Policy: To ensure that the selection criteria are consistently followed and documented. Meridian Health Plan (MHP) considers liver transplantation medically necessary for the indications listed below. Indications for liver transplant include irreversible liver dysfunction or the general effects of liver dysfunction after alternative medical or surgical treatments have been utilized and where the benefits of transplantation outweigh the risk of alternative modalities. Because liver transplantation has a 10% to 15% mortality rate during the first year post transplantation, only patients who are projected to survive less than 2 years because of their chronic liver disease should be considered for transplantation.

Procedure: Social and environmental variables, adherence history, poor understanding of illness and the transplant process, certain diagnosed mental illnesses, personality disorders and other psychological factors may represent relative contraindications to transplant, and members with any of these risk factors must receive psychiatric assessment. Any minor presenting with relative or absolute contraindication to transplant must receive psychiatric pre-transplant assessment. All candidates for transplant should be free of:

1. Systemic of uncontrolled infection including sepsis.
2. Significant uncorrectable life-limiting medical conditions other than those treated by liver transplant.
3. Severe end stage organ damage including diabetes with end organ damage, irreversible severe pulmonary disease, with FEV1<1 L or FVC <50%, irreversible severe renal disease.

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4. Active untreated or untreatable malignancy
5. Irreversible, severe brain damage
6. Active alcoholism and substance abuse, There should be 6 months of documented abstinence through participation in a structured alcohol/substance abuse program with regular meeting attendance and negative random drug testing,
7. Emotional instability, significant depression or other psychiatric illness that cannot be controlled that would impact on ability to comply with a complex evaluation process, surgical procedure and post-transplant plan of care.
8. dementia, memory loss or cognitive disability that would impact on ability to comply with transplant requirements (unless there is a representative/guardian/conservator)
9. Lack of psychological support as indicated by either no identified caregiver or an uncommitted caregiver. This includes lack of transportation, inability to adhere to transplant program requirements
10. Lack of sufficient financial means to purchase post-transplant medications.
11. non remediated non-compliance
12. Inability to give informed consent, unless there is an authorized guardian
13. limited irreversible rehabilitative potential
14. Post-transplant lymphoproliferative disease, unless no active disease is demonstrated by PET scan, CT scan or MRI.

**Medically Necessary Indications:** MHP considers orthotopic (normal anatomical position) liver transplantation (with cadaver organ, reduced-size organ, living related organ, and split liver) medically necessary for members with end-stage liver disease (ESLD) due to any of the following conditions.

1. Cholestatic diseases:
   a. Biliary atresia *
   b. Primary biliary cirrhosis
   c. Primary sclerosing cholangitis with development of secondary biliary cirrhosis
   d. Nonalcoholic Steatohepatitis (NASH)
2. Hepatocellular diseases:
   a. Alcoholic cirrhosis
   b. Chronic active hepatitis with cirrhosis (hepatitis B or C) *
   c. Idiopathic autoimmune hepatitis *
   d. Cryptogenic cirrhosis
3. Malignancies:
   a. Primary hepatocellular carcinoma confined to the liver when all of the following criteria are met:
      i. Member is not a candidate for subtotal liver resection; and
      ii. Member meets criteria for a single tumor that is less than or equal to 5 cm or two/three tumors that are less than or equal to 3 cm each. Tumors can be downstaged with hepatic artery chemoembolization with or without radiofrequency ablation. If successfully downstaged to be within Milan criteria, the tumor(s) must meet the Milan criteria after the downstaging procedure, as assessed by imaging requirements, and there will be a minimum time-out or

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observation period of 3 months from the date on which imaging is documented to meet the Milan Criteria before eligibility for transplant is approved and

iii. There is no macrovascular involvement, and

iv. There is no identifiable extrahepatic spread of tumor to surrounding lymph nodes, abdominal organs, bone or other sites.

