OPTN/UNOS Policy Notice Changes to HCC Criteria for Auto Approval

Sponsoring Committee: **Liver and Intestinal Organ Transplantation**
Policy/Bylaws Affected: **Policy 9.3.F: Candidates with Hepatocellular Carcinoma (HCC)**
Public Comment: **August 2016**
Effective Date: **Upon implementation and notice to members**

Problem Statement

The model for end-stage liver disease (MELD) allocation policy provides "exception" scores for patients with hepatocellular carcinoma (HCC). Candidates with a MELD score exception for HCC receive increased priority on the liver waiting list. Therefore, policy must appropriately balance prioritization between HCC candidates and non-HCC candidates, as well as prioritization among HCC candidates.

Current HCC exceptions policy does not adequately filter HCC candidates whose characteristics indicate poor post-transplantation outcomes. Current policy excludes candidates outside the T2 definition of lesions from automatic exception points. There is, however, a subset of HCC candidates within T2 (specifically those with a high alpha-fetoprotein (AFP)) that exhibits characteristics suggesting a high probability of post-transplant recurrence or mortality.

Current policy excludes candidates that initially present outside of automatic approval criteria, but could benefit from transplant. The downstaging of HCC lesions involves decreasing the size of the lesion using local-regional treatment, specifically to reach the eligibility criteria for liver transplant. Data suggests that HCC candidates successfully downstaged to within T2 exhibit a low rate of HCC recurrence and have excellent post-transplant survival, comparable to those meeting T2 without downstaging. Current policy does not describe eligibility criteria for candidates suitable for HCC downstaging through local-regional treatment.

Summary of Changes

This proposal contains two primary policy changes:

1. Candidates with lesions meeting T2 criteria but with an AFP greater than 1000 are not initially eligible for a standardized MELD exception. If these lesions fall below 500 after local-regional therapy, the candidate is eligible for a standardized MELD exception. Candidates with an AFP level greater than or equal to 500 at any time following local-regional therapy will be referred to the review board.
2. The policy addition describes the eligibility criteria for being included in the downstaging protocol. Candidates meeting the criteria will be eligible for automatic priority after they've had local-regional treatment, and if their residual lesions fall within T2 criteria.

The transplant program will be required to submit an updated exception request at the time of extension indicating that their candidate still meets the initial eligibility criteria. This ensures that at the time of extension, their candidate continues to meet the criteria that initially qualified them for MELD exception points.

Current policy contains recommendations on the imaging characteristics used for CT scans and MRIs performed for a HCC MELD or PELD score exception. We will remove those recommendations from policy and add them to the forthcoming HCC guidance document.

What Members Need to Do

Transplant hospitals need to be aware of the new criteria for automatic approval of HCC exception requests.

Affected Policy Language:

New language is underlined (example) and language that is removed is struck through (~~example~~).

9.3.F Candidates with Hepatocellular Carcinoma (HCC)

~~Upon submission of the required information to the OPTN Contractor, candidates with Hepatocellular Carcinoma (HCC) that have stage T2 lesions and meet the criteria according to *Policies 9.3.F.i* through *vi* below will be listed at their calculated MELD or PELD score.~~
Upon submission of the first exception request, a candidate that is:

- At least 18 years old with Hepatocellular Carcinoma (HCC) and meets the criteria according to Policies *9.3.F.i* through *vi* will receive a MELD score according to *Table 9-4: Exception Score Assignment for Candidates at least 18 Years Old upon Submission of Initial Exception Request*.
- Twelve to 17 years old, and the Regional Review Board (RRB) has determined that the candidate's calculated MELD score does not reflect the candidate's medical urgency, will be listed at a MELD score of 28.
- Less than 12 years old, and the RRB has determined that the candidate's calculated MELD score does not reflect the candidate's medical urgency, will be listed at a PELD score of 41.

