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EVIDENCE-BASED CRITERIA  
SECTION: MEDICINE

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## HEMATOPOIETIC CELL TRANSPLANTATION FOR AUTOIMMUNE DISEASES

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Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Evidence-Based Criteria must be read in its entirety to determine coverage eligibility, if any.

This Evidence-Based Criteria provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Evidence-Based Criteria are subject to change as new information becomes available.

For purposes of this Evidence-Based Criteria, the terms "experimental" and "investigational" are considered to be interchangeable.

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## **HEMATOPOIETIC CELL TRANSPLANTATION FOR AUTOIMMUNE DISEASES**

### **Description:**

Most individuals with autoimmune disorders respond to conventional drug therapies; however, conventional drug therapies are not curative and a proportion of individuals suffer from autoimmune diseases that range from severe to recalcitrant to rapidly progressive. It is in this group of individuals with a severe autoimmune disease that alternative therapies have been sought, including hematopoietic cell transplantation (HCT).

### **Autoimmune Disease Treatment**

Immune suppression is a common treatment strategy for many autoimmune diseases, particularly rheumatic diseases (e.g., rheumatoid arthritis [RA], systemic lupus erythematosus [SLE], scleroderma). Most individuals with autoimmune disorders respond to conventional therapies, which consist of anti-inflammatory agents, immunosuppressants, and immunomodulating drugs; however, conventional drug therapies are not curative, and a proportion of individuals suffer from autoimmune diseases that range from severe to recalcitrant to rapidly progressive. It is for this group of individuals with a severe autoimmune disease that alternative therapies have been sought, including hematopoietic cell transplantation (HCT). The primary concept underlying the use of HCT for these diseases is this: ablating and “resetting” the immune system can alter the disease process by inducing a sustained remission that possibly leads to cure.

### **Hematopoietic Cell Transplantation**

HCT is a procedure in which hematopoietic stem cells are intravenously infused to restore bone marrow and immune function in cancer individuals who receive bone marrow-toxic doses of cytotoxic drugs with or without whole-body radiotherapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HCT) or a donor (allogeneic HCT [allo-HCT]). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after delivery of neonates.

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HCT. In allogeneic stem cell transplantation, immunologic compatibility between donor and individual is a critical factor for achieving a successful outcome. Compatibility is established by typing of human leukocyte antigens (HLA) using cellular, serologic, or molecular techniques. The term HLA refers to the gene complex expressed at the HLA-A, -B, and -DR (antigen-D related) loci on each arm of chromosome 6. An acceptable donor will match the individual at all or most of the HLA loci.

### **Hematopoietic Cell Transplantation for Systemic Sclerosis**

Autologous hematopoietic cell transplantation (HCT) should be considered for individuals with systemic sclerosis only if the condition is rapidly progressing and the prognosis for survival is poor. An important factor influencing the occurrence of treatment-related adverse effects and response to treatment is the level of internal organ involvement. If organ involvement is severe and irreversible, HCT is not recommended.

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### Definitions:

Adult: Age 18 years and older

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### Criteria:

**All stem cell transplants will be reviewed by the medical director(s) and/or clinical advisor(s).**

- Autologous hematopoietic cell transplantation (HCT) for the treatment of systemic sclerosis (scleroderma) is considered **medically necessary** with documentation of **ALL** of the following:
  1. Adult individuals < 60 years of age
  2. Maximum duration of condition of 5 years
  3. Modified Rodnan Scale Scores  $\geq 15$
  4. History of < 6 months of treatment with cyclophosphamide
  5. No active gastric antral vascular ectasia
  6. Individuals with internal organ involvement indicated by **ONE** of the following measurements:
    - Abnormal electrocardiogram
    - Diffusing capacity of carbon monoxide (DLCo) < 80% of predicted value
    - Decline of forced vital capacity (FVC) of  $\geq 10\%$  in last 12 months
    - Pulmonary fibrosis
    - Ground glass appearance on high-resolution chest computed tomography (CT)
    - Scleroderma-related renal disease
  7. Lack of **ANY** of the following measurements for internal organ involvement:
    - Left ventricular ejection fraction < 50%
    - Tricuspid annular plane systolic excursion < 1.8 cm
    - Pulmonary artery systolic pressure > 40 mm Hg
    - Mean pulmonary artery pressure > 25 mm Hg
    - DLCo < 40% of predicted value
    - FVC < 45% of predicted value
    - Creatinine clearance < 40 ml/minute