Milan Selection Criteria:
1. Not a candidate for a subtotal hepatic resection
2. Tumor is HCC state II (T2, one nodule 2.0-5.0 cm; two or three nodules, all <3.0cm
3. No macrovascular involvement, no extrahepatic spread.

b. Special consideration may be given to Hepatocellular carcinoma, T2 lesion, eligible for MELD exception points.

c. Hepatocellular carcinoma that has been “downstaged”. (Pomfret et al, Yao et al and Ravaioili et al)
  i. The inclusion criteria for downstaging should be a single tumor < 8 cm or 2 to 3 tumors, each < 5 cm, with a total tumor diameter < 8 cm and no vascular invasion by imaging criteria.
  ii. The criteria for successful downstaging should be as follows:
      a. The tumor must meet the Milan Criteria after the downstaging procedure(s), as assessed by imaging requirements for priority listing and maintaining listing for liver transplant every 3 months.
      b. Successful downstaging also requires a significant decrease in the AFP level to <500 ng/ml for those patients with an initial AFP level > 1000 ng/ml.
  iii. There will be a minimum time-out or observation period of 3 months from the date on which the imaging is documented to meet the Milan Criteria before eligibility for active priority listing.
  iv. Those with acute hepatic decompensation after downstaging procedures are not eligible for transplant unless they meet the above criteria.

d. Hepatoblastoma in children (less than 18 years old) when all of the following criteria are met: *
   i. Member is not a candidate for subtotal liver resection; and
   ii. There is no identifiable extrahepatic spread of tumor to surrounding lungs, abdominal organs, bone or other sites
   iii. Children with Hepatoblastoma will be given PELD score exception.

4. Vascular diseases:
   a. Budd-Chiari syndrome

5. Metabolic disorders and metabolic liver diseases with cirrhosis
   a. Alpha 1-antitrypsin deficiency *
   b. Hemochromatosis
   c. Inborn errors of metabolism: *
      Tyrosinemia
      Galactosemia
      Fatty acid metabolism—Zellweger syndrome
      Glycogen storage disease type IV
      Alpha -1 antitrypsin deficiency
      Niemann-Pick disease type c
   d. Wilson's disease *
   e. Protoporphyria
   f. Primary Oxaluria
6. Miscellaneous
   a. Toxic reactions (fulminant hepatic failure due to poisonings: Mushroom, acetaminophen, etc.) *
   b. Hepato-pulmonary syndrome --when the following selection criteria are met:
      i. Arterial hypoxemia (PaO2 less than 60 mm Hg or AaO2 gradient greater than 20 mm Hg in supine or standing position); and
      ii. Chronic liver disease with non-cirrhotic portal hypertension; and
      iii. Intrapulmonary vascular dilatation (as indicated by contrast-enhanced echocardiography, technetium-99 macroaggregated albumin perfusion scan, or pulmonary angiography).

7. Re-transplantation—MHP considers re-transplantation following a failed liver transplant medically necessary if the initial transplant was performed for a covered indication or medical diagnosis.
   * Denotes diagnoses most commonly associated with indications for pediatric transplant.

**General required criteria for potential recipients:**

1. Less than 70 years of age
2. No advanced cardiopulmonary disease
3. Absence of significant systemic infection or disease
4. Good nutritional status
5. Adequate support systems
6. Adequate psychosocial profile
7. No evidence of current dependence on alcohol (6 months) or illicit substances (6 months). In order to ensure the best outcomes, blood or urine testing will be undertaken between evaluation and procurement phase with documented evidence of ongoing compliance with abstinence of these substances, as well as the member’s plan of care, routine preventative visits and disease management. If there is evidence of alcohol or illicit substance abuse it will be required that the member has weekly substance abuse/dependence support group and/or participation in an outpatient treatment program. Member is required to have successful completion of the program and/or support group.
8. No evidence of extra-hepatic malignancy with the exclusion of carcinoma in situ of the cervix and squamous cell skin cancer
9. No evidence of metastatic hepatobiliary malignancy
10. No evidence of permanent brain damage
11. Absence of HIV infection, as defined by all of the following:
    a. CD4 count greater than 200 cells/mm3 for more than 6 months; and
    b. HIV-1 RNA (viral load) undetectable; and
    c. On stable anti-viral therapy for more than 3 months; and
    d. No other complications from AIDS, such as opportunistic infection (e.g., aspergillus, coccidiomycosis, resistant fungal infections, tuberculosis), Kaposi’s sarcoma or other neoplasm.
12. MELD (age greater than 12) score or PELD (age less than 12) score greater than or equal to 15
   **(MELD/PELD exception points may be given for the presence of hepatopulmonary syndrome, hyponatremia, primary oxaluria, Familial Amyloidosis, combined liver/intestine transplant, children with Hepatoblastoma, children with urea cycle disorders and organic academia, children in need of combined liver/intestine transplant)**
13. Nonsmoker for 6 months with documentation through physician certification and/or negative cotinine urine test
14. Ability to give and understand informed consent for the procedure by the member or patient’s healthcare proxy otherwise the non-comprehension will be considered a contraindication

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* (Ward, Slutsker, Buehler, Jaffe, Berkelman, & Curran, 1992)
**Model for End-Stage Liver Disease (MELD score)** = 3.78(serum albumin in mg/dl) + 11.2(INR) + 9.57 (serum creatinine in mg/dl) + 6.43.

