## *At-a-Glance*

- **Proposal to Allow Transplant Centers to Place Liver Candidates with HCC Exceptions on 'HCC Hold' Without Loss of Accumulated Exception Score**

- **Affected/Proposed Policy:** 3.6.4.4 (Liver Candidates with Hepatocellular Carcinoma (HCC))

- **Liver and Intestinal Organ Transplantation Committee**

  This proposal would allow transplant programs to voluntarily place well-compensated candidates with stable or well-treated HCC in inactive status ("HCC Hold", where no livers will be offered) without losing accumulated exception points. These candidates may then be reactivated at the discretion of the transplant center if the tumor shows growth or other concerning features. Candidates listed with an HCC exception continue to receive additional points every three months regardless of whether the HCC tumors have changed in size or have responded to ablative therapy. In some cases, a center may wish to put a candidate with an HCC exception 'on hold' (in inactive status) at a particular MELD score until the tumor(s) show growth or change if the tumor is stable or if there has been a successful response to therapy. Currently, the UNet℠ application does not allow this without loss of exception points. If an exception expires while a candidate is inactive, the application must be resubmitted as an initial application with loss of accumulated points, or the case must go to the Regional Review Board (RRB) for prospective review.

  The proposed change would facilitate more appropriate timing of liver transplantation for candidates with HCC based on the size and number of their tumors, as well as encourage alternative therapies for HCC besides transplantation.

- **Affected Groups**
  Transplant Administrators
  Transplant Data Coordinators
  Transplant Physicians/Surgeons
  Transplant Program Directors

- **Number of Potential Candidates Affected**
  Based on data from 2008-2010, approximately 2500 candidates with a MELD/PELD exception for HCC are waiting for a transplant during any given year. This represents 14% of all liver candidates listed waiting during the period and 20% of deceased donor liver transplants.

- **Compliance with OPTN Key Goals and Final Rule**
  This addresses the OPTN Key Goals of increased patient safety (avoiding unnecessary transplantation by allowing transplant centers to observe the growth of HCC tumors) and increased access to transplant for more urgent candidates. The OPTN Final Rule, §121.8(a)(5) states that "Such allocation policies…Shall be designed to avoid wasting organs, to avoid futile transplants, to promote patient access to transplantation, and to promote the efficient management of organ placement."

- **Specific Requests for Comment**
  The current proposal would limit this to HCC exceptions placed on 'HCC hold' until evidence of tumor progression, but there may be reasons to expand this to other reasons or types of exceptions (e.g., the patient is non-compliant, or there is a medical issue that would prevent immediate transplant, or the patient is late for a follow-up imaging appointment and in danger of missing an extension deadline) or for other standard exceptions (e.g., hepatopulmonary syndrome). The Committee seeks feedback on potential expansion of this proposal beyond HCC. Further, the Committee seeks feedback on whether to develop a proposal for a mandatory hold until there is demonstrated tumor progression.

**Proposal to Allow Transplant Centers to Place Liver Candidates with HCC Exceptions on 'HCC Hold' Without Loss of Accumulated Exception Score**

**Affected Policy:** Policy 3.6.4.4 (Liver Candidates with Hepatocellular Carcinoma (HCC))

**Liver and Intestinal Organ Transplantation Committee**

**Summary and Goals of the Proposal:**

This proposal would allow transplant centers to place candidates with an HCC exception on "HCC hold" without loss of accumulated exception points. This will facilitate more appropriate timing of liver transplantation for candidates with HCC based on the growth of the tumors.

**Background and Significance of the Proposal:**

In November 2008, the OPTN and three major organ transplant professional societies (ASTS, AST, and ILTS) sponsored a national conference to address specific HCC issues related to liver allocation policy. One area of concern highlighted during the conference is the increased access to deceased donor livers that the current policy provides candidates with HCC exceptions when compared to other candidates, which may not be justified by their post-transplant outcomes. Conference attendees agreed that the allocation policy should result in similar risks of removal from the waiting list and similar transplant rates for HCC and non-HCC candidates[1].