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- Autologous hematopoietic cell transplantation (HCT) as a treatment of systemic sclerosis (scleroderma) if above criteria not met is considered **experimental or investigational** when any **ONE** or more of the following criteria are met:
  1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
  3. Insufficient evidence to support improvement of the net health outcome; or
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
  5. Insufficient evidence to support improvement outside the investigational setting.
  
- Autologous or allogeneic hematopoietic cell transplantation (HCT) as a treatment of autoimmune diseases is considered **experimental or investigational** when any **ONE** or more of the following criteria are met:
  1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
  3. Insufficient evidence to support improvement of the net health outcome; or
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
  5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to*:

- Chronic inflammatory demyelinating polyneuropathy
- Juvenile idiopathic or rheumatoid arthritis
- Multiple sclerosis
- Systemic lupus erythematosus
- Type 1 diabetes

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### Resources:

Literature reviewed 03/05/24. We do not include marketing materials, poster boards and non-published literature in our review.

Resources prior to 03/05/24 may be requested from the BCBSAZ Medical Policy and Technology Research Department.

1. Atkins HL, Bowman M, Allan D, et al. Immunoablation and autologous haemopoietic stem-cell transplantation for aggressive multiple sclerosis: a multicentre single-group phase 2 trial. *Lancet*. Aug 6 2016;388(10044):576-85. doi:10.1016/s0140-6736(16)30169-6

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2. Boffa G, Massacesi L, Inglese M, et al. Long-Term Clinical Outcomes of Hematopoietic Stem Cell Transplantation in Multiple Sclerosis. *Neurology*. Jan 20 2021;doi:10.1212/wnl.0000000000011461
3. Brierley CK, Castilla-Llorente C, Labopin M, et al. Autologous Haematopoietic Stem Cell Transplantation for Crohn's Disease: A Retrospective Survey of Long-term Outcomes From the European Society for Blood and Marrow Transplantation. *J Crohns Colitis*. Aug 29 2018;12(9):1097-1103. doi:10.1093/ecco-jcc/jjy069
4. Bruera S, Sidanmat H, Molony DA, et al. Stem cell transplantation for systemic sclerosis. *Cochrane Database Syst Rev*. Jul 29 2022;7(7):CD011819. doi:10.1002/14651858.CD011819.pub2
5. Bryant A, Atkins H, Pringle CE, et al. Myasthenia Gravis Treated With Autologous Hematopoietic Stem Cell Transplantation. *JAMA Neurol*. Jun 1 2016;73(6):652-8. doi:10.1001/jamaneurol.2016.0113
6. Burman J, Iacobaeus E, Svenningsson A, et al. Autologous haematopoietic stem cell transplantation for aggressive multiple sclerosis: the Swedish experience. *J Neurol Neurosurg Psychiatry*. Oct 2014;85(10):1116-21. doi:10.1136/jnnp-2013-307207
7. Burt RK, Balabanov R, Burman J, et al. Effect of Nonmyeloablative Hematopoietic Stem Cell Transplantation vs Continued Disease-Modifying Therapy on Disease Progression in Patients With Relapsing-Remitting Multiple Sclerosis: A Randomized Clinical Trial. *Jama*. Jan 15 2019;321(2):165-174. doi:10.1001/jama.2018.18743
8. Burt RK, Balabanov R, Han X, et al. Association of nonmyeloablative hematopoietic stem cell transplantation with neurological disability in patients with relapsing-remitting multiple sclerosis. *Jama*. Jan 20 2015;313(3):275-84. doi:10.1001/jama.2014.17986
9. Burt RK, Balabanov R, Tavee J, et al. Hematopoietic stem cell transplantation for chronic inflammatory demyelinating polyradiculoneuropathy. *J Neurol*. Nov 2020;267(11):3378-3391. doi:10.1007/s00415-020-10010-6
10. Burt RK, Han X, Gozdzia P, et al. Five year follow-up after autologous peripheral blood hematopoietic stem cell transplantation for refractory, chronic, corticosteroid-dependent systemic lupus erythematosus: effect of conditioning regimen on outcome. *Bone Marrow Transplant*. Jun 2018;53(6):692-700. doi:10.1038/s41409-018-0173-x
11. Burt RK, Han X, Quigley K, Helenowski IB, Balabanov R. Real-world application of autologous hematopoietic stem cell transplantation in 507 patients with multiple sclerosis. *J Neurol*. May 2022;269(5):2513-2526. doi:10.1007/s00415-021-10820-2