**Pediatric End-Stage Liver Disease (PELD score)** = 4.08(serum bilirubin) + 18.57(INR) – 6.87(albumin in g/dl) + 4.36(if <1 year old) + 6.67(growth failure).

Members with A MELD or PELD score < 15 may be considered when Hepatocellular carcinoma that meets the Milan selection criteria is present, hepatopulmonary syndrome, primary oxaluria, familial Amyloidosis, combined liver/intestine transplant, children with hepatoblastoma, children with urea cycle disorders and organic academia, children in need of combined liver/intestine transplant

**Liver Transplant evaluation:** The transplantation evaluation is typically started once a patient has a MELD score >10. This permits the patient to meet the transplantation team prior to developing end-stage liver disease and ensures adequate time for the patient to complete the pretransplantation evaluation.

**Contraindications:** MHP considers liver transplantation experimental and investigational for members with any of the following absolute contraindications to liver transplantation:

1. Active sepsis outside the biliary tract
2. Other effective medical treatments or surgical options are available
3. Presence of significant organ system failure other than kidney, liver or small bowel.
4. Malignancy outside the liver
5. Metastatic hepatobiliary malignancy
6. Advanced cardiopulmonary disease: severe valvular disease complicated by severe pulmonary hypertension; alcoholic cardiomyopathy; aortic stenosis with LV dysfunction; coronary artery disease uncorrected or with residual LV dysfunction are all contraindications.
7. Severe hypoxemia due to right to left shunts with the exception of hepatopulmonary syndrome: (PaO2 less than 60 mm Hg or AaO2 gradient greater than 20 mm Hg in supine or standing position)
8. Psychologically unsuitable/lack of adequate support or understanding (patients who present with liver failure as the result of a deliberate and sincere suicide attempt are not considered appropriate candidates)
9. Irreversible brain damage
10. Morbid obesity with BMI > 40

**Additional Selection Criteria:** Transplant will not be approved if any one of the following indicators of non-compliance are observed or documented:

1. For members with a history of tobacco use, if the member fails or refuses to submit to monthly cotinine testing for the preceding 6 months prior to the transplant and while listed, or refuses to actively and continuously participate in an accepted smoking cessation program.
2. For members with a history of alcohol abuse, member fails or refuses to submit to testing for alcohol use. Absence of documentation showing member has not engaged in alcohol use for at least six months prior to transplant and monthly while listed.
3. For members with a history of illicit drug use, member fails or refuses to submit to testing for illegal drug use. Absence of documentation showing member has not engaged in illegal drug use for at least six months prior to transplant and monthly while listed.
4. Tobacco, Alcohol and Drug Addiction: Refusal or failure to participate in available addiction interventions for actively using members must be documented in non-compliance determinations.
5. Documentation of non-impactable social issues that substantially increase the risks of an adverse outcome of the medical therapy or transplant at issue
6. Severely Mentally Ill Adults and Severely Emotionally Disturbed Minors: Non-adherence to psychotropic medications or medical regimen in SMI or SED members for whom core symptoms include lack of insight into illness, must be assessed for adequacy of and engagement with psychosocial resource supports in Care Coordination prior to non-compliance determinations.

7. Developmental or Acquired Cognitive Impairment and Dementia: Psychosocial and guardianship support as well as reversibility of impairment must be assessed and documented prior to non-compliance determinations.