Several papers published[2,3] subsequent to the conference have further demonstrated that candidates with HCC exceptions have a significantly lower rate of dropping off the waiting list (i.e., due to death or becoming unsuitable for transplant) than those listed with their calculated MELD score. One reason may be effective modes of loco-regional therapy of small HCC, such as transarterial chemoembolization (TACE) or radiofrequency ablation (RFA). The Committee has identified one minor change to the current policy and UNet℠ programming for these patients.

*Problem Being Addressed*

Under the current policy, candidates listed with an HCC exception continue to receive increases in priority every three months regardless of whether the HCC tumors have shown progression. Thus, candidates with small tumors that do not demonstrate progression such as an increase in size, rising AFP or development of new lesions continue to receive higher and higher MELD scores even though their risk of drop-out from the waiting list (i.e., death or becoming unsuitable for transplant) is low. These candidates continue to receive offers as their MELD score increases, despite the fact that the transplant center may not be ready to transplant the candidate yet, causing inefficiency in organ placement.

[1] Pomfret, E. A., Washburn, K., Wald, C., Nalesnik, M. A., Douglas, D., Russo, M., Roberts, J., Reich, D. J., Schwartz, M. E., Mieles, L., Lee, F. T., Florman, S., Yao, F., Harper, A., Edwards, E., Freeman, R. and Lake, J. (2010), Report of a national conference on liver allocation in patients with hepatocellular carcinoma in the United States. Liver Transplantation, 16: 262–278.

[2] Washburn K, Edwards E, Harper A, Freeman R. Hepatocellular Carcinoma Patients Are Advantaged in the Current Liver Transplant Allocation System. *American Journal of Transplantation 2010; 10: 1652–1657.*

[3] Massie A, Caffo B, Gentry S, Hall E, Axelrod D, Lentine K, Schnitzler M, Gheorghian A, Salvalaggio P, Segev D. MELD Exceptions and Rates of Waiting List Outcomes. *American Journal of Transplantation 2011; 11: 2362–2371*

Conversely, the high priority assigned to these candidates may lead to more transplants in a patient population that could potentially avoid transplantation perhaps indefinitely, or is in less urgent need of a transplant when compared to patients with similar calculated MELD/PELD scores.

For those candidates initially listed with small tumors, a transplant center may wish to put an HCC exception application 'on hold' and inactivate the candidate until there is demonstrated tumor progression. These candidates may have a well-treated tumor that is stable, but continue to gain points every 3 months until they are at the top of the allocation sequence. The center may wish to observe the response of a tumor rather than transplant the candidate, but may feel compelled to transplant the candidate given the high MELD score achieved. Alternatively, the center may opt to repeatedly decline offers, causing inefficiencies in organ placement. The HCC application process in UNet℠ does not allow the center to inactivate a candidate indefinitely without loss of exception points. The current programming also results in an automatic increase in the MELD score after each approved extension; there is no way for centers to "freeze" the score until the candidate is determined to be ready for transplant and re-activated. If a candidate is placed in inactive status and the exception expires, the application must be resubmitted as an initial application, or the case must go to the RRB for prospective review.

This proposal would allow transplant centers to place candidates in a "hold" status without loss of accumulated exception points, to facilitate more appropriate timing of liver transplantation for candidates with HCC based on the size and number of their tumors, and encourage use of alternative therapies for HCC. The proposed changes are shown in Table 1. Examples of how this would be used are found in Table 2.