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12. Burt RK, Shah SJ, Dill K, et al. Autologous non-myeloablative haemopoietic stem-cell transplantation compared with pulse cyclophosphamide once per month for systemic sclerosis (ASSIST): an open-label, randomised phase 2 trial. *Lancet*. Aug 6 2011;378(9790):498-506. doi:10.1016/s0140-6736(11)60982-3
13. Burt RK, Traynor A, Statkute L, et al. Nonmyeloablative hematopoietic stem cell transplantation for systemic lupus erythematosus. *Jama*. Feb 1 2006;295(5):527-35. doi:10.1001/jama.295.5.527
14. Cantú-Rodríguez OG, Lavallo-González F, Herrera-Rojas M, et al. Long-Term Insulin Independence in Type 1 Diabetes Mellitus Using a Simplified Autologous Stem Cell Transplant. *J Clin Endocrinol Metab*. May 2016;101(5):2141-8. doi:10.1210/jc.2015-2776
15. Cao C, Wang M, Sun J, et al. Autologous peripheral blood haematopoietic stem cell transplantation for systemic lupus erythematosus: the observation of long-term outcomes in a Chinese centre. *Clin Exp Rheumatol*. May-Jun 2017;35(3):500-507.
16. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) for Stem Cell Transplantation(Formerly 110.8.1) (110.23). 2016. Accessed November 14, 2023. <https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=366>
17. El-Badawy A, El-Badri N. Clinical Efficacy of Stem Cell Therapy for Diabetes Mellitus: A Meta-Analysis. *PLoS One*. 2016;11(4):e0151938. doi:10.1371/journal.pone.0151938
18. Fassas A, Kimiskidis VK, Sakellari I, et al. Long-term results of stem cell transplantation for MS: a single-center experience. *Neurology*. Mar 22 2011;76(12):1066-70. doi:10.1212/WNL.0b013e318211c537
19. Ge F, Lin H, Li Z, Chang T. Efficacy and safety of autologous hematopoietic stem-cell transplantation in multiple sclerosis: a systematic review and meta-analysis. *Neurol Sci*. Mar 2019;40(3):479-487. doi:10.1007/s10072-018-3670-1
20. Hawkey CJ, Allez M, Clark MM, et al. Autologous Hematopoietic Stem Cell Transplantation for Refractory Crohn Disease: A Randomized Clinical Trial. *Jama*. Dec 15 2015;314(23):2524-34. doi:10.1001/jama.2015.16700
21. Henes J, Oliveira MC, Labopin M, et al. Autologous stem cell transplantation for progressive systemic sclerosis: a prospective non-interventional study from the European Society for Blood and Marrow Transplantation Autoimmune Disease Working Party. *Haematologica*. Feb 1 2021;106(2):375-383. doi:10.3324/haematol.2019.230128
22. Henes JC, Schmalzing M, Vogel W, et al. Optimization of autologous stem cell transplantation for systemic sclerosis -- a single-center longterm experience in 26 patients with severe organ manifestations. *J Rheumatol*. Feb 2012;39(2):269-75. doi:10.3899/jrheum.110868