See special instructions for additional Medicaid contraindications

**Labs to confirm the diagnosis was well as exclude other diagnoses:**

**Confirm diagnosis:**
- Alpha fetoprotein
- Alpha 1 antitrypsin
- ANA
- Anti-Liver kidney microsomal
- Anti-mitochondrial antibody
- Anti-smooth muscle antigen

**Ensure Success of Transplant:**
- Albumin
- Amylase/lipase
- Bilirubin
- Blood type
- CBC
- CEA
- CMV
- Cholesterol
- CPK
- EBV
- GGT
- Ferritin, Iron and binding capacity
- Hepatitis A antibody
- Hepatitis B surface antibody
- Hepatitis B and C
- Thyroid studies
- Ceruloplasmin
- Herpes simplex virus
- HIV
- LDH
- Liver profile
- Phosphorus
- PT, PTT, INR
- PSA all males (yearly)
- RPR
- Varicella antibodies (IgG)
- Basic Chem Panel: Lytes, bun, creatinine, glucose, calcium
- Magnesium

Laboratory tests to be done at least every 3 months include: electrolytes, creatinine, CBC, alpha fetoprotein, bilirubin, albumin, PT, INR

**Other screening tests:**
- CXR
- EKG
- MRI or CT of abdomen to evaluate the liver for vascular patency and exclude hepatic malignancy, providing the creatinine is normal. (every 6 months)
- Baseline renal ultrasound
- Mammograms on women age 40 or older or with a family history of breast cancer (yearly)
- EGD
- Full colonoscopy on all patients 50 years of age or older
- Recent PAP/pelvic exam for all females (yearly)
- ABGs
- Dobutamine ECHO and other studies to exclude CAD and pulmonary hypertension (yearly)
- Dental exam to evaluate for oral cancer and to determine if further action is required to remove diseased teeth.
- Patients with a diagnosis of hepatocellular cancer will also routinely undergo a Chest CT (every 6 months)
Special Instructions:

Medicaid/All:
Member must follow MHP’s Member Compliance Policy I.07

Contraindications:
1. History of multiple suicide attempts
2. Current suicidal ideation
3. Liver failure as the result of a deliberate and sincere suicide attempt (adults)
4. Dementia

Medicaid/Iowa:
Coverage for liver transplantation will be provided under the following circumstances:
1. Persons with extrahepatic biliary atresia or any other form of end-stage liver disease;
2. Coverage is not provided for persons with a malignancy extending beyond the margins of the liver

Line of Business Applicability:
For Medicaid/Medicaid Expansion Plan members, this policy will apply. Coverage is based on medical necessity criteria being met and the codes being submitted and considered for review being included on either the Michigan Medicaid Fee Schedule (located at: http://www.michigan.gov/mdch/0,1607,7-132-2945,42542,42543,42546,42551-159815--,00.html), the Illinois Medicaid Fee Schedule (located at: http://www.illinois.gov/hfs/MedicalProviders/MedicaidReimbursement/Pages/default.aspx), or the Iowa Medicaid Fee Schedule (located at: http://dhs.iowa.gov/ime/providers/csrf/fee-schedule). If there is a discrepancy between this policy and either the Michigan Medicaid Provider Manual (located at: http://www.michigan.gov/mdch/0,1607,7-132-2945,5100-87572--,00.html), the Illinois Medicaid Provider Manual (located at: http://www.illinois.gov/hfs/MedicalProviders/Handbooks/Pages/default.aspx), or the Iowa Medicaid Provider Manual (located at: http://dhs.iowa.gov/policy-manuals/medicaid-provider) the applicable Medicaid Provider Manual will govern.

For Medicare members, coverage is determined by the Centers for Medicare and Medicaid Services (CMS). If a coverage determination has not been adopted by CMS, this policy applies. Medicare Fee Schedules can be found on the CMS website (https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/FeeScheduleGenInfo/index.html).

For Exchange members, please refer to the Meridian Choice Certificate of Coverage located here: https://share13.mhplan.com/sites/communications/Bronson%20Healthcare/MCH%20Certificate%20of%20Coverage%202016.pdf. If there is a discrepancy between this policy and the Certificate of Coverage for Meridian Choice, the Certificate will govern.

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<tr>
<th>Approved by:</th>
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<tr>
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<tr>
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<tr>
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References:
6. Michigan Department of Community Health, Medicaid Provider Manual- Hospital, Sec. 3.22, p. 25-27 (Version Date April 1, 2015)
8. State of Iowa Department of Human Services (DHS), Medicaid Provider Manual, Physician Services- Chapter III. Provider Specific Policies. Pg. 52. (Version Date: July 1, 2014)