIPSS experimental and investigational for all other indications including any of the following conditions because the effectiveness of TIPSS for these conditions has not been proven:

- Cirrhosis-related chylothorax; or
- Controlling bleeding from gastro antral vascular ectasia in persons with cirrhosis; or
- Correction of hypersplenism and thrombocytopenia; or
- Hepatopulmonary syndrome; or
- Hepatorenal syndrome; or
- Initial therapy for acute variceal hemorrhage; or
- Initial therapy to prevent first or recurrent variceal hemorrhage; or
- Portal hypertension associated with polycystic liver disease or Caroli disease; or
- Portal-mesenteric venous thrombosis; or
- Pre-hepatic portal hypertension; or
- Pre-operative reduction in portal hypertension before liver transplantation; or
- Prevention of re-bleeding in cirrhotic individuals with cavernous transformation of the portal vein; or
- Prophylaxis of variceal hemorrhage; or
- Pulmonary hypertension; or
- Sinusoidal obstruction syndrome (veno-occlusive disease).

**Background**

Transjugular intrahepatic portosystemic shunt (TIPSS) has been shown in a number of clinical studies to be an option in the treatment of acute variceal bleeding that can not be successfully controlled with sclerotherapy and for treatment of recurrent variceal bleeding that can not be successfully controlled with medical management or sclerotherapy.

Transjugular intrahepatic portosystemic shunt does not involve an incision; rather, a catheter is placed percutaneously into the jugular vein through which a permanent intrahepatic shunt is created between the hepatic and portal veins. Blood flow is diverted around the diseased liver, thus easing portal hypertension. It is usually performed in the angiography or interventional radiology laboratory under intravenous anesthesia.

The efficacy of TIPSS as the initial treatment of variceal bleeding or in the prevention of secondary variceal bleeding has not been established.
The American Association for the Study of Liver Diseases (AASLD) practice guidelines on the role of TIPSS creation in the management of portal hypertension has a number of recommendations, including the following (Boyer and Haskal, 2005):

- The use of TIPSS to treat hepatopulmonary syndrome cannot be recommended (grade II-3).
- The use of TIPSS to treat sinusoidal obstruction syndrome cannot be recommended (grade II-3).
- TIPSS is effective in the control of hepatic hydrothorax, but it should be used only in patients whose effusion cannot be controlled by diuretics and sodium restriction (grade II-3).
- TIPSS is effective in the prevention of rebleeding from gastric and ectopic varices (including intestinal, stomal, and anorectal varices) and is the preferred approach for the prevention of rebleeding in this group of patients (grade II-3).

Grade II-3 refers to multiple time series, dramatic uncontrolled experiments.

Pan et al (2008) identified factors predictive of survival after TIPSS creation. Log-rank tests were used to compare the cumulative survival functions among groups of patients who underwent TIPSS creation for various indications. Thirty-day mortality after TIPSS creation was examined by logistic regression. Cox proportional-hazards analyses were performed to analyze the cumulative 90-day and 1-year survival. Selected variables such as creatinine, bilirubin, and International Normalized Ratio (INR) were assessed with respect to survival. The study included 352 patients, of whom 229 (65.1%) were male. The mean age at the time of TIPSS creation was 53.6 years (range of 21 to 82). A Model for End-stage Liver Disease (MELD) score greater than 15 was significantly associated with poor survival (p < 0.05) at 30 days, 90 days, and 1 year after TIPSS creation. Independently, a serum total bilirubin level greater than 2.5 mg/dL, an INR greater than 1.4 (p < 0.05), and a serum creatinine level greater than 1.2 mg/dL were predictive of poor survival. Finally, age greater than 70 years was associated with poor survival at 90 days and 1 year after TIPSS creation (p < 0.05). The authors concluded that the choice to create a TIPSS in individuals whose MELD score is greater than 15 and/or whose age is greater than 70 years should involve a careful consideration of risk/benefit ratio, taking into account the finding that such patients have significantly poorer survival after TIPSS creation.
Garcia-Pagán et al (2008) reported the long-term results and prognostics factors in 124 patients with Budd-Chiari syndrome (BCS) who were treated with TIPSS. Subjects were followed until death, orthotopic liver transplantation (OLT), or last clinical evaluation. Prior to treatment with TIPSS, BCS patients had a high MELD and high Rotterdam BCS prognostic index (98 % of patients at intermediate-risk or high-risk) indicating severity of liver dysfunction. However, 1- and 5-year OLT-free survival were 88 % and 78 %, respectively. In the high-risk patients, 5-year OLT-free survival was much better than that estimated by the Rotterdam BCS index (71 % versus 42 %, respectively). In the whole population, bilirubin, age, and INR for prothrombin time independently predicted 1-year OLT-free survival. A prognostic score with a good discriminative capacity (area under the curve, 0.86) was developed from these variables. Seven out of 8 patients with a score greater than 7 died or underwent transplantation versus 5 out of 114 patients with a score of less than 7. The authors concluded that long-term outcome for patients with severe BCS treated with TIPSS is excellent even in high-risk patients, suggesting that TIPS may improve survival. Furthermore, these researchers identified a small subgroup of BCS patients with poor prognosis despite TIPSS who might benefit from early OLT.