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23. Higashitani K, Takase-Minegishi K, Yoshimi R, et al. Benefits and risks of Hematopoietic Stem Cell Transplantation for Systemic Sclerosis: A Systematic Review and Meta-Analysis. *Mod Rheumatol*. Mar 12 2022;doi:10.1093/mr/roac026
24. Host L, Nikpour M, Calderone A, Cannell P, Roddy J. Autologous stem cell transplantation in systemic sclerosis: a systematic review. *Clin Exp Rheumatol*. Sep-Oct 2017;35 Suppl 106(4):198-207.
25. Ioannidis JP, Vlachoyiannopoulos PG, Haidich AB, et al. Mortality in systemic sclerosis: an international meta-analysis of individual patient data. *Am J Med*. Jan 2005;118(1):2-10. doi:10.1016/j.amjmed.2004.04.031
26. J MFS, Ladomenou F, Carpenter B, et al. Allogeneic hematopoietic stem cell transplantation for severe, refractory juvenile idiopathic arthritis. *Blood Adv*. Apr 10 2018;2(7):777-786. doi:10.1182/bloodadvances.2017014449
27. Kanate AS, Majhail NS, Savani BN, et al. Indications for Hematopoietic Cell Transplantation and Immune Effector Cell Therapy: Guidelines from the American Society for Transplantation and Cellular Therapy. *Biol Blood Marrow Transplant*. Jul 2020;26(7):1247-1256. doi:10.1016/j.bbmt.2020.03.002
28. Kazmi MA, Mahdi-Rogers M, Sanvito L. Chronic inflammatory demyelinating polyradiculoneuropathy: a role for haematopoietic stem cell transplantation? *Autoimmunity*. Dec 2008;41(8):611-5. doi:10.1080/08916930802198253
29. Kvistad SAS, Lehmann AK, Trovik LH, et al. Safety and efficacy of autologous hematopoietic stem cell transplantation for multiple sclerosis in Norway. *Mult Scler*. Dec 2020;26(14):1889-1897. doi:10.1177/1352458519893926
30. Lehmann HC, Hughes RA, Hartung HP. Treatment of chronic inflammatory demyelinating polyradiculoneuropathy. *Handb Clin Neurol*. 2013;115:415-27. doi:10.1016/b978-0-444-52902-2.00023-0
31. Leng XM, Jiang Y, Zhou DB, et al. Good outcome of severe lupus patients with high-dose immunosuppressive therapy and autologous peripheral blood stem cell transplantation: a 10-year follow-up study. *Clin Exp Rheumatol*. May-Jun 2017;35(3):494-499.
32. Leone A, Radin M, Almarzooqi AM, et al. Autologous hematopoietic stem cell transplantation in Systemic Lupus Erythematosus and antiphospholipid syndrome: A systematic review. *Autoimmun Rev*. May 2017;16(5):469-477. doi:10.1016/j.autrev.2017.03.008
33. Lindsay JO, Allez M, Clark M, et al. Autologous stem-cell transplantation in treatment-refractory Crohn's disease: an analysis of pooled data from the ASTIC trial. *Lancet Gastroenterol Hepatol*. Jun 2017;2(6):399-406. doi:10.1016/s2468-1253(17)30056-0

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34. Mancardi GL, Sormani MP, Di Gioia M, et al. Autologous haematopoietic stem cell transplantation with an intermediate intensity conditioning regimen in multiple sclerosis: the Italian multi-centre experience. *Mult Scler*. Jun 2012;18(6):835-42. doi:10.1177/1352458511429320
35. Mancardi GL, Sormani MP, Gualandi F, et al. Autologous hematopoietic stem cell transplantation in multiple sclerosis: a phase II trial. *Neurology*. Mar 10 2015;84(10):981-8. doi:10.1212/wnl.0000000000001329
36. Milanetti F, Abinun M, Voltarelli JC, Burt RK. Autologous hematopoietic stem cell transplantation for childhood autoimmune disease. *Pediatr Clin North Am*. Feb 2010;57(1):239-71. doi:10.1016/j.pcl.2009.12.003
37. Milanetti F, Bucha J, Testori A, Burt RK. Autologous hematopoietic stem cell transplantation for systemic sclerosis. *Curr Stem Cell Res Ther*. Mar 2011;6(1):16-28. doi:10.2174/157488811794480663
38. Muraro PA, Pasquini M, Atkins HL, et al. Long-term Outcomes After Autologous Hematopoietic Stem Cell Transplantation for Multiple Sclerosis. *JAMA Neurol*. Apr 1 2017;74(4):459-469. doi:10.1001/jamaneurol.2016.5867
39. Nabizadeh F, Pirahesh K, Rafiei N, et al. Autologous Hematopoietic Stem-Cell Transplantation in Multiple Sclerosis: A Systematic Review and Meta-Analysis. *Neurol Ther*. Dec 2022;11(4):1553-1569. doi:10.1007/s40120-022-00389-x
40. Nash RA, Hutton GJ, Racke MK, et al. High-dose immunosuppressive therapy and autologous HCT for relapsing-remitting MS. *Neurology*. Feb 28 2017;88(9):842-852. doi:10.1212/wnl.0000000000003660
41. Nash RA, McSweeney PA, Crofford LJ, et al. High-dose immunosuppressive therapy and autologous hematopoietic cell transplantation for severe systemic sclerosis: long-term follow-up of the US multicenter pilot study. *Blood*. Aug 15 2007;110(4):1388-96. doi:10.1182/blood-2007-02-072389
42. Nikolov NP, Pavletic SZ. Technology Insight: hematopoietic stem cell transplantation for systemic rheumatic disease. *Nat Clin Pract Rheumatol*. Apr 2008;4(4):184-91. doi:10.1038/ncprheum0756
43. Peltier AC, Donofrio PD. Chronic inflammatory demyelinating polyradiculoneuropathy: from bench to bedside. *Semin Neurol*. Jul 2012;32(3):187-95. doi:10.1055/s-0032-1329194
44. Reston JT, Uhl S, Treadwell JR, Nash RA, Schoelles K. Autologous hematopoietic cell transplantation for multiple sclerosis: a systematic review. *Mult Scler*. Feb 2011;17(2):204-13. doi:10.1177/1352458510383609
45. Saccardi R, Di Gioia M, Bosi A. Haematopoietic stem cell transplantation for autoimmune disorders. *Curr Opin Hematol*. Nov 2008;15(6):594-600. doi:10.1097/MOH.0b013e3283136700



