MEDICAL NECESSITY GUIDELINES

Subject: Stem-Cell Transplantation for Aplastic Anemia and Fanconi Anemia
Number: 0293

Effective Date: 5/15/2008
Revision Date: 5/15/2009, 5/15/2010, 5/15/2011, 5/15/2012, 5/15/2013

INSTRUCTIONS FOR USE
This Medical Necessity Guideline outlines the factors CareAllies considers in determining medical necessity for this indication. Please note, the terms of a customer's particular benefit plan document or summary plan description (SPD) may differ significantly from the standard upon which this Medical Necessity Guideline is based. For example, a customer's benefit plan document or SPD may contain a specific exclusion related to the topic addressed. In the event of a conflict, a customer's benefit plan document or SPD always supercedes the information in this Medical Necessity Guideline. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document or SPD. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document or SPD in effect on the date of service; 2) any applicable laws/regulations, and; 3) the specific facts of the particular situation. Medical Necessity Guidelines are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of Cigna Health Management, Inc. © Copyright 2013.

Allogeneic hematopoietic stem-cell transplantation (HSCT) from an appropriately-matched human leukocyte antigen (HLA) donor is considered medically necessary for the treatment of EITHER of the following conditions:

- severe aplastic anemia (AA)
- Fanconi anemia

General Background

Aplastic Anemia
Aplastic anemia, along with Diamond-Blackfan anemia, Fanconi anemia, and others is an inherited bone marrow failure syndrome (IBMFS). IBMFS are rare disorders in which there is usually some form of aplastic anemia (failure of the bone marrow to produce blood. Some of these conditions have typical changes in physical appearance or in laboratory findings which suggest a specific diagnosis. Failure of the bone marrow to produce blood cells predisposes an individual to the future development of other hematological disorders, including leukemia and myelodysplastic syndrome.

Aplastic anemia (AA), also called hypoplastic anemia, is a potentially fatal bone marrow failure disorder that is characterized by pancytopenia and a hypocellular bone marrow (DeZern, 2012). This failure, which can be congenital or acquired, is related to either a defect in the stem-cell pool, or an injury to the microenvironment that supports the bone marrow. Immunosuppression improves marrow function in up to 80% of individuals with AA; however, it is not uncommon for those who respond to immunosuppressive therapy to experience disease relapse. Aplastic anemia is classified as non-severe (NSAA), severe (SAA) and very severe based on the degree of the peripheral blood cytopenias.

Severe AA is diagnosed according to the following criteria (Young, 2005):

- No other hematologic disease
- Bone marrow cellularity < 30%
- **TWO** of the following blood criteria:
  - neutrophils < 500/mm^3
  - platelets < 20,000/mm^3
  - absolute reticulocyte count < 40,000/mm^3

Allogeneic HSCT for Aplastic Anemia: Allogeneic hematopoietic stem-cell transplantation (HSCT) is a standard treatment option for individuals with severe AA. Allogeneic HSCT from a human leukocyte antigen (HLA)-matched sibling donor provides curative therapy for individuals with severe AA. It is considered a standard of care for individuals younger than 45 o 50 years of age, despite treatment-related morbidity and mortality (Young, 2008).

Hematopoietic recovery is often incomplete after immunosuppressive treatment, but tends to be complete and stable after HSCT (Young, 2008). The probability of survival with sustained donor engraftment for individuals with severe AA undergoing allogeneic HSCT is >80%, with younger patients having even better outcomes (Velardi, 2007). In children, matched-sibling-donor allogeneic HSCT has a >90% five-year overall survival (OS) rate (Bakhshi S., 2006), with ten-year outcomes of 97% reported for some children (Davies, 2007).