Murad et al (2008) noted that the clinical outcome of a covered versus uncovered TIPSS for patients with BCS is as yet largely unknown. These investigators compared patency rates of bare and polytetrafluoroethylene (PTFE)-covered stents, and examined clinical outcome using 4 prognostic indices (Child-Pugh score, Rotterdam BCS index, modified Clichy score and MELD). A total of 23 TIPSS procedures were performed on 16 patients. The primary patency rate at 2 years was 12 % using bare and 56 % using covered stents (p = 0.09). These researchers found marked clinical improvement at 3 months post-TIPSS as determined by a drop in median Child-Pugh score (10 to 7, p = 0.04), Rotterdam BCS index (1.90 to 0.83, p = 0.02) and modified Clichy score (7.77 to 2.94, p = 0.003), but not in MELD (18.91 to 17.42, p = 0.9). Survival at 1 and 3 years post-TIPSS was 80 % (95 % confidence interval [CI]: 59 to 100 %) and 72 % (95 % CI: 48 to 96 %). Four patients (25 %) died and 1 required liver transplantation. The authors concluded that a TIPSS using PTFE-covered stents shows better patency rates than bare stents in BCS. Moreover, TIPSS leads to an improvement in important prognostic indicators for the survival of patients with BCS.
Corso et al (2008) evaluated the safety and effectiveness of TIPSS in the treatment of patients affected by BCS. A total of 15 patients (7 male and 8 female subjects, age range of 7 to 52 years) with BCS uncontrolled by medical therapy were treated with TIPSS placement. In 7 cases BCS was idiopathic, in 4 it was caused by myeloproliferative disorders and in 4 by other disorders. One patient also had portal vein thrombosis. In 5/15 cases TIPSS was created through a transcaval approach. Eight patients (53.4 %) received a bare stent, and 7 (46.6 %) received a stent graft. The follow-up lasted a median of 29.4 (range of 3.2 to 68) months. Technical success was achieved in all patients without major complications. Transjugular intrahepatic portosystemic shunt was very effective in decreasing the portosystemic pressure gradient from 26.2 +/- 5.8 to 10 +/- 6.2 mmHg. All patients but 2 were alive at the time of writing. Acute leukemia was the cause of the single early death and was unrelated to the procedure. The patient with portal vein thrombosis underwent thrombolysis before TIPSS, but the vein occluded again after 3 weeks, and the patient died 6 months later. The other patients showed significant improvements in liver function, ascites and symptoms related to portal hypertension. Primary patency was 53.3 %, and primary assisted patency was 93.3 %. No patient required or was scheduled for liver transplantation. The authors concluded that TIPSS is an effective and safe treatment for BCS and may be considered a valuable alternative to traditional surgical portosystemic shunting or liver transplantation.

Amarapurkar and associates (2008) assessed patterns of obstruction, etiological spectrum and non-surgical treatment in patients with BCS. A total of 49 consecutive cases were prospectively evaluated. All patients with refractory ascites or deteriorating liver function were, depending on morphology of inferior vena cava (IVC) and/or hepatic vein (HV) obstruction, triaged for radiological intervention, in addition to anti-coagulation therapy. Asymptomatic patients, patients with diuretic-responsive ascites and stable liver function, and patients unwilling for surgical intervention were treated symptomatically with anti-coagulation. Mean duration of symptoms was 41.5 +/- 11.2 (range of 1 to 240) months. Hepatic vein thrombosis (HVT) was present in 29 (59.1 %), IVC thrombosis in 8 (16.3 %), membranous obstruction of IVC in 2 (4 %) and both IVC-HV thrombosis in 10 (20.4 %) cases. Of 35 cases tested for hyper-coagulability, 27 (77.1 %) were positive for 1 or more hyper-coagulable states. Radiological intervention was technically successful in 37/38 (97.3 %): IVC stenting in 7 (18.9 %), IVC balloon angioplasty in 2 (5.4 %), combined IVC-HV stenting in 2 (5.4 %), HV stenting in 11 (29.7 %), TIPSS in 13 (35.1 %) and combined TIPSS-IVC stenting in 2 (5.4 %). Complications
encountered in follow-up: death in 5, re-stenosis of the stent in 5 (17.1 %), hepatic encephalopathy in 2 and hepatocellular carcinoma in 1 patient. Of 9 patients treated medically, 2 showed complete resolution of HVT. The authors concluded that in their series, HVT was the predominant cause of BCS. In the last 5 years with the availability of sophisticated tests for hyper-coagulability, etiologies were defined in 85.7 % of cases. Non-surgical management was successful in most cases.

Current guidelines from the AASLD on TIPSS (Boyer and Haskal, 2010) indicated that Teflon-coated stents are preferred over bare stents to lower the risk of shunt dysfunction. This position is supported by a number of studies of PTFE-covered stents in TIPSS.

Tripathi et al (2006) assessed the shunt function and clinical efficacy of PTFE-covered stents in a single center. A total of 316 patients with uncovered stents before the introduction of covered stents (group 1) and 157 patients with the Viatorr Gore PTFE-covered stents at the time of TIPSS creation (group 2) were studied. The mean follow-up was 22.8 +/- 25.4 and 13.1 +/- 12.5 months, respectively (p < 0.01). Shunt insufficiency was greater in group 1 [54 % versus 8 % at 12 months; relative hazard (RH) 8.6; 95 % CI: 4.8 to 15.5; p < 0.001]. The incidence of variceal re-bleeding was greater in group 1 (11 % versus 6 % at 12 months; RH 2.4; 95 % CI: 1.1 to 5.1; p < 0.05). The incidence of hepatic encephalopathy was greater in group 1 (32 % versus 22 % at 12 months; RH 1.5; 95 % CI: 1.1 to 2.3; p < 0.05). Mortality was similar in the two groups. The authors concluded that the Viatorr type of PTFE-covered stent results in vastly improved patency compared with uncovered stents, with reduced rates of variceal re-bleeding and hepatic encephalopathy. This type of covered stent has the potential for superior clinical efficacy compared with uncovered stents.

