April 10, 2019

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Dear Sir or Madam:

As a compendium recognized by the Centers for Medicare and Medicaid Services (CMS), Medicare Part D plans utilize the information in Micromedex® DRUGDEX® for determination of medically-accepted off-label indications. This determination is critical, as it dictates whether a drug claim will be reliably paid by a Medicare Part D plan for a specific beneficiary. Current monographs for many immunosuppressive drugs in Micromedex® DRUGDEX® do not adequately address off-label organ transplant uses. As a result, transplant recipients are vulnerable to, and some have experienced, denial of coverage by Part D plans for their lifesaving immunosuppressive drug therapy.

The American Society of Transplantation became aware of this issue in 2016 and formalized a position (Appendix A). Per our proposed approaches for resolution, we hereby implore you to review your Micromedex® DRUGDEX® content on the following drugs, and consider expanding your “Non-FDA Uses” section to include the off-label indications listed below (these are also summarized in Appendix B):

1. Tacrolimus
   a. Add vascular composite allograft rejection, prophylaxis
2. Cyclosporine
   a. Add pancreas transplant rejection, prophylaxis
3. Mycophenolate mofetil
   a. Add lung transplant rejection, prophylaxis
   b. Add intestine transplant rejection, prophylaxis
   c. Add vascular composite allograft rejection, prophylaxis
4. Mycophenolate sodium
   a. Add liver transplant rejection, prophylaxis
   b. Add heart transplant rejection, prophylaxis
   c. Add lung transplant rejection, prophylaxis
   d. Add pancreas transplant rejection, prophylaxis
5. Azathioprine
   a. Add heart transplant rejection, prophylaxis
   b. Add lung transplant rejection, prophylaxis
   c. Add intestine transplant rejection, prophylaxis
6. Leflunomide
   a. Add kidney transplant rejection, prophylaxis
   b. Add liver transplant rejection, prophylaxis
7. Sirolimus
   a. Add liver transplant rejection, prophylaxis
   b. Add heart transplant rejection, prophylaxis
   c. Add lung transplant rejection, prophylaxis
   d. Add pancreas transplant rejection, prophylaxis
   e. Add intestine transplant rejection, prophylaxis

8. Everolimus
   a. Add heart transplant rejection, prophylaxis
   b. Add lung transplant rejection, prophylaxis
   c. Add pancreas transplant rejection, prophylaxis

9. Belatacept
   a. Add liver transplant rejection, prophylaxis
   b. Add heart transplant rejection, prophylaxis
   c. Add lung transplant rejection, prophylaxis
   d. Add pancreas transplant rejection, prophylaxis

10. Basiliximab
    a. Add heart transplant rejection, prophylaxis
    b. Add lung transplant rejection, prophylaxis
    c. Add pancreas transplant rejection, prophylaxis
    d. Add intestine transplant rejection, prophylaxis

11. Rabbit antithymocyte globulin
    a. Add liver transplant rejection, prophylaxis
    b. Add liver transplant rejection
    c. Add intestine transplant rejection, prophylaxis
    d. Add vascular composite allograft rejection, prophylaxis

12. Alemtuzumab
    a. Add lung transplant rejection, prophylaxis
    b. Add pancreas transplant rejection, prophylaxis
    c. Add intestine transplant rejection, prophylaxis
    d. Add vascular composite allograft rejection

13. Immune globulin
    a. Add liver transplant rejection
    b. Add liver transplant, pre-transplant desensitization
    c. Add heart transplant, pre-transplant desensitization
    d. Add lung transplant rejection
    e. Add pancreas transplant rejection
    f. Add intestine transplant rejection
    g. Add intestine transplant, pre-transplant desensitization

14. Rituximab
    a. Add kidney transplant rejection
    b. Add kidney transplant, pre-transplant desensitization
    c. Add liver transplant rejection
    d. Add liver transplant, pre-transplant desensitization
    e. Add heart transplant rejection
    f. Add heart transplant, pre-transplant desensitization
    g. Add lung transplant rejection
    h. Add pancreas transplant rejection
    i. Add intestine transplant rejection, prophylaxis
    j. Add intestine transplant rejection
15. Bortezomib
   a. Add kidney transplant rejection
   b. Add kidney transplant, pre-transplant desensitization
   c. Add liver transplant rejection
   d. Add heart transplant rejection
   e. Add heart transplant, pre-transplant desensitization
   f. Add lung transplant rejection
   g. Add pancreas transplant rejection
   h. Add intestine transplant rejection

16. Carfilzomib
   a. Add lung transplant rejection

17. Eculizumab
   a. Add kidney transplant rejection
   b. Add kidney transplant, pre-transplant desensitization
   c. Add liver transplant rejection
   d. Add lung transplant rejection
   e. Add pancreas transplant rejection
   f. Add intestine transplant rejection

18. Tocilizumab
   a. Add kidney transplant rejection
   b. Add kidney transplant, pre-transplant desensitization

19. Adalimumab
   a. Add intestine transplant rejection

20. Infliximab
   a. Add intestine transplant rejection

We realize that you require at least one citation from the medical literature to support each of these revisions. We have reviewed the literature, and Appendix C contains the citations that we believe meet this need.

Thank you in advance for your attention to this matter.