**Table 1: Comparison of Current and Proposed Processes**

| **Current Process in UNet℠** | **Proposed Change** |
|---|---|
| Transplant centers can extend an approved HCC Exception while candidate is in inactive status. | No change. |
| Approved HCC Exception applications must be extended every 3 months, even while the candidate is in inactive status. If the application is not extended, the candidate will lose the accumulated exception score upon re-activation. | Approved HCC Exception applications may remain on 'HCC hold' as long as a candidate is in inactive status; once re-activated, the candidate will retain the accumulated exception score (most recent tumor information must be provided). |
| Upon extension of an approved HCC Exception, the MELD score increases by the equivalent of a 10 percentage point increase in the risk of 3-month mortality. | Upon extension of an approved HCC Exception, the MELD score could remain fixed when the candidate is re-activated. |

**Table 2 – Examples**

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|---|
| **Example A**. A candidate is listed with an approved HCC exception on January 1, 2011, with one tumor that is 2.1 cm in size (MELD 22). The exception is extended on April 1 (MELD 25) and July 1 (MELD 28). The candidate begins receiving offers, however the size of the tumor remains 2.1cm and the transplant team wishes to continue to observe the tumor behavior before proceeding to transplant. The candidate is placed on "HCC hold" while periodically undergoing CT to monitor the lesion. On December 10, 2011, a CT shows the tumor has grown to 2.8cm. The transplant center then activates the candidate, submits the routine tumor information, and the candidate's score of 28 is maintained until the next extension or transplant. |
| **Example B**. A candidate is listed with an approved HCC exception on January 1, 2011, with one tumor that has been treated with RFA and is 2.5cm in size (MELD 22). The exception is extended on April 1 (MELD 25) and July 1 (MELD 28). The candidate begins receiving offers, however the candidate has an ablation defect with no evidence of viable tumor and the transplant team wishes to continue to observe the tumor behavior before proceeding to transplant. The candidate is placed on "HCC hold" while periodically undergoing CT to monitor the lesion. On January 2, 2012, a CT shows no evidence of viable tumor at the ablation site but a new 1cm hypervascular lesion with wash out on delayed phase imaging. The transplant center activates the candidate at a score of 28, which is maintained until the next extension or transplant. |

- ***Alternatives considered:*** One alternative to the current proposal would be to require transplant centers to follow the 3-month extension schedule for candidates who are in inactive status, but allow centers to 'opt out' of the 10 percentage point increases for these candidates.

  The Committee discussed expanding this option to other reasons, e.g., when a patient is non-compliant, or there is a medical issue that would prevent immediate transplant, or the patient is late for a follow-up imaging appointment and in danger of missing an extension deadline. The option could also be expanded to non-HCC exceptions.

- ***Strengths and weaknesses:*** This proposal may facilitate increased access to transplant for more medically urgent patients and allows transplant centers to make best use of donated organs. As an *optional* pathway for centers to manage their patients, this will serve as an experiment for a future proposal that would require HCC exceptions scores to be placed on hold until tumor growth is demonstrated. As tumor size and rate of tumor growth are suggested components of the "HCC allocation score," which was proposed by the HCC Consensus Conference participants as a way to better prioritize candidates with HCC relative to other candidates, this is also a way to begin to incorporate these concepts into the allocation policy.

- ***Unintended Consequences:*** The Committee has not identified any potential unintended consequences, but would appreciate feedback from the transplant community on this topic.

**Supporting Evidence and/or Modeling:**

As stated above, several recently published papers have shown that candidates with small HCC tumors have a low probability of waiting list dropout or growth beyond current transplant criteria within 12 months of listing.

**Expected Impact on Living Donors or Living Donation:**

Not applicable.

**Expected Impact on Specific Patient Populations:**

This proposed change will facilitate more appropriate timing of liver transplantation for candidates with HCC based on the size of their tumor(s).

**Compliance with OPTN Key Goals and the Final Rule:**

OPTN Key Goals: This proposal addresses the key goals of patient safety (avoiding unnecessary transplantation) and increased access to transplant for more urgent patients.

This proposal addresses the OPTN Final Rule, § 121.8 (a) (5) Such allocation policies…Shall be designed to avoid wasting organs, to avoid futile transplants, to promote patient access to transplantation, and to promote the efficient management of organ placement.