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46. Shevchenko JL, Kuznetsov AN, Ionova TI, et al. Autologous hematopoietic stem cell transplantation with reduced-intensity conditioning in multiple sclerosis. *Exp Hematol*. Nov 2012;40(11):892-8. doi:10.1016/j.exphem.2012.07.003
47. Shevchenko JL, Kuznetsov AN, Ionova TI, et al. Long-term outcomes of autologous hematopoietic stem cell transplantation with reduced-intensity conditioning in multiple sclerosis: physician's and patient's perspectives. *Ann Hematol*. Jul 2015;94(7):1149-57. doi:10.1007/s00277-015-2337-8
48. Shouval R, Furie N, Raanani P, Nagler A, Gafter-Gvili A. Autologous Hematopoietic Stem Cell Transplantation for Systemic Sclerosis: A Systematic Review and Meta-Analysis. *Biol Blood Marrow Transplant*. May 2018;24(5):937-944. doi:10.1016/j.bbmt.2018.01.020
49. Snarski E, Milczarczyk A, Hałaburda K, et al. Immunoablation and autologous hematopoietic stem cell transplantation in the treatment of new-onset type 1 diabetes mellitus: long-term observations. *Bone Marrow Transplant*. Mar 2016;51(3):398-402. doi:10.1038/bmt.2015.294
50. Song XN, Lv HY, Sun LX, et al. Autologous stem cell transplantation for systemic lupus erythematosus: report of efficacy and safety at 7 years of follow-up in 17 patients. *Transplant Proc*. Jun 2011;43(5):1924-7. doi:10.1016/j.transproceed.2011.03.039
51. Sormani MP, Muraro PA, Schiavetti I, et al. Autologous hematopoietic stem cell transplantation in multiple sclerosis: A meta-analysis. *Neurology*. May 30 2017;88(22):2115-2122. doi:10.1212/wnl.0000000000003987
52. Sullivan KM, Goldmuntz EA, Keyes-Elstein L, et al. Myeloablative Autologous Stem-Cell Transplantation for Severe Scleroderma. *N Engl J Med*. Jan 4 2018;378(1):35-47. doi:10.1056/nejmoa1703327
53. Sullivan KM, Muraro P, Tyndall A. Hematopoietic cell transplantation for autoimmune disease: updates from Europe and the United States. *Biol Blood Marrow Transplant*. Jan 2010;16(1 Suppl):S48-56. doi:10.1016/j.bbmt.2009.10.034
54. Sun SY, Gao Y, Liu GJ, Li YK, Gao W, Ran XW. Efficacy and Safety of Stem Cell Therapy for T1DM: An Updated Systematic Review and Meta-Analysis. *J Diabetes Res*. 2020;2020:5740923. doi:10.1155/2020/5740923
55. van Bijnen S, de Vries-Bouwstra J, van den Ende CH, et al. Predictive factors for treatment-related mortality and major adverse events after autologous haematopoietic stem cell transplantation for systemic sclerosis: results of a long-term follow-up multicentre study. *Ann Rheum Dis*. Aug 2020;79(8):1084-1089. doi:10.1136/annrheumdis-2020-217058
56. van Laar JM, Farge D, Sont JK, et al. Autologous hematopoietic stem cell transplantation vs intravenous pulse cyclophosphamide in diffuse cutaneous systemic sclerosis: a randomized clinical trial. *Jama*. Jun 25 2014;311(24):2490-8. doi:10.1001/jama.2014.6368

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57. Vonk MC, Marjanovic Z, van den Hoogen FH, et al. Long-term follow-up results after autologous haematopoietic stem cell transplantation for severe systemic sclerosis. *Ann Rheum Dis*. Jan 2008;67(1):98-104. doi:10.1136/ard.2007.071464
58. Walicka M, Milczarczyk A, Snarski E, et al. Lack of persistent remission following initial recovery in patients with type 1 diabetes treated with autologous peripheral blood stem cell transplantation. *Diabetes Res Clin Pract*. Sep 2018;143:357-363. doi:10.1016/j.diabres.2018.07.020
59. Xiang H, Chen H, Li F, et al. Predictive factors for prolonged remission after autologous hematopoietic stem cell transplantation in young patients with type 1 diabetes mellitus. *Cytotherapy*. Nov 2015;17(11):1638-45. doi:10.1016/j.jcyt.2015.07.006

### **Coding:**

CPT: 38204, 38205, 38206, 38207, 38208, 38209, 38210, 38211, 38212, 38213, 38214, 38215, 38220, 38230, 38232, 38240, 38241, 38242, 38243, 86812, 86813, 86816, 86817, 86821  
HCPCS: S2140, S2142, S2150

### **History:**

<b><u>History:</u></b>	<b><u>Date:</u></b>	<b><u>Activity:</u></b>
Medical Policy Panel	03/05/24	Review with revisions
Medical Policy Panel	03/07/22	Review with revisions
Medical Policy Panel	08/30/22	Approved guideline (Effective 9/19/22)
Medical Director (Dr. Deering)	07/18/22	Development

### **Policy Revisions:**

03/05/24	Updated	Resources section
03/07/23	Added:	“Insufficient evidence to support improvement of the net health outcome; or”, and “Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, or” to experimental or investigational bullets in systemic sclerosis and autoimmune disease criteria.
03/07/23	Revised:	“Insufficient evidence to support improvement outside the investigational setting” from #3 to #5 in experimental or investigational bullets in systemic sclerosis and autoimmune disease criteria.
03/07/23	Updated:	Description Section, Resources section



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### Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, [crc@azblue.com](mailto:crc@azblue.com). You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at <https://ocrportal.hhs.gov/ocr/portal/lobby.jsf>, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1-800-368-1019, 800-537-7697 (TDD). Complaint forms are available at <http://www.hhs.gov/ocr/office/file/index.html>

### Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un intérprete, llame al 602-864-4884.

Navajo: Dii kwe'é atah nilinigií Blue Cross Blue Shield of Arizona haada yit'éego bina'idilkidgo éi doodago Háida bíjá anilyeedigií t'áadoo le'é yina'idilkidgo beehaz'ánii hóloq dii t'áa hazaadk'ehjí háká a'doowolgo bee haz'á doo baqah ilinígóo. Ata' halne'ígíí kojí' bich'í' hodílnih 877-475-4799.

Chinese: 如果您，或是您正在協助的對象，有關於插入項目的名稱 Blue Cross Blue Shield of Arizona 方面的問題，您有權利免費以您的母語得到幫助和訊息。洽詢一位翻譯員，請撥電話 在此插入數字 877-475-4799。

Vietnamese: Nếu quý vị, hay người mà quý vị đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quý vị sẽ có quyền được giúp và có thêm thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thông dịch viên, xin gọi 877-475-4799.

Arabic:

إن كان لديك أو لدى شخص تساعد أسئلة بخصوص Blue Cross Blue Shield of Arizona، فلديك الحق في الحصول على المساعدة والمعلومات الضرورية بلغتك من دون أية تكلفة. للتحدث مع مترجم اتصل بـ 877-475-4799.



An Independent Licensee of the Blue Cross Blue Shield Association

EVIDENCE-BASED CRITERIA SECTION: MEDICINE

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Multi-Language Interpreter Services:

Tagalog: Kung ikaw, o ang iyong tinutulungan, ay may mga katanungan tungkol sa Blue Cross Blue Shield of Arizona...

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona 에 관해서 질문이 있다면...

French: Si vous, ou quelqu'un que vous êtes en train d'aider, a des questions à propos de Blue Cross Blue Shield of Arizona...

German: Falls Sie oder jemand, dem Sie helfen, Fragen zum Blue Cross Blue Shield of Arizona haben, haben Sie das Recht...

Russian: Если у вас или лица, которому вы помогаете, имеются вопросы по поводу Blue Cross Blue Shield of Arizona...

Japanese: ご本人様、またはお客様の身の回りの方でも、Blue Cross Blue Shield of Arizona についてご質問がございましたら...

Farsi: اگر شما، یا کسی که شما به او کمک میکنید، سوال در مورد Blue Cross Blue Shield of Arizona داشته باشید حق این را دارید که کمک و اطلاعات به زبان خود را به طور رایگان دریافت نمایید 877-475-4799 [تماس حاصل نمائید.]

Assyrian: Blue Cross Blue Shield of Arizona ... 877-475-4799.

Serbo-Croatian: Ukoliko Vi ili neko kome Vi pomažete ima pitanje o Blue Cross Blue Shield of Arizona, imate pravo da besplatno dobijete pomoć i informacije na Vašem jeziku.

Thai: หากคุณ หรือคนที่คุณกำลังช่วยเหลือถามเกี่ยวกับ Blue Cross Blue Shield of Arizona คุณสมสิทธิ์ที่จะได้รับความช่วยเหลือและขอมลในภาษา ของคุณได้โดยไมมคาคาไขจ่าย พดคยทลลท โทร 877-475-4799