Sincerely,

Dianne B. McKay, MD
President

Attachments:
- Appendix A: AST Position Statement on Immunosuppressant Drug Coverage Under Medicare Part D Benefit
- Appendix B: Overview of drug/indication pairs with on- or off-label indications already endorsed by Micromedex (green) and those for which we request endorsement (yellow)
- Appendix C: Citations from the medical literature in support of the proposed off-label indication
Appendix A:

AST Position Statement on Immunosuppressant Drug Coverage Under Medicare Part D Benefit

Appendix B:

Overview of drug/indication pairs with on- or off-label indications already endorsed by Micromedex (green) and those for which we request endorsement (yellow)

<table>
<thead>
<tr>
<th>Indication Pathology</th>
<th>Tacrolimus</th>
<th>Cyclosporine</th>
<th>Mycophenolate mofetil</th>
<th>Mycophenolate sodium</th>
<th>Azathioprine</th>
<th>Leflunomide</th>
<th>Sirolimus</th>
<th>Everolimus</th>
<th>Belatacept</th>
<th>Basiliximab</th>
<th>Rabbit antithymocyte globulin</th>
<th>Alemtuzumab</th>
<th>Immune globulin</th>
<th>Rituximab</th>
<th>Bortezomib</th>
<th>Carfilzomib</th>
<th>Eculizumab</th>
<th>Tocilizumab</th>
<th>Adalimumab</th>
<th>Infliximab</th>
</tr>
</thead>
</table>
Appendix C:

Citations from the medical literature in support of the proposed off-label indication

1. Tacrolimus

   a. Add vascular composite allograft rejection, prophylaxis

2. Cyclosporine

   a. Add pancreas transplant rejection, prophylaxis

3. Mycophenolate mofetil

   a. Add lung transplant rejection, prophylaxis
      ii. Zuckermann A, Reichenspurner H, Birsan T, et al. Cyclosporine A versus tacrolimus in combination with mycophenolate mofetil and steroids as primary immunosuppression after lung transplantation:


b. Add intestine transplant rejection, prophylaxis


c. Add vascular composite allograft rejection, prophylaxis


4. Mycophenolate sodium

a. Add liver transplant rejection, prophylaxis


b. Add heart transplant rejection, prophylaxis


c. Add lung transplant rejection, prophylaxis

d. Add pancreas transplant rejection, prophylaxis

5. Azathioprine

a. Add heart transplant rejection, prophylaxis

b. Add lung transplant rejection, prophylaxis

c. Add intestine transplant rejection, prophylaxis

6. Leflunomide

   a. Add kidney transplant rejection, prophylaxis

   b. Add liver transplant rejection, prophylaxis

7. Sirolimus

   a. Add liver transplant rejection, prophylaxis

   b. Add heart transplant rejection, prophylaxis


c. Add lung transplant rejection, prophylaxis

d. Add pancreas transplant rejection, prophylaxis


e. Add intestine transplant rejection, prophylaxis

8. Everolimus

a. Add heart transplant rejection, prophylaxis


b. Add lung transplant rejection, prophylaxis


c. Add pancreas transplant rejection, prophylaxis


9. Belatacept

a. Add liver transplant rejection, prophylaxis

i. LaMattina JC, Jason MP, Hanish SI, et al. Safety of belatacept bridging immunosuppression in hepatitis C-positive liver transplant recipients with renal dysfunction. *Transplantation* 2014; 97(2):
b. Add heart transplant rejection, prophylaxis

c. Add lung transplant rejection, prophylaxis

d. Add pancreas transplant rejection, prophylaxis

10. Basiliximab

a. Add heart transplant rejection, prophylaxis

b. Add lung transplant rejection, prophylaxis

c. Add pancreas transplant rejection, prophylaxis

d. Add intestine transplant rejection, prophylaxis

11. Rabbit antithymocyte globulin
a. Add liver transplant rejection, prophylaxis

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12. Alemtuzumab
a. Add lung transplant rejection, prophylaxis

b. Add pancreas transplant rejection, prophylaxis

c. Add intestine transplant rejection, prophylaxis

d. Add vascular composite allograft rejection

13. Immune globulin

a. Add liver transplant rejection
b. Add liver transplant, pre-transplant desensitization

c. Add heart transplant, pre-transplant desensitization

d. Add lung transplant rejection

e. Add pancreas transplant rejection

f. Add intestine transplant rejection

g. Add intestine transplant, pre-transplant desensitization

14. Rituximab

a. Add kidney transplant rejection

b. Add kidney transplant, pre-transplant desensitization

c. Add liver transplant rejection
**Transplantation** 2006; 82(7): 988-9.

d. Add liver transplant, pre-transplant desensitization

e. Add heart transplant rejection

f. Add heart transplant, pre-transplant desensitization

g. Add lung transplant rejection

h. Add pancreas transplant rejection

i. Add intestine transplant rejection, prophylaxis

j. Add intestine transplant rejection
15. Bortezomib

a. Add kidney transplant rejection


b. Add kidney transplant, pre-transplant desensitization

c. Add liver transplant rejection

d. Add heart transplant rejection

e. Add heart transplant, pre-transplant desensitization

f. Add lung transplant rejection

g. Add pancreas transplant rejection

h. Add intestine transplant rejection

16. Carfilzomib

a. Add lung transplant rejection

17. Eculizumab

a. Add kidney transplant rejection

b. Add kidney transplant, pre-transplant desensitization

c. Add liver transplant rejection

d. Add lung transplant rejection

e. Add pancreas transplant rejection

f. Add intestine transplant rejection

18. Tocilizumab

a. Add kidney transplant rejection
b. Add kidney transplant, pre-transplant desensitization

19. Adalimumab

   a. Add intestine transplant rejection

20. Infliximab

   a. Add intestine transplant rejection