Saad et al (2010) compared functional and anatomic outcomes of TIPSs created with the specialized Viatorr stent versus a Wallstent/Fluency stent combination. Retrospective review of patients who underwent TIPS creation with stent-grafts was conducted over a 54-month period ending in June 2008. Patients were divided into 3 groups: (i) Viatorr only, (ii) Fluency only, and (iii) combined Viatorr/Fluency, the latter of which was included in the overall evaluation but excluded from the comparative analysis between the Viatorr and Fluency groups. Patient demographics, Child-Pugh scores, and PSG reduction were compared. Patencies were calculated using the Kaplan-Meier method and compared. A total of 126
TIPSs created with stent-grafts were found: 28 with Fluency stents, 93 with Viatorr devices, and 5 combined. No significance in demographic factors or PSGs was found among groups (p > 0.05). Major encephalopathy rates were 3.6 % and 4.3 % in the Fluency and Viatorr groups, respectively (p = 1.000). Hemodynamic success rates were 93 % and 98 % in the Fluency and Viatorr groups, respectively (p = 0.099). The primary unassisted patency rates at 6, 9, and 12 months were 87 %, 81 %, and 81 %, respectively, in the Fluency group and 95 %, 93 %, and 89 %, respectively, in the Viatorr group (p = 0.03). Portal and hepatic end stenoses were the causes of TIPS narrowing in the Fluency and Viatorr groups, respectively. The authors concluded that the Wallstent/Fluency stent combination is associated with a 1-year patency rate greater than 80 %, with no significant difference versus the Viatorr stent regarding technical and hemodynamic success and encephalopathy rate. However, the Viatorr stent is associated with improved patency (89 %) versus this bare stent/stent-graft combination.

In a meta-analysis, Yang et al (2010) compared the patency and clinical outcomes of TIPS with PTFE-covered stent-grafts versus bare stents. Pertinent studies were retrieved through PubMed (1950 to 2010), MEDLINE (1950 to 2010), and reference lists of key articles. Outcome measures were primary patency, risk of encephalopathy and survival. Time-to-event data analysis was used to calculate the overall hazard ratios (HR). A total of 6 studies were identified including a total of 1,275 patients (346 TIPS with PTFE-covered stent-grafts and 929 TIPS with bare stents). Pooled shunt patency data from 4 eligible studies suggested a significant improvement of primary patency in patients who were treated with PTFE-covered stent-grafts (HR = 0.28, 95 % CI: 0.20 to 0.35). Pooled encephalopathy data from 3 eligible studies suggested a significant reduction of risk in the PTFE-covered group (HR = 0.65, 95 % CI: 0.45 to 0.86). Pooled survival data from 4 eligible studies also suggested a significant decrease of mortality in the PTFE-covered group (HR = 0.76, 95 % CI: 0.58 to 0.94). No statistical heterogeneity was observed between studies for either outcome. The authors concluded that this meta-analysis showed that the use of PTFE-covered stent-grafts clearly improves shunt patency without increasing the risk of hepatic encephalopathy and with a trend towards better survival.

Wu et al (2010) examined the outcome of a modified TIPSS (MTIPSS) in the treatment of the BCS. A total of 11 patients with severe BCS were selected for MTIPS treatment -- 3 patients had an acute history (less than 2 months) and 8 had a subacute or a chronic course of the disease. All patients were associated with
variceal bleeding and massive ascites. The diagnosis of BCS was established by duplex sonography, computed tomography scan, magnetic resonance imaging, angiography of hepatic veins and inferior vena cava, and liver biopsy. The shunt was established using conventional self-expandable stents with diameter of 10 cm in all patients. The mean follow-up was 60.55 +/- 42.76 months. The shunt reduced the portosystemic pressure gradient from 30.32 +/- 7.69 to 9.08 +/- 3.43 mmHg and improved the portal flow velocity from 11.24 +/- 2.75 to 52.16 +/- 13.68 cm/s. Clinical symptoms as well as the biochemical test results improved significantly during 3 weeks after shunt treatment except for 1 death caused by hepatic failure. Ten patients are alive without clinical symptoms. Three revisions in 2 patients were needed during the follow-up. The inflation of stenosised shunt was performed in 1 patient, and the inflation of stenosised shunt and the re-implantation of stent in another patient. The other 8 patients had no revisions. The authors concluded that MTIPSS provides an excellent outcome in patients with BCS. It may be regarded as an option for the acute and long-term managements of these patients.

The AASLD's guideline on the role of TIPSS in the management of portal hypertension (Boyer and Haskal, 2005) stated that the decision to create a TIPSS in a patient with BCS should be based on the severity of disease, and only patients with moderate disease appear to be reasonable candidates for a TIPSS. Patients with BCS and mild disease can be managed medically, whereas those with more severe disease or acute hepatic failure are best managed by liver transplantation. Furthermore, the use of TIPSS to treat sinusoidal obstruction syndrome or hepatopulmonary syndrome can not be recommended.

The AASLD's 2009 updated guidelines on the role of TIPS in the management of portal hypertension (Boyer and Haskal, 2010) has the following recommendations:

- The use of TIPS in the management of portal hypertensive gastropathy should be limited to those who have recurrent bleeding despite the use of betablockers. Evidence-II-3.
- TIPS is ineffective in controlling bleeding from gastro antral vascular ectasia in patients with cirrhosis and should not be used in this situation. Evidence-II-3.
- TIPS will decrease the need for repeated large volume paracentesis in patients with refractory cirrhotic ascites. However, given the uncertainty as to the effect of TIPS creation on survival and the increased risk of
encephalopathy, TIPS should be used in those patients who are intolerant of repeated large volume paracentesis. Evidence-I.