9.3.F.~~i~~ii Initial Assessment ~~for Registration~~ and Requirements for HCC Exception Requests

Prior to applying for a standardized MELD exception, the candidate must undergo a thorough assessment that includes *all* of the following:

1. An evaluation of the number and size of ~~tumors~~ lesions before local-regional therapy that meet Class 5 criteria using a dynamic contrast enhanced computed tomography (CT) or magnetic resonance imaging (MRI)
2. ~~A CT or MRI to rule out any extrahepatic spread or macrovascular involvement~~ A CT of the chest to rule out metastatic disease
3. ~~A CT of the chest to rule out metastatic disease~~ A CT or MRI to rule out any other sites of extrahepatic spread or macrovascular involvement
4. An indication that the candidate is not eligible for resection
5. An indication whether the candidate has undergone local-regional therapy
~~5~~6. The candidate's alpha-fetoprotein (AFP) level

The transplant hospital must maintain documentation of the radiologic images and assessments of all OPTN Class 5 lesions in the candidate's medical record. If growth criteria are used to classify a lesion as HCC, the radiology report must contain the prior and current dates of imaging, type of imaging, and measurements of the lesion.

For those candidates who receive a liver transplant while receiving additional priority under the HCC exception criteria, the transplant hospital must submit the *Post-Transplant Explant Pathology Form* to the OPTN Contractor within 60 days of transplant. If the pathology report does not show evidence of HCC, the transplant hospital must also submit documentation or imaging studies confirming HCC at the time of assignment. The Liver and Intestinal Organ Transplantation Committee will review a transplant hospital when more than 10 percent of the HCC cases in a one-year period are not supported by the required pathologic confirmation or submission

of clinical information.

9.3.F.ii Eligible Candidates Definition of T2 Lesions

~~Stage T2 lesions include *any* of the following:~~ Candidates who initially present with T2 HCC lesions are eligible for a standardized MELD exception if they have an alpha-fetoprotein (AFP) level less than 1000 ng/mL and *either* of the following:

- One lesion greater than or equal to 2 cm and less than or equal to 5 cm in size.
- Two or three lesions each greater than or equal to 1 cm and less than or equal to 3 cm in size.

9.3.F.iii Lesions Eligible for Downstaging Protocols

Candidates are eligible for inclusion in a downstaging protocol if they initially present with lesions that meet *one* of the following criteria:

- One lesion greater than 5 cm and less than or equal to 8 cm
- Two or three lesions each less than 5 cm and a total diameter of all lesions less than or equal to 8 cm
- Four or five lesions each less than 3 cm and a total diameter of all lesions less than or equal to 8 cm

For candidates who meet the downstaging criteria and then complete local-regional therapy, their residual lesions must subsequently meet the requirements for T2 lesions according to *Policy 9.3.F.ii: Eligible Candidates Definition of T2 Lesions* to be eligible for a standardized MELD exception. Downstaging to meet eligibility requirements for T2 lesions must be demonstrated by CT or MRI performed after local-regional treatment. Candidates with lesions that do not initially meet the downstaging protocol inclusion criteria who are later downstaged and then meet eligibility for T2 lesions are not automatically eligible for a standardized MELD exception and must be referred to the RRB for consideration of a MELD exception.

9.3.F.iv Candidates with Alpha-fetoprotein (AFP) Levels Greater than 1000

Candidates with lesions meeting T2 criteria according to *Policy 9.3.F.ii Eligible Candidates Definition of T2 Lesions* but with an alpha-fetoprotein (AFP) level greater than 1000 ng/mL may be treated with local-regional therapy. If the candidate's AFP level falls below 500 ng/mL after treatment, they are eligible for a standardized MELD exception. Candidates with an AFP level greater or equal to 500 ng/mL following local-regional therapy at any time must be referred to the RRB for consideration of a MELD exception.

9.3.F.~~iii~~iv Requirements~~commended Minimum Specifications~~ for Dynamic Contrast-enhanced CT or MRI of the Liver

CT scans and MRIs performed for a Hepatocellular Carcinoma (HCC) MELD or PELD score exception ~~application~~ request ~~should meet the criteria in Table 9-3 and Table 9-4 and~~ must be interpreted by a radiologist at a transplant hospital. If the scan is inadequate or incomplete then the lesion will be classified as OPTN Class 0 and imaging must be repeated or completed to receive an HCC MELD~~/~~ or PELD exception.

Table 9-3: Recommendations for Dynamic Contrast-enhanced CT of the Liver

Feature:	CT scans should meet the below specifications:
Scanner type	Multidetector row scanner
Detector type	Minimum of 8 detector rows and must be able to image the entire liver during brief late arterial phase time window
Slice thickness	Minimum of 5 mm reconstructed slice thickness; thinner slices are preferable especially if multiplanar reconstructions are performed
Injector	Power injector, preferably dual chamber injector with saline flush and bolus tracking recommended
Contrast injection rate	3 mL/sec minimum, better 4-6 mL/sec with minimum of 300 mg I/mL or higher, for dose of 1.5 mL/kg body weight
Mandatory dynamic phases on contrast-enhanced MDCT	1. Late arterial phase: artery fully enhanced, beginning contrast enhancement of portal vein 2. Portal venous phase: portal vein enhanced, peak liver parenchymal enhancement, beginning contrast enhancement of hepatic veins 3. Delayed phase: variable appearance, greater than 120 seconds after initial injection of contrast
Dynamic phases (Timing)	Use the bolus tracking or timing bolus

Table 9-4: Recommendations for Dynamic Contrast-enhanced MRI of the Liver

Feature	MRIs should meet the below specifications:
Scanner type	1.5T Tesla or greater main magnetic field strength. Low field magnets are not suitable.
Coil type	Phased array multichannel torso coil, unless patient-related factors precludes its use.
Minimum sequences	Pre-contrast and dynamic post gadolinium T1-weighted gradient echo sequence (3D preferable), T2 (with and without fat saturation), T1-weighted in and out of phase imaging.
Injector	Dual chamber power injector with bolus tracking recommended.
Contrast injection rate	2-3 mL/sec of extracellular gadolinium chelate that does not have dominant biliary excretion, preferably resulting in vendor-recommended total dose.
Mandatory dynamic phases on contrast-enhanced MRI	1. Pre-contrast T1W: do not change scan parameters for post contrast imaging. 2. Late arterial phase: artery fully enhanced, beginning contrast enhancement of portal vein. 3. Portal venous phase: portal vein enhanced, peak liver parenchymal enhancement, beginning contrast enhancement of hepatic veins. 4. Delayed phase: variable appearance, greater than 120 seconds after initial injection of contrast.
Dynamic phases (Timing)	The use of the bolus tracking method for timing contrast arrival for late arterial phase imaging is preferable. Portal vein phase images should be acquired 35 to 55 seconds after initiation of late arterial phase. Delayed phase images should be acquired 120 to 180 seconds after the initial contrast injection.

~~Feature~~	~~MRIs should meet the below specifications:~~
~~Slice thickness~~	~~5 mm or less for dynamic series, 8 mm or less for other imaging.~~
~~Breath-holding~~	~~Maximum length of series requiring breath-holding should be about 20 seconds with a minimum matrix of 128 x 256. Technologists must understand the importance of patient instruction about breathholding before and during scan.~~

9.3.F.~~iv~~vi Imaging Requirements for Class 5 Lesions

~~Nodules~~ Lesions found on images of cirrhotic livers are classified according to *Table 9-5~~3~~3*. ~~Use the largest dimension of each tumor to report the size of Hepatocellular Carcinoma (HCC) lesions. Nodules less than 1 cm are indeterminate and are not eligible for additional priority.~~

Table 9-~~5~~3: Classification System for ~~Nodules~~Lesions Seen on Imaging of Cirrhotic Livers

Class	Description
0	Incomplete or technically inadequate study
5A	Must meet *all* of the following: 1. ~~Single nodule~~ Maximum diameter of at least ≥1 cm and less than~~<~~ 2 cm~~. The maximum diameter of lesions should be~~, as measured on late arterial or portal phase images. 2. Increased contrast enhancement, relative to hepatic parenchyma, on late arterial phase ~~(relative to hepatic parenchyma)~~. 3. *Either* of the following: • Washout during the later contrast phases and peripheral rim enhancement ~~(capsule/pseudocapsule)~~ on delayed phase~~ *or*~~ • ~~a b~~Biopsy ~~(A pre-listing biopsy is not mandatory.)~~
5A-g ~~(growth)~~	Must meet *all* of the following: 1. ~~Single nodule~~ Maximum diameter of at least ≥1 cm and less than~~<~~ 2 cm~~. The maximum diameter of lesions should be~~, as measured on late arterial or portal phase images. 2. Increased contrast enhancement, relative to hepatic parenchyma, on late arterial phase ~~(relative to hepatic parenchyma)~~. 3. ~~Growth (m~~Maximum diameter increase~~) by~~ of at least 50%~~ or more~~ documented on serial MRI or CT obtained ≤ at least 6 months apart. ~~Growth criteria do not apply to ablated lesions.~~
5B	Must meet *all* of the following: 1. ~~Single nodule~~ Maximum diameter of at least ≥ 2 cm and less than or equal to ≤ 5 cm~~. The maximum diameter of lesions should be~~, as measured on late arterial or portal phase images. 2. Increased contrast enhancement, relative to hepatic parenchyma, on late hepatic arterial images ~~(relative to hepatic parenchyma)~~. 3. *One* of the following: a. Washout on portal venous/delayed phase. b. ~~Late capsule or pseudocapsule~~ Peripheral rim enhancement. c. ~~Growth (m~~Maximum diameter increase, in the absence of ~~ablative therapy)~~ ablation, by 50% or more and documented on serial MRI or CT obtained ≤ at least 6 months apart. Serial imaging and measurements must be performed on corresponding contrast phases ~~with the same modality preferred. Growth criteria do not apply to previously ablated lesions~~. d. Biopsy. ~~A pre-listing biopsy is not mandatory.~~

Class	Description
5T ~~(Treated)~~	Any ~~OPTN~~ Class ~~5~~ 5A, 5A-g, 5B ~~or biopsy-proven HCC~~ lesion that was automatically approved upon initial ~~application~~ request or extension and has subsequently ~~undergone loco-regional treatment~~been ablated. ~~OPTN Class 5T nodules qualify for continued priority points based on the pre-treatment classification of the nodules and are defined as:~~ ~~Past loco-regional treatment for HCC (OPTN Class 5 lesion or biopsy proven prior to ablation).~~ ~~Evidence of persistent/recurrent HCC such as, but not limited to, nodular or crescentic extra-zonal or intra-zonal enhancing tissue on late arterial imaging (relative to hepatic parenchyma) may be present.~~
~~**5X**~~	~~Lesions that meet radiologic criteria for HCC but are *Eligible Candidates Definition of T2 Lesions* outside stage T2 as defined above will be considered Class 5X and are not eligible for automatic exception points.~~

~~9.3.F.v HCC Lesions Eligible for Automatic Upgrade~~

~~Individual OPTN Class 5B and 5T are eligible for automatic priority. A single OPTN Class 5A nodule corresponds to T1 stage hepatocellular carcinoma and does not qualify for automatic priority MELD points but must be considered towards the overall staging of the patient according to criteria listed above. Combinations of OPTN Class 5A nodules that meet stage T2 criteria as described above are eligible for automatic priority.~~

~~9.3.F.vii Candidates Not Meeting Criteria (Class 5X)~~

~~A candidate not meeting any of the above criteria will not be given a standardized MELD/PELD exception and must be registered at the calculated MELD or PELD score with no additional priority given because of the HCC diagnosis. All such candidates with HCC, including those with downsized tumors whose original or presenting tumor was greater than a stage T2, must be referred to the applicable RRB for prospective review in order to receive additional priority.~~

9.3.F.vi**i** Extensions of HCC Exceptions

In order for a candidate to maintain an ~~HCC~~ approved exception for HCC, the transplant program must submit an updated MELD/PELD Exception Score Request Form ~~MELD/PELD exception application~~ every three months. The candidate will receive the additional priority as long as they continue to meet initial eligibility criteria. ~~until transplanted or is found unsuitable for transplantation based on the HCC progression.~~

Exception scores for candidates that were at least 18 years old upon submission of their initial exception request are assigned according to *Table 9-4* below. The candidate's MELD exception score will be capped at 34.

~~Upon submission of the first extension, the candidate will be listed at the calculated MELD/PELD score. Upon submission of the second extension, the candidate will be assigned a MELD/PELD score equivalent to a 35 percent risk of 3-month mortality (MELD 28/PELD 41). For each subsequent extension, the candidate will receive~~

~~additional MELD or PELD points equivalent to a 10 percentage point increase in the candidate's mortality risk every three months.~~

~~The HCC exception score will be capped at 34. Upon implementation, candidates with HCC exception scores greater than 34 will receive a score of 34 for their remaining HCC exception extensions. Candidates with scores greater than 34 at the time of implementation may be referred to the RRB if they demonstrate the need for higher priority.~~

Table 9-4: Exception Score Assignment for Candidates at least 18 Years Old upon Submission of Initial Exception Request

Exception Request	MELD Exception Score
Initial	Calculated MELD score
1st extension	Calculated MELD score
2nd extension	28
3rd extension	30
4th extension	32
5th extension and all subsequent extensions	34

If a candidate was less than 18 years old upon submission of their initial exception request, the candidate will receive additional MELD or PELD points equivalent to a 10 percentage point increase in the candidate's mortality risk every three months according to *Table 9-5* below.

Table 9-5: First Seven Exception Score Assignments for Candidates less than 18 Years Old upon Submission of Initial Exception Request

Exception Request	MELD or PELD Exception Score
Initial	MELD 28 or PELD 41
1st extension	MELD 30 or PELD 44
2nd extension	MELD 32 or PELD 47
3rd extension	MELD 34 or PELD 50
4th extension	MELD 36 or PELD 53
5th extension	MELD 39 or PELD 56
6th extension	MELD 40 or PELD 60

To receive the extension, the transplant program must submit an updated MELD/PELD Exception Score Request Form ~~MELD exception~~ that contains all of the following:

1. ~~Submit an Hepatocellular Carcinoma (HCC) MELD/PELD score exception application with a~~An updated narrative
2. Document the tumor using a CT or MRI
3. Specify the type of treatment if the number of tumors decreased since the last ~~application~~ request~~.~~
4. The candidate's alpha-fetoprotein (AFP) level

~~Invasive studies such as biopsies or ablative procedures and repeated chest CT scans are not required after the initial application is approved.~~ If a candidate's tumors have been resected since the previous ~~application~~ request, then the transplant

program must submit an updated MELD/PELD Exception Score Request Form ~~the extension application~~ to ~~its~~ the RRB for prospective review.

Candidates with Class 5T lesions will receive a MELD or PELD equivalent to a 10 percentage point increase in the candidate's mortality risk every three months, without RRB review, even if the estimated size of residual viable tumors falls below stage T2 criteria due to ablative therapy.

9.3.F.viii Appeal for Candidates not Meeting Criteria

If the RRB denies the initial HCC MELD/PELD Exception Score Request Form ~~exception application~~, the transplant program may appeal to the RRB, but the candidate will not receive the additional MELD or PELD priority until approved by the RRB. The RRB ~~will~~ may refer the matter to the Liver and Intestinal Organ Transplantation Committee for further review and possible action if the RRB finds the transplant program to be noncompliant with these Policies.

~~Applications~~ Requests and appeals not resolved by the RRB within 21 days will be referred to the Liver and Intestinal Organ Transplantation Committee for review. The Liver and Intestinal Organ Transplantation Committee may refer these matters to the MPSC for appropriate action according to *Appendix L* of the OPTN Bylaws.

~~9.3.F.ix Compliance Monitoring~~

~~The transplant hospital must maintain documentation of the radiologic characteristics of each OPTN Class 5 nodule. If growth criteria are used to classify a nodule as HCC, the radiology report must contain the prior and current dates of imaging, type of imaging and measurements of the nodule.~~

~~For those candidates who receive a liver transplant while receiving additional priority under the HCC exception criteria, the transplant hospital must submit the *Post-Transplant Explant Pathology Form* to the OPTN Contractor within 60 days of transplant. If the pathology report does not show evidence of HCC, the transplant hospital must also submit documentation or imaging studies confirming HCC at the time of assignment. The Liver and Intestinal Organ Transplantation Committee will review a transplant hospital when more than 10 percent of the HCC cases in a one-year period are not supported by the required pathologic confirmation or submission of clinical information.~~

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