**Plan for Evaluating the Proposal:**

If approved, the Committee will review on an annual basis how often this option is used once implemented. The Committee will also monitor the mean MELD/PELD scores at transplant the number and percentage of candidates that are removed from the waiting list for reasons other than transplant (death, too sick, and 'other' related to the tumor size) for candidates with HCC exceptions versus those without, by Region. The Committee will also review outcomes for candidates whose exception is placed on hold.

**Additional Data Collection:**

This proposal does not require additional data collection in UNet℠ or on TIEDI® forms.

**Expected Implementation Plan:**

Additional programming in UNet℠ will be required to modify the allocation algorithm for adult deceased donor livers. This will require an additional reason for inactive status to be added to the current drop-down menu, and a mechanism to prevent candidates that are inactivated for this reason from losing their accumulated MELD/PELD exception score. The Liver and Intestinal Organ Transplantation Committee will work with the UNOS IT Department to implement this policy.

**Communication and Education Plan:**

| Communication Activities | | | |
|---|---|---|---|
| **Type of Communication** | **Audience(s)** | **Deliver Method(s)** | **Timeframe** |
| Policy Notice following Board Approval | Liver candidates, transplant surgeons, transplant physicians, transplant coordinators, transplant administrators | OPTN and UNOS websites | 1 month after Board approval |

| | | | |
|---|---|---|---|
| System Notice upon implementation | All UNet℠ Users | Blast e-mail, UNet℠ notice | 30 days before the implementation, and again upon implementation |

| Education/Training Activities | | | |
|---|---|---|---|
| **Education/Training Description** | **Audience(s)** | **Deliver Method(s)** | **Timeframe and Frequency** |
| Brief Training Session | All UNet℠ Users | Webinar | Prior to Implementation |

**Compliance Monitoring:**

The proposed policy change will be optional for transplant centers that choose to inactivate candidates with an approved HCC exception; as such no compliance monitoring will be required.

**Policy or Bylaw Proposal**

Proposed new language is underlined (example) and language that is proposed for removal is struck through (~~example~~).

**3.6.4.4 Liver Transplant Candidates with Hepatocellular Carcinoma (HCC).**

**A. – E. (no change)**

**F. Extensions of HCC Exception Applications**. Candidates will receive additional MELD/PELD points equivalent to a 10 percentage point increase in candidate mortality to be assigned every 3 months until these candidates receive a transplant or are determined to be unsuitable for transplantation based on progression of their HCC. To receive the additional points at 3-month intervals, the transplant program must re-submit an HCC MELD/PELD score exception application with an updated narrative every three months. Continued documentation of the tumor via repeat CT or MRI is required every three months for the candidate to receive the additional 10 percentage point increase in mortality points while waiting. Invasive studies such as biopsies or ablative procedures and repeated chest CTs are not required after the initial upgrade request is approved to maintain the candidate's HCC priority scores.

The following options are available while a candidate with an approved HCC Exception application is in inactive status:

- The center may choose to submit an extension application every 3 months, as described above; the candidate will receive a MELD/PELD score equivalent to a 10 percentage point increase in candidate mortality following each approved extension.

- The center may keep the candidate in inactive status for any length of time, without submission of an extension application every 3 months. However, prior to reactivation, an extension application must

be submitted. Once the extension application is approved, the candidate will be listed with the candidate's previously approved exception score prior to inactivation (i.e., without loss of the accumulated MELD/PELD exception score) upon re-activation.

If the number of tumors that can be documented at the time of extension is less than upon initial application or prior extension, the type of ablative therapy must be specified on the extension application. Candidates whose tumors have been ablated after previously meeting the criteria for additional MELD/PELD points (OPTN Class 5T) will continue to receive additional MELD/PELD points (equivalent to a 10 percentage point increase in candidate mortality) every 3 months without RRB review, even if the estimated size of residual viable tumor falls below stage T2 criteria.

For candidates whose tumors have been resected since the initial HCC application or prior extension, the extension application must receive prospective review by the applicable RRB.

**G. – I. (no change)**