- TIPS is effective in the control of hepatic hydrothorax, but it only should be used in patients whose effusion can not be controlled by diuretics and sodium restriction. Evidence-II-3.

- TIPS is of investigatory use for the treatment of HRS, especially type 1, pending the publication of controlled trials. Evidence-II-3.

- The decision to create a TIPS in a patient with Budd-Chiari syndrome should be based on the severity of their disease and only those with moderate disease and who have failed to respond to anticoagulation appear to be reasonable candidates for a TIPS. Evidence-II-3.

- Patients with Budd-Chiari syndrome and mild disease can be managed medically whereas those with more severe disease or acute hepatic failure are best managed by liver transplantation. Evidence-II-3.

- The use of TIPS to treat sinusoidal obstruction syndrome (veno-occlusive disease) can not be recommended. Evidence-II-3.

- The use of TIPS to treat hepatopulmonary syndrome is not recommended. Evidence-II-3.

García-Pagán et al (2010) stated that patients with cirrhosis in Child-Pugh class C or those in class B who have persistent bleeding at endoscopy are at high-risk for treatment failure and a poor prognosis, even if they have undergone rescue treatment with a TIPSS. These researchers evaluated the earlier use of TIPSS in such patients; they randomly assigned, within 24 hours after admission, 63 patients with cirrhosis and acute variceal bleeding who had been treated with vasoactive drugs plus endoscopic therapy to treatment with a PTFE-covered stent within 72 hours after randomization (early-TIPSS group, n = 32) or continuation of vasoactive-drug therapy, followed after 3 to 5 days by treatment with propranolol or nadolol and long-term endoscopic band ligation (EBL), with insertion of a TIPSS if needed as rescue therapy (pharmacotherapy-EBL group, n = 31). During a median follow-up of 16 months, re-bleeding or failure to control bleeding occurred in 14 patients in the pharmacotherapy-EBL group as compared with 1 patient in the early-TIPSS group (p = 0.001). The 1-year actuarial probability of remaining free of this composite end point was 50 % in the pharmacotherapy-EBL group versus 97 % in the early-TIPSS group (p < 0.001). Sixteen patients died (12 in the pharmacotherapy-EBL group and 4 in the early-TIPSS group, p = 0.01). The 1-year actuarial survival was 61 % in the pharmacotherapy-EBL group versus 86 % in the early-TIPSS group (p < 0.001). Seven patients in the pharmacotherapy-EBL
group received TIPSS as rescue therapy, but 4 died. The number of days in the intensive care unit and the percentage of time in the hospital during follow-up were significantly higher in the pharmacotherapy-EBL group than in the early-TIPSS group. No significant differences were observed between the 2 treatment groups with respect to serious adverse events. The authors concluded that in these patients with cirrhosis who were hospitalized for acute variceal bleeding and at high-risk for treatment failure, the early use of TIPSS was associated with significant reductions in treatment failure and in mortality.

In an editorial that accompanied the afore-mentioned study, Afdhal and Curry (2010) state that additional clinical trials of adequate size should be carried out to confirm these findings and to examine the effect of a rapid reduction in portal pressure on disease progression in patients with cirrhosis of other causes.

Qi and colleagues (2014) conducted a meta-analysis to compare the incidence of shunt dysfunction, variceal re-bleeding, encephalopathy, and death between patients treated with TIPS alone and those treated with TIPS combined with variceal embolization. All relevant studies were searched via PubMed, EMBASE, and Cochrane Library databases. Odds ratios (ORs) with 95 % CIs were pooled. Heterogeneity among studies and publication bias were assessed. A total of 6 articles were included in this study. Type of stents was covered (n = 2), bare (n = 2), mixed (n = 1), and unknown (n = 1). Varices were angiographically embolized by coils in 6 studies. Additional liquids agents were employed in 3 studies. Compared with TIPS alone group, TIPS combined with variceal embolization group had a significantly lower incidence of variceal re-bleeding (OR = 2.02, 95 % CI: 1.29 to 3.17, p = 0.002), but a similar incidence of shunt dysfunction (OR = 1.26, 95 % CI: 0.76 to 2.08, p = 0.38), encephalopathy (OR = 0.81, 95 % CI: 0.46 to 1.43, p = 0.47), and death (OR = 0.90, 95 % CI: 0.55 to 1.47, p = 0.68). Neither any significant heterogeneity nor proof of publication bias among studies was found in all meta-analyses. The authors concluded that adjunctive variceal embolization during TIPS procedures might be beneficial in the prevention of variceal re-bleeding. However, they stated that given the heterogeneity of type of stents, embolic agents, type of varices, and indications of variceal embolization among studies, additional well-designed randomized controlled trials with larger sample size and use of covered stents should be warranted to confirm these findings.
Qi et al (2015) performed a meta-analysis to compare the outcomes of TIPS to those of medical/endoscopic therapy for acute variceal bleeding in cirrhotic patients. The PubMed, EMBASE, and Cochrane Library databases were searched for all relevant comparative studies. Odds ratios and HR with 95 % CI were pooled for dichotomous and time-dependent variables, respectively. Subgroup analyses were performed according to the type of study design (randomized or non-randomized studies), source of bleeding (esophageal or gastric varices), type of stent (covered or bare stent), and patient selection (high risk or unselected patients). A total of 6 papers were eligible. Transjugular intrahepatic portosystemic shunt was superior to medical/endoscopic therapy in decreasing the incidence of treatment failure (OR = 0.22; 95 % CI: 0.11 to 0.44), improving overall survival (HR = 0.55; 95 % CI: 0.38 to 0.812), and decreasing the incidence of bleeding-related death (OR = 0.19; 95 % CI: 0.06 to 0.59). Although TIPS did not significantly decrease the incidence of re-bleeding (OR = 0.27; 95 % CI: 0.06 to 1.29), it became significantly greater in the subgroup meta-analyses of randomized studies (OR = 0.09; 95 % CI: 0.03 to 0.32) than in those of non-randomized studies (OR = 0.76; 95 % CI: 0.40 to 1.45; subgroup difference, p = 0.003), and in the subgroup meta-analyses of studies including high-risk patients (OR = 0.06; 95 % CI: 0.01 to 0.23) than in those including low-risk patients (OR = 0.83; 95 % CI: 0.44 to 1.56; subgroup difference, p = 0.0007). In addition, TIPS did not significantly increase the incidence of post-treatment hepatic encephalopathy (OR = 1.37; 95 % CI: 0.63 to 2.99). The authors concluded that with the exception of the benefit of prevention from treatment failure, TIPS with covered stents might improve the overall survival of high-risk patients with acute variceal bleeding.

Deltenre and colleagues (2015) stated that there is conflicting evidence on the benefit of early TIPSS on the survival of patients with acute variceal bleeding (AVB). These researchers evaluated the effect of early TIPSS on patient prognosis. They performed a meta-analysis of studies evaluating early TIPSS in cirrhotic patients with AVB. A total of 4 studies were included. Early TIPSS was associated with fewer deaths [OR = 0.38, 95 % CI: 0.17 to 0.83, p =0.02], with moderate heterogeneity between studies (p = 0.15, I = 44 %). Early TIPSS was not significantly associated with fewer deaths among Child-Pugh B patients (OR = 0.35, 95 CI: 0.10 to 1.17, p = 0.087) nor among Child-Pugh C patients (OR = 0.34, 95 % CI: 0.10 to 1.11, p = 0.074). There was no heterogeneity between studies in the Child-Pugh B analysis (p = 0.6, I = 0 %), but there was a high heterogeneity in the Child-Pugh C analysis (p = 0.06, I = 60 %). Early TIPSS was associated with lower rates of bleeding within 1 year (OR = 0.08, 95 % CI: 0.04 to 0.17, p < 0.001)
both among Child-Pugh B patients, (OR = 0.15, 95 % CI: 0.05 to 0.47, p = 0.001) and among Child-Pugh C patients (OR = 0.05, 95 % CI: 0.02 to 0.15, p < 0.001), with no heterogeneity between studies. Early TIPSS was not associated with higher rates of encephalopathy (OR = 0.84, 95 % CI: 0.50 to 1.42, p = 0.5). The authors concluded that cirrhotic patients with AVB treated with early TIPSS had lower death rates and lower rates of clinically significant bleeding within 1 year compared with patients treated without early TIPSS. Moreover, they stated that additional studies are needed to identify the potential risk factors leading to a poor prognosis after early TIPSS in patients with AVB and to determine the impact of the degree of liver failure on the patient's prognosis.

An UpToDate review on “Transjugular intrahepatic portosystemic shunts: Indications and contraindications” (Sanyal and Bajaj, 2016) states that TIPS should not be used for:

- Correction of hypersplenism and thrombocytopenia
- Portal hypertension associated with polycystic liver disease or Caroli disease
- Pre-hepatic portal hypertension
- Primary prophylaxis of variceal hemorrhage
- Pulmonary hypertension and hepatopulmonary syndrome

Lahat and associates (2018) stated that portal hypertension (PHTN) increases the risk of non-hepatic surgery in cirrhotic patients. This first systematic review analyzed the place of TIPS in preparation for non-hepatic surgery in such patients. Medline, Embase, and Scopus databases were searched from 1990 to 2017 to identify reports on outcomes of non-hepatic surgery in cirrhotic patients with PHTN prepared by TIPS. Feasibility of TIPS and the planned surgery, and the short- and long-term outcomes of the latter were assessed. A total of 19 studies (64 patients) were selected; TIPS was indicated for past history of variceal bleeding and/or ascites in 22 (34 %) and 33 (52 %) patients, respectively. The planned surgery was gastro-intestinal (GI) tract cancer in 38 (59 %) patients, benign digestive or pelvic surgery in 21 (33 %) patients, and others in 4 (6 %) patients. The TIPS procedure was successful in all, with a zero mortality rate. All patients could be operated within a median delay of 30 days from TIPS (mortality rate = 8 %; overall morbidity rate = 59.4 %). One year overall survival (OS) was 80 %. The authors concluded that TIPS allows non-hepatic surgery in cirrhotic patients deemed non-operable due to PHTN. Moreover, they stated that further evidence in larger cohort of patients is essential for wider applicability.
Cirrhosis-Related Chylothorax

Lutz and associates (2013) reported on the case of a 59-year old woman with severe dyspnea due to a large chylothorax. She was known to have liver cirrhosis but no ascites. There was no history of trauma, cardiac function was normal and thorough diagnostic work-up did not reveal any signs of malignancy. In summary, no other etiology of the chylothorax than portal hypertension could be found. Therapy with diuretics as well as parenteral feeding failed to relieve symptoms. After a TIPSS had successfully been placed, pleural effusion decreased considerably. Eight months later, TIPSS revision had to be performed because of stenosis, resulting in remission from chylothorax. This case showed that even in the absence of ascites, chylothorax might be caused by portal hypertension and that TIPSS can be an effective treatment option. However, the authors noted that “The success of the TIPSS placement in this patient confirmed the hepatic origin of the chylothorax. It has been suggested that in liver cirrhosis, chyle flow increases substantially due to increased formation of hepatic lymph and due to portal hypertension. Since drainage into the venous system is limited by a valve at the junction of the thoracic duct and the subclavian vein, pressure in the lymphatic vessels is increased, leading to an elevated risk of spontaneous rupture. Thus, in this patient, such a spontaneous leak might have persisted as long as portal hypertension was high, maintaining the pleural effusion via small gaps in the diaphragm as in hepatic hydrothorax, which occurs in about 5% to 12% of liver cirrhosis patients. A recent review described a clinical response rate of about 70% in 198 patients with hepatic hydrothorax after TIPS placement. However, controlled studies are still missing. No case of chylothorax was described in these patients”.

Tsauo and colleagues (2016) stated that cirrhosis-related chylothorax and chylous ascites are rare conditions. The pathophysiologic mechanism of cirrhosis-related chylous fluid collections is believed to be excessive lymph flow resulting from portal hypertension. These investigators reported the case of a 61-year old man with cirrhosis-related chylothorax treated successfully with a TIPSS. They also performed a systematic review of the literature, which revealed 9 additional cases of chylothorax or chylous ascites treated successfully with a TIPSS. The authors concluded that these cases showed that TIPS creation may be safe and effective for the treatment of chylous fluid collections in patients with cirrhosis. These preliminary findings need to be validated by well-designed studies.

Furthermore, an UpToDate review on “Management of chylothorax” (Heffner, 2016)
does not mention TIPSS as a management tool.

**Covered Stents for Transjugular Intrahepatic Portosystemic Shunt**

In a meta-analysis of randomized controlled trials (RCTs), Qi and co-workers (2017) compared the outcomes of covered stents (CS) versus bare stents (BS) for TIPS. PubMed, Embase, and Cochrane Library databases were searched to identify the relevant RCTs; OS, shunt patency, and hepatic encephalopathy (HE) were the major end-points; HRs with 95 % CIs were calculated. Heterogeneity was calculated. Cochrane risk of bias tool was employed. A total of 119 papers were identified. Among them, 4 RCTs were eligible. Viatorr CS alone, Fluency CS alone, and Viatorr plus Fluency CS were employed in 1, 2, and 1 RCTs, respectively. Risk of bias was relatively low. Meta-analyses demonstrated that the CS group had significantly higher probabilities of OS (HR = 0.67, 95 % CI: 0.50 to 0.90, p = 0.008) and shunt patency (HR = 0.42, 95 % CI: 0.29 to 0.62, p < 0.0001) than the BS group. Additionally, the CS group might have a lower risk of HE than the BS group (HR = 0.70, 95 % CI: 0.49 to 1.00, p = 0.05). The heterogeneity among studies was not statistically significant in the meta-analyses. The authors concluded that compared with BS, CS for TIPS may improve the OS. These researchers stated that in the era of CS, the indications for TIPS may be further expanded.

In a meta-analysis, Triantafyllou and colleagues (2018) reviewed polytetrafluoroethylene-CS grafts versus BS in TIPS procedure. Systematic search of literature databases was done from January 1990 till April 2017, using pre-decided keywords. Outcome measures studied were primary-patency (PP) at 1 year (defined as absence of shunt insufficiency at 1 year), re-bleeding (RE), new-onset HE (new-onset or worsening encephalopathy following the procedure), and survival at 1 year (SU). Odds ratio (OR) was calculated for each outcome variable. Between-study heterogeneity was assessed by the I2 statistics and \( \chi^2 \) Q-test. A total of 14 studies (4 RCTs, 2 prospective non-randomized, and 8 retrospective) were included with 2,519 patients (1,548 patients in BS group and 971 patients in CS group). Three-quarter outcome measures showed significantly better results with CS; PP was pooled from 13 studies and showed an OR = 4.75 (95 % CI: 3.32 to 6.79; p < 0.00001; I2 = 44 %) in favor of CS; RE was pooled from 6 studies with OR = 0.37 (95 % CI: 0.24 to 0.56; p < 0.00001; I2 = 0 %) in favor of CS; SU was pooled from 11 studies with OR = 1.85 (95 % CI: 1.44 to 2.38; p < 0.00001; I2 = 0 %) in favor of CS. On subset analysis for RCTs, 3 outcome variables favored CS with
minimal heterogeneity [PP: OR = 4.18 (95 % CI: 2.66 to 6.55; p < 0.00001; I² = 0 %); RE: OR = 0.43 (95 % CI: 0.25 to 0.72; p < 0.001; I² = 0 %); SU: OR = 1.85 (95 % CI: 1.44 to 2.38, p < 0.00001; I² = 0 %)]; HE showed no difference between 2 stents on the overall and subset pooled analysis. Overall: OR = 0.86 (95 % CI: 0.68 to 1.08; p = 0.19; I² = 4 %). Only RCTs: OR = 0.91 (95 % CI: 0.63 to 1.32, p = 0.63; I² = 0 %).

The authors concluded that CS is associated with better primary patency and survival and lesser rate of re-bleeding than BS in patients undergoing TIPS procedure. Furthermore, there was no difference in new-onset HE.

**Portal Vein Thrombosis**

In a retrospective analysis, Goykhman et al (2010) reviewed their experience with TIPSS and analyzed the results with emphasis on patient selection and indication (conventional versus atypical). All cases were managed by a single-center multi-disciplinary team comprising liver surgery and transplantation, hepatology, imaging, interventional radiology and intensive care). Between August 2003 and December 2009, a total of 34 patients (mean age of 51, range of 27 to 76 years) were treated with TIPSS. The cause of portal hypertension was cirrhosis (n = 23), hyper-coagulability complicated by BCS (n = 6), and acute portal vein thrombosis (PVT; n = 5). Clinical indications for TIPSS included treatment or secondary prevention of variceal bleeding (n = 10), refractory ascites (n = 18), mesenteric ischemia due to acute portal vein thrombosis (n = 5), and acute liver failure (n = 1). Transjugular intrahepatic portosystemic shunt was urgent in 18 cases (53 %) and elective in 16. Three deaths occurred following urgent TIPSS. The overall related complication rate was 32 %: transient encephalopathy (n = 6), ischemic hepatitis (n = 2), acute renal failure (n = 2) and bleeding (n = 1). Long-term results of TIPSS were defined as good in 25 cases (73 %), fair in 4 (12 %) and failure in 5 (15 %). In 3 of 5 patients with mesenteric ischemia following acute portal vein thrombosis, surgery was obviated. Revision of TIPSS due to stenosis or thrombosis was needed in 7 cases (20 %). The authors concluded that TIPSS is safe and effective.

Furthermore, they noted that while its benefit for patients with portal hypertension is clear, the role of TIPSS in treatment of portal-mesenteric venous thrombosis needs further evaluation.

Valentin and colleagues (2018) stated that the role of TIPS in the management of PVT remains controversial. These investigators performed a systematic review and meta-analysis to examine the role of TIPS for the management of PVT in adult patients with liver disease. Multiple databases were searched through April 2017.
Data were gathered to estimate the rates of technical success, portal vein re-canalization, portal patency, HE, and mean change in portal pressure gradient in patients with PVT who underwent TIPS; estimates were pooled across studies using the random effects model. A total of 18 studies were included in the analysis. The pooled technical success rate was 86.7 % [95 % CI: 78.6 to 92.1 %]. Rate of portal vein re-canalization was 84.4 % (95 % CI: 78.4 to 89.0 %). The rate of complete re-canalization was 73.7 % (95 % CI: 64.3 to 81.3 %). Portal patency was 86.9 % (95 % CI: 79.7 to 91.8 %). Mean change in portal pressure gradient was 14.5 mmHg (95 % CI: 11.3 to 17.7 mmHg); HE was 25.3 % (95 % CI: 19.2 to 32.6 %). The number of major adverse events (AEs) reported across studies was low. The majority of the analyses were not associated with substantial heterogeneity. The authors concluded that the use of TIPS in the management of PVT was feasible and effective in achieving a significant and sustainable reduction in clot burden with a low risk of major complications; and TIPS should be considered as a viable therapeutic option in patients with PVT. Moreover, these researchers stated that given the limited amount of randomized, comparative studies reported, additional studies are needed to evaluate the safety and efficacy of TIPS as a treatment modality in PVT, in comparison to other therapeutic options, such as anti-coagulation.

Prevention of Re-Bleeding in Cirrhotic Individuals with Cavernous Transformation of the Portal Vein

Zuo and associates (2019) examined the role of early overt HE (OHE) as a clinical marker of prognosis in cirrhosis with a TIPS and evaluated the relationship between recurrence of OHE and survival after TIPS. From January 2012 to December 2013, a retrospective study of consecutive patients with cirrhosis and a TIPS was performed at a single institution. A total of 304 patients (196 men; mean age of 52 years) were enrolled during the study period. The mean MELD score was 11.6; and time-dependent Cox regression was applied to estimate the predictive ability of early OHE (within 3 months after TIPS) and the effect of its frequency on survival. During a median follow-up of 28.3 months, 115 patients experienced OHE after the TIPS procedure; of these, 54 had at least 2 OHE episodes. Long-term survival worsened in patients with early OHE (HR = 2.75; 95 % CI: 1.75 to 4.32; p < 0.001). When early OHE was further divided into early-recurrent and single OHE, death was more common in patients with early-recurrent OHE (p < .001) than in patients with early-single OHE (p = 0.24). After adjustment by MELD score, ascites, serum albumin, indication for TIPS, and age, patients with early-recurrent OHE had a
lower probability of survival (HR = 2.91; 95% CI: 1.04 to 4.89; p < 0.001). Furthermore, landmark and propensity score analyses confirmed the predictive value of early-recurrent OHE. The authors concluded that early recurrence of OHE was associated with an increased risk of mortality for patients with cirrhosis who underwent TIPS.

Li and colleagues (2019) compared the effectiveness of TIPS and endoscopic variceal ligation (EVL) plus propranolol in reducing re-bleeding and improving survival rate in cirrhotic patients with cavernous transformation of the portal vein (CTPV). Cirrhotic patients with CTPV and variceal bleeding history treated for a second prophylaxis of recurrent variceal bleeding between June 2010 and July 2016 were identified and classified based on the treatment that they received (TIPS or EVL + propranolol). Patients’ demographics and clinical data were recorded. The PRISM method was applied to compare the re-bleeding and long-term survival rate. A total of 51 patients were included, 25 of them were treated with TIPS and 26 received EVL + propranolol during the study period. The mean follow-up duration was 21 months in the TIPS group (range of 1 to 47 month) and 27 months in the EVL + propranolol group (range of 6 to 73 month). The recurrent variceal bleeding free probability was increased remarkable in the TIPS group compared with the EVL + propranolol group (p = 0.047); 3 (14.29%) patients died in the TIPS group, and 1 (3.85%) in the EVL + propranolol group; however, there were no significant differences in the survival rate (p = 0.305); and HE occurred in 14.29% (3 of 21) of patients in the TIPS group, and 3.85% (1 of 26) in the EVL + propranolol group (p = 0.202). The authors concluded that the effectiveness of TIPS appeared to be greater in preventing re-bleeding in patients with CTPV comparing with EVL + propranolol in on this study, without improving survival. The higher rate of HE in the TIPS group was a concern; these findings need to be further investigated.

An UpToDate review on chronic portal vein thrombosis in adults (Sanyal, et al., 2019) stated: "Transjugular intrahepatic portosystemic shunting (TIPS) has been shown to be technically feasible in some cases of extrahepatic portal vein thrombosis, such as patients without cavernous transformation in whom the thrombosed vein can be accessed, dilated, and stented, and it may be considered in selected cases with symptoms related to portal hypertension that fail to respond to other treatments. However, the ability to adequately decompress the portal vein is unpredictable. In addition, although TIPS may be technically feasible in patients..."
with cavernous transformation, it is unlikely to adequately decompress the liver. When performed, it is advisable to perform a thorough assessment for prothrombotic states and consider anticoagulation after the bleeding is controlled."

Appendix

Selection Criteria of TIPSS for the Treatment of Varices and Ascites

Aetna considers transjugular intrahepatic portosystemic shunt (TIPSS) medically necessary in members who meet any of the following criteria:

- Surgery is contraindicated and the member requires bleeding control from varices; or
- The member has failed sclerotherapy and has acute bleeding from varices; or
- The member has failed sclerotherapy and has had 2 or more episodes of re-bleeding requiring a transfusion during a 2-week period; or
- The member has severe debilitating ascites or hepatic hydrothorax refractory to medical management (e.g., oral diuretics and sodium restriction; and repeated large-volume paracentesis); or
- The member is a liver transplant candidate who requires bleeding control from varices.

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>
</tr>
</thead>
<tbody>
<tr>
<td>37182</td>
<td>Insertion of transvenous intrahepatic portosystemic shunt(s) (TIPS) (includes venous access, hepatic and portal vein catheterization, portography with hemodynamic evaluation, intrahepatic tract formation/dilatation, stent placement and all associated imaging guidance and documentation)</td>
</tr>
</tbody>
</table>
Revision of transvenous intrahepatic portosystemic shunt(s) (TIPS) (includes venous access, hepatic and portal vein catheterization, portography with hemodynamic evaluation, intrahepatic tract recanalization/dilatation, stent placement and all associated imaging guidance and documentation)

HCPCS codes covered if selection criteria are met:

C1874  Stent, coated/covered, with delivery system [PTFE coated]
C1875  Stent, coated/covered, without delivery system [PTFE coated]

ICD-10 codes covered if selection criteria are met:

I82.0  Budd-Chiari syndrome [moderate with failed response to anticoagulation] [not covered for sinusoidal obstruction syndrome or veno-occlusive disease]
I85.00  Esophageal varices without bleeding
I85.01  Esophageal varices with bleeding [not covered for prophylaxis of variceal hemorrhage]
I85.10  Secondary esophageal varices without bleeding
I85.11  Secondary esophageal varices with bleeding [not covered for prophylaxis of variceal hemorrhage]
I86.4  Gastric varices
I86.8  Varicose veins of other specified sites
J90  Pleural effusion, not elsewhere classified [hepatic hydrothorax]
K31.89  Other diseases of stomach and duodenum [portal hypertensive gastropathy with recurrent bleeding despite the use of beta-blockers]
K64.0 - K64.9  Hemorrhoids and perianal venous thrombosis
K74.0  Hepatic fibrosis
K74.3 - K74.69  Other and unspecified cirrhosis of liver
K76.6  Portal hypertension
K92.0  Hematemesis
K92.1  Melena
K92.2  Gastrointestinal hemorrhage, unspecified
R18.0 - R18.8  Ascites

ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>D69.3 - D69.6</td>
<td>Thrombocytopenia</td>
</tr>
<tr>
<td>D73.1</td>
<td>Hypersplenism</td>
</tr>
<tr>
<td>I27.20 - I27.29</td>
<td>Other secondary pulmonary hypertension</td>
</tr>
<tr>
<td>I27.2</td>
<td>Other secondary pulmonary hypertension</td>
</tr>
<tr>
<td>I81</td>
<td>Portal vein thrombosis [portal-mesenteric venous thrombosis]</td>
</tr>
<tr>
<td>I89.8</td>
<td>Other specified noninfective disorders of lymphatic vessels and lymph nodes</td>
</tr>
<tr>
<td></td>
<td>[cirrhosis-related chylothorax]</td>
</tr>
<tr>
<td>K31.811</td>
<td>Angiodysplasia of stomach and duodenum with bleeding [with cirrhosis]</td>
</tr>
<tr>
<td>K55.011 - K55.1</td>
<td>Acute and chronic vascular disorders of intestine [portal-mesenteric venous thrombosis]</td>
</tr>
<tr>
<td>K76.5</td>
<td>Hepatic veno-occlusive disease [Sinusoidal obstruction syndrome]</td>
</tr>
<tr>
<td>K76.6</td>
<td>Portal hypertension</td>
</tr>
<tr>
<td>K76.7</td>
<td>Hepatorenal syndrome</td>
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<tr>
<td>K76.81</td>
<td>Hepatopulmonary syndrome</td>
</tr>
<tr>
<td>Q44.6</td>
<td>Cystic disease of liver [Caroli disease]</td>
</tr>
<tr>
<td>Z76.82</td>
<td>Awaiting organ transplant status [preoperative reduction in portal hypertension before liver transplantation]</td>
</tr>
</tbody>
</table>

The above policy is based on the following references:


05/31/2019


70. Sanyal AJ. Chronic portal vein thrombosis in adults: Clinical manifestations, diagnosis, and management. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed January 2019.


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Amendment to
Aetna Clinical Policy Bulletin Number: Transjugular Intrahepatic Portosystemic Shunt (TIPSS)

There are no amendments for Medicaid.