Young adults have a reasonable opportunity for cure with bone marrow transplantation but also face more complications than children (Young, 2006). Older individuals and those without HLA-identical related donors generally receive first-line therapy with immunosuppressive drugs. Alternative donor transplantation may be an option in children who do not have an -matched donor. Pienemann et al. (2011) published a meta-analysis of 26 studies comparing results achieved by use of a matched related donor HSCT compared with immunosuppression (IST) as first-line therapy. No randomized clinical trial was identified. A systematic review was performed on overall survival. On multivariate analysis, younger age was identified as a statistically significant factor for improved survival in individuals who received HSCT. Overall mortality was reported in 23 studies (HSCT vs. IST: 3%–67% vs. 9%–58%, respectively).

Although data from randomized controlled trials (RCTs) are lacking, a large number of case series and retrospective analyses report improved outcomes with the use of allogeneic HSCT. In several recent studies OS rates are 51% to 100% for a range of time intervals (Perez-Albuerne, 2008; Inamoto, 2007; Unal, 2007). In a prospective study of individuals who were treated with allogeneic HSCT after failure with immunosuppressive therapy compared with those who received only immunosuppression, four-year failure-free survival, defined as survival with response, was 83.9% in the transplantation group compared with 9.1% in the group who received immunosuppressive therapy alone (Kosada, 2008).

Disadvantages to allogeneic HSCT are procedure-related morbidity and mortality, especially graft-versus-host disease (GVHD) in older patients, and an increased incidence of solid organ malignancies (Young, 2005; Ades, et al., 2004). Graft failure after HSCT remains a significant problem in patients with AA, especially in those patients who have been heavily transfused (Champlin, 2007).

The toxicity of myeloablative allogeneic HSCT has led to investigation of non-myeloablative conditioning and allogeneic HSCT for selected individuals who have failed previous immunosuppressive therapy and/or who are transfusion dependent. Data from RCT are lacking; however, several small case series and retrospective analyses report durable engraftment and four-year OS of 93% and 89%, respectively, for individuals receiving sibling-matched and unrelated donor allografts, and five-year OS rates of 84% (Kennedy-Nasser, 2006; Resnick, 2006).

Although data are not robust, allogeneic hematopoietic stem-cell transplantation (HSCT) is considered a standard treatment option for individuals with severe aplastic anemia.

Fanconi Anemia

Fanconi anemia (also called Fanconi's anemia, FA, and aplastic anemia with congenital anomalies) is a form of congenital aplastic anemia. It is a rare, genetic disorder of autosomal recessive inheritance, characterized by congenital abnormalities, progressive bone marrow failure, spontaneous and induced chromosome breakage and increased cancer susceptibility (Gluckman, 2007). At least thirteen genes have been implicated in the disease (Gluckman, 2007). Survival after diagnosis can range from two to 25 years. By age 40 to 48 years, the estimated cumulative incidence of bone marrow failure is 90%.

Allogeneic hematopoietic stem-cell transplantation (HSCT) can rescue aplastic anemia and prevent the occurrence of clonal hematopoietic disorders and is considered the treatment of choice for patients with

severe hematological changes (Bonfim, 2007; Freedman, 2007; Velardi, 2007; Bitan, 2006; Motwani, 2005).

Allogeneic HSCT for Fanconi Anemia (FA): HSCT is currently the only curative therapy for the hematological abnormalities of FA. Although randomized controlled trials (RCT) data are lacking and evidence is not robust, FA is a universally accepted indication for allogeneic HSCT with a human leukocyte antigen (HLA)-identical sibling donor. Pooled published data on HSCT using HLA-matched sibling donors show a survival of greater than 80% in FA patients less than 10 years of age, and greater than 65% for FA patients of all ages (Freedman, 2008). Alternative donors may be considered for individuals without other options; however, survival is generally less than 50% (Guardiola, 2000; Gluckman, 1995). Graft-versus-host disease (GVHD) is more likely to be severe in patients with FA because of the underlying defect.

FA is a rare disease, and, consequently, patient populations for many transplantation series have been comparatively small. Data from case series, retrospective analyses and review of registry data suggest improved long-term outcomes with allogeneic HSCT. In a retrospective review of one cohort of 43 individuals with FA, overall survival (OS) was 93% at 3.7 years (Bonfirm, 2007). In a retrospective analysis of 64 individuals who received allogeneic HSCT for FA overall eight-year event-free survival for the total population was 66%; eight-year OS was 67% (Locatelli, 2007). Farzin et al. (2007) reported 10-year OS rates of 89% in a cohort of 35 patients with FA who underwent allogeneic HSCT.

Reduced-dose or non-myeloablative conditioning regimens may result in acceptable toxicity, high engraftment rates, improved survival and comparable incidences of GVHD compared with standard dose regimens utilized for hematological malignancies (Balci, 2008; Bonfirm, 2007; Bitan, 2006; Tan, 2006; Yabe, 2006; Janis-Netro, 2005). Data are not robust, and patient populations are small; nonetheless, this therapy may allow allogeneic transplantation in patients who are older, have co-morbid conditions, or have toxicities from previous treatment. Patients with minimal and chemotherapy-sensitive disease transplanted early in their disease course may have better outcomes.

Although randomized control trial data are lacking, allogeneic HSCT is considered a standard treatment option for individuals with Fanconi anemia.

Stem-Cell Transplantation
Stem-cell transplantation refers to the transplantation of hematopoietic stem cells (HSCs) from a donor into a recipient. HSCs are immature cells that can develop into any of the three types of blood cells (i.e., red cells, white cells or platelets). Allogeneic HSCT uses stem cells from a donor.

In allogeneic HSCT it is preferable for donors to have a human leukocyte antigen (HLA) type that is identical to the recipient. Matching is performed on the basis of variability at three of more loci of the HLA gene (e.g., HLA-A, HLA-B, HLA-DRB1). Alternative donor sources are being evaluated for individuals with aplastic anemia and Fanconi anemia who do not have an HLA-identical donor. As HLA variability increases, transplant-related morbidity and mortality, including graft rejection and graft-versus-host disease, also increase. Long-term survival after mismatched related donation is inferior to genotypically matched donor transplantation (Young, 2008).

Contraindications to Stem-Cell Transplantation
The presence of any significant co-morbid conditions which would significantly compromise clinical care and chances of survival is a contraindication to transplantation. Relative contraindications to HSCT include, but are not limited to:

- poor cardiac function (ejection fraction less than 45%)
- poor liver function (bilirubin greater than 2.0 mg/dL and transaminases greater than two times normal)
- poor renal function (creatinine clearance less than 50 mL/min)
- poor pulmonary function (diffusion capacity [DLCO] less than 60% of predicted)
- presence of human immunodeficiency virus or an active form of hepatitis B, hepatitis C or human T-cell lymphotropic virus (HTLV-1)

- Karnofsky rating less than 60% and/or Eastern Cooperative Oncology Group (ECOG) performance status greater than two

Professional Societies/Organizations
British Committee for Standards in Hematology (BCSH) General Hematology Task Force (2009): On behalf of the NCSH, Marsh et al. (2009) published guidelines recommending allogeneic hematopoietic stem-cell transplantation (HSCT) as the initial treatment of choice for newly diagnosed patients with very severe or severe aplastic anemia, and a human leukocyte antigen (HLA)-compatible sibling donor. Immunosuppressive therapy is recommended for patients with non-severe aplastic anemia who are transfusion dependent, patients with severe or very severe disease who are >40 years old, and younger patients with severe or very severe disease who do not have an HLA-identical sibling donor. Matched unrelated donor bone marrow transplant may be considered when a patient has severe aplastic anemia, has no matched sibling donor but a matched unrelated donor, is <50 years old (or 50–60 years old with good performance
status), and has failed at least one course of ATG and cyclosporine.

National Marrow Donor Program (NMDP): The NMDP lists severe aplastic anemia and other bone marrow failure states including Fanconi anemia as indications for HSCT.

Summary
Allogeneic HSCT is considered a standard treatment option for individuals with severe aplastic anemia or Fanconi anemia. Although data are not robust, the published, peer-reviewed evidence supports the safety and effectiveness of allogeneic hematopoietic stem-cell transplantation (HSCT) for this indication.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.

When medically necessary:

CPT®* Codes	Description
38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic
38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing, per donor
38209	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, with washing, per donor
38210	Transplant preparation of hematopoietic progenitor cells; specific cell depletion within harvest, T-cell depletion
38212	Transplant preparation of hematopoietic progenitor cells; red blood cell removal
38213	Transplant preparation of hematopoietic progenitor cells; platelet depletion
38214	Transplant preparation of hematopoietic progenitor cells; plasma (volume) depletion
38215	Transplant preparation of hematopoietic progenitor cells; cell concentration in plasma, mononuclear or buffy-coat layer
38230	Bone marrow harvesting for transplantation, allogeneic
38240	Hematopoietic progenitor cell (HPC); allogeneic, per donor
38242	Allogeneic lymphocyte infusions

HCPCS Codes	Description
S2140	Cord blood harvesting for transplantation, allogeneic
S2142	Cord blood-derived stem cell transplantation, allogeneic

S2150[†]	Bone marrow or blood-derived stem cells (peripheral or umbilical), allogeneic or autologous, harvesting, transplantation, and related complications; including pheresis and cell preparation/storage; marrow ablative therapy; drugs; supplies; hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services; and the number of days or pre-and post-transplant care in the global definition

[†]Note: Medically necessary when used to report allogeneic bone marrow or blood-derived stem-cell procedures.

References

1. Ades L, Mary JY, Robin M, Ferry C, Porcher R, Esperou H, et al. Long-term outcome after bone marrow transplantation for severe aplastic anemia. Blood. 2004 Apr 1;103(7):2490-7.

2. American Cancer Society. Aplastic anemia. Updated 2012 Jan 23. Accessed Mar 25, 2013. Available at URL address: http://documents.cancer.org/901.00/901.00.pdf

3. Bacigalupo A, Bruno B, Saracco P, Di Bona E, Locasciulli A, Locatelli F, et al. Antilymphocyte globulin, cyclosporine, prednisolone, and granulocyte colony-stimulating factor for severe aplastic anemia: an update of the GITMO/EBMT study on 100 patients. Blood. 2000 Mar 15;1931-4.

4. Bacigalupo A, Locatelli F, Lanino E, Marsh J, Socie G, Maury S, et al. Fludarabine, cyclophosphamide and anti-thymocyte globulin for alternative donor transplants in acquired severe aplastic anemia: a report from the EBMT-SAA Working Party. Bone Marrow Transplant. 2005 Dec;36(11):947-50.

5. Bakhshi S. Aplastic anemia. Updated 2011 Nov 1. Accessed Mar 25, 2013. Available at URL address: http://www.emedicine.com/med/topic162.htm

6. Balci YI, Akdemir Y, Gumruk F, Cetin M, Arpaci F, Uckan D. CD-34 selected hematopoietic stem cell transplantation from HLA identical family members for Fanconi anemia. Pediatr Blood Cancer. 2008 May;50(5):1065-7

7. Bitan M, Or R, Shapira MY, Aker M, Resnick IB, Ackerstein A, et al. Fludarabine-based reduced intensity conditioning for stem cell transplantation of Fanconi anemia patients from fully matched related and unrelated donors. Biol Blood Marrow Transplant. 2006 Jul;12(7):712-8.

8. Bonfim CM, de Medeiros CR, Bitencourt MA, Zanis-Neto V, Funke VA, Setubal DC, et al. HLA-matched related donor hematopoietic cell transplantation in 43 patients with Fanconi anemia conditioned with 60 mg/kg of cyclophosphamide. Biol Blood Marrow Transplant. 2007 Dec;13(12):1455-60. Epub 2007 Oct 18.

9. Brodsky RA. Acquired Aplastic Anemia. In: Greer JP, Foerster J, Rodgers GM, Paraskevas F, Glader B, Arber DA, Means RT, editors. Wintrobe's Clinical oncology, 12th ed. Philadelphia: Lippincott Williams & Wilkins; 2009.

10. Bunin N, et al. Unrelated donor bone marrow transplantation for children with severe aplastic anemia: minimal GVHD and durable engraftment with partial T cell depletion. Bone Marrow Transplant. 2005 Jan 10 (35) 369-373.

11. Champlin RE, Perez WS, Passweg JR, Klein JP, Camitta BM, Gluckman E, et al. Bone marrow transplantation for severe aplastic anemia: a randomized controlled study of conditioning regimens. Blood. 2007 Feb 1; [Epub ahead of print]

12. Davies JK, Guinan GC. An update on the management of severe idiopathic aplastic anaemia in children. Br J Haematol. 2007 Feb;136(4):549-64.

13. Deeg HJ, O'Donnell M, Tolar J, Agarwal J, Harris RE, Feig SA, et al. Optimization of conditioning for marrow transplantation from unrelated donors for patients with aplastic anemia after failure of immunosuppressive therapy. Blood. 2006 Sep 1;108(5):1485-91. Epub 2006 May 9.

14. DeZern AE, Brodsky RA. Clinical management of aplastic anemia. Expert Rev Hematol. 2011 Apr;4(2):221-30.

15. Farzia A, Davies SM, Smith FO, Filipovich A, Hansen M, Auerbach RD, et al. Matched sibling donor haematopoietic stem cell transplantation in Fanconi anaemia: an update of the Cincinnati Children's experience. Br J Haematol. 2007 Feb;136(4):633-40.

16. Freedman MH. Inherited forms of bone marrow failure. In: Hoffman R, Benz EJ, Shattil SJ, Silberstein LE, Heslop HE, Weitz JI, editors. Hematology: basic principles and practice, 6th ed. Orlando: Churchill Livingstone; 2012.

17. Freedman MH. The pancytopenias. In: Kleigman RM, Stanton BF, St. Geme III JW, Schor NF, Berhman RE, editors. Nelson textbook of pediatrics, 19th ed. Philadelphia: W.B. Saunders; 2011

18. George B, Mathews V, Viswabandya A, Kavitha ML, Srivastava A, Chandy M. Fludarabine based reduced intensity conditioning regimens in children undergoing allogeneic stem cell transplantation for severe aplastic anemia. Pediatr Transplant. 2008 Feb;12(1):14-9. Epub 2007 Dec 14.

19. Gluckman E, Auerbach AD, Horowitz MM, Sobocinski KA, Ash RA, Bortin MM, et al. Bone marrow transplantation for Fanconi anemia. Blood. 1995 Oct 1;86(7):2856-62.

20. Gluckman E, Wagner JE. Hematopoietic stem cell transplantation in childhood inherited bone marrow failure syndrome. Bone Marrow Transplant. 2008 Jan;41(2):127-32. Epub 2007 Dec 17.

21. Guardiola P, Pasquini R, Dokal I, Ortega JJ, van Weel-Sipman M, Marsh JC, et al. Outcome of 69 allogeneic stem cell transplantations for Fanconi anemia using HLA-matched unrelated donors: a study on behalf of the European Group for Blood and Marrow Transplantation. Blood. 2000 Jan 15;95(2):422-9.

22. Guardiola P, Socie G, Li X, Ribaud P, Devergie A, Esperou H, et al. Acute graft-versus-host disease in patients with Fanconi anemia or acquired aplastic anemia undergoing bone marrow transplantation from HLA-identical sibling donors: risk factors and influence on outcome. Blood. 2004 Jan 1;103(1):73-7.

23. Kennedy-Nasser AA, Leung KS, Mahajan A, Weiss HL, Arce JA, Gottschalk S, et al. Comparable outcomes of matched-related and alternative donor stem cell transplantation for pediatric severe aplastic anemia. Biol Blood Marrow Transplant. 2006 Dec;12(12):1277-84.

24. Koh LP, Koh MB, Ng HY, Kwang WY, Goh YT, Linn YC, et al. Allogeneic hematopoietic stem cell transplantation for patients with severe aplastic anemia following nonmyeloablative conditioning using 200-cGy total body irradiation and fludarabine. Biol Blood Marrow Transplant. 2006 Aug;12(8):887-90.

25. Kojima S, Matsuyama T, Kato S, Kigasawa H, Kobayashi R, Kikuta A, et al. Outcome of 154 patients with severe aplastic anemia who received transplants from unrelated donors: the Japan Marrow Donor Program. Blood. 2002 Aug 1;100(3):799-803.

26. Kutler DI, Singh B, Satagopan J, Batish SD, Berwick M, Giampietro PF, et al. A 20-year perspective on the International Fanconi Anemia Registry (IFAR). Blood. 2003 Feb 15;101(4):1249-56.

27. Locatelli F, Zecca M, Pession A, Morreale G, Longoni D, D Bartolomeo P, et al. The outcome of children with Fanconi anemia given hematopoietic stem cell transplantation and the influence of fludarabine in the conditioning regimen: a report from the Italian pediatric group. Haematologica. 2007 Oct;92(10):1381-8.

28. Marsh JC, Ball SE, Cavenagh J, Darbyshire P, Dokal I, Gordon-Smith EC, et al. Guidelines for the diagnosis and management of aplastic anaemia. Br J Haematol. 2009 Oct;147(1):43-70.

29. Motwani J, Lawson SE, Darbyshire PJ. Successful HSCT using non-radiotherapy-based conditioning regimens and alternative donors in patients with Fanconi anaemia-experience in a single UK centre. Bone Marrow Transplant. 2005 Sep;36(5):408-10.

30. National Cancer Institute. Inherited bone marrow failure syndromes. Accessed Mar 25, 2013. Available at URL address: http://marrowfailure.cancer.gov/

31. National Marrow Donor Program. Evaluating adult patients prior to hematopoietic cell transplant. Copyright © 1996-2013 National Marrow Donor Program. Accessed Mar 25, 2013. Available at URL address: http://www.marrow.org/PHYSICIAN/Tx_Indications_Timing_Referral/Evaluating_Adult_Patients_Prio/index.html

32. National Marrow Donor Program. Recommended timing for transplant consultation. Copyright © 1996-2013 National Marrow Donor Program. Accessed Mar 25, 2013. Available at URL address: http://www.marrow.org/PHYSICIAN/Tx_Indications_Timing_Referral/Diseases_Treatable_by_HCT/index.html

33. National Marrow Donor Program. Severe aplastic anemia and fanconi anemia-NMDP transplant outcomes. Copyright © 1996-2013 National Marrow Donor Program. Accessed Mar 25, 2013. Available at URL address: http://marrow.org/Physicians/Outcomes_Data/Outcomes_Data.aspx#transplant

34. Peinemann F, Grouven U, Kroger N, Bartel C, Pittler MH, Lange F. First-line matched related donor hematopoietic stem cell transplantation compared to immunosuppressive therapy in acquired severe aplastic anemia. PLoS One. 2011 Apr 25;6(4):e18572.

35. Perez-Albuerne ED, Eapen M, Klein J, Gross TJ, Lipton JM, Baker JS, et al. Outcome of unrelated donor stem cell transplantation for children with severe aplastic anemia. Br J Haematol. 2008 Apr;141(2):216-23. Epub 2008 Feb 26.

36. Resnick IB, Aker M, Shapira MY, Tsirigotis PD, Bitan M, Abdul-Hai A, et al. Allogeneic stem cell transplantation for severe acquired aplastic anaemia using a fludarabine-based preparative regimen. Br J Haematol. 2006 Jun;133(6):649-54.

37. Rosenberg PS, Alter BP, Ebell W. Cancer risks in Fanconi anemia: findings from the German Fanconi Anemia Registry. Haematologica. 2008 Apr;93(4):511-7. Epub 2008 Mar 5.

38. Rubinstein P, Carrier C, Scaradavou A, Kurtzberg J, Adamson J, Migliaccio AR, et al. Outcomes among 562 recipients of placental-blood transplants from unrelated donors. N Engl J Med. 1998 Nov 26;339(22):1565-77.

39. Srinivasan R, Takahashi Y, McCoy JP, Espinoza-Delgado I, Dorrance C, Igarashi T, et al. Overcoming graft rejection in heavily transfused and allo-immunised patients with bone marrow failure syndromes using fludarabine-based haematopoietic cell transplantation. Br J Haematol. 2006 May;133(3):305-14.

40. Storb R, Blume KG, O'Donnell MR, Chauncey T, Forman SJ, Deeg HJ, et al. Cyclophosphamide and antithymocyte globulin to condition patients with aplastic anemia for allogeneic marrow transplantations: the experience in four centers. Biol Blood Marrow Transplant. 2001.7:39-44.

41. Stucki A, Leisenring W, Sandmaier BM, Sanders J, Anasetti C, Storb R. Decreased rejection and improved survival of first and second marrow transplants for severe aplastic anemia (a 26-year retrospective analysis). Blood. 1998 Oct 15;2742-9.

42. Tajika K, Mizuki T, Nakayama K, Yamaguchi H, Dan K. Umbilical-cord blood cell transplantation conditioned with a reduced intensity-regimen is a practical salvage therapy for severe aplastic anemia refractory to immunosuppressive therapy with antithymocyte globulin/ciclosporin. J Nippon Med Sch. 2007 Dec;74(6):424-9.

43. Tan PL. Wagner JE, Auerbach AD, Defor TE, Slungaard A, Macmillan ML. Successful engraftment without radiation after fludarabine-based regimen in Fanconi anemia patients undergoing genotypically identical donor hematopoietic cell transplantation. Pediatr Blood Cancer. 2006 May 1;46(5):630-6

44. Tisdale JF, Maciejewski JP, Nunez O, Rosenfeld SJ, Young NS. Late complications following treatment for severe aplastic anaemia (SAA) with high-dose cyclophosphamide (Cy): follow-up of a randomized trial. Blood. 2002 Dec 15;100(13):4668-70.

45. Unal S, Cetin M, Tavil B, Caliskan M, Yetgin S, Uckan D. Favorable outcome with allogeneic hematopoietic stem cell transplantation in pediatric acquired aplastic anemia patients. Pediatr Transplant. 2007 Nov;11(7):788-91.

46. Velardi A, Locatelli F. Hematopoietic stem cell transplantation: clinical indications. In: Kliegman RM, Stanton BF, St Geme II JW, Schor NF, Behrman RE, editors. Nelson textbook of pediatrics, 19th ed. Philadelphia: W.B. Saunders; 2011.

47. Yabe H, Inoue H, Matsumoto M, Hamanoue S, Koike H, Suzuki K, et al. Allogeneic haematopoietic cell transplantation from alternative donors with a conditioning regimen of low-dose irradiation, fludarabine and cyclophosphamide in Fanconi anaemia. Br J Haematol. 2006 Jul;134(2):208-12.

48. Young NS, Calado RT, Scheinberg P. Current concepts in the pathophysiology and treatment of aplastic anemia. Blood. 2006 Oct 15;108(8):2509-19. Epub 2006 Jun 15.

49. Young NS, Maciejewski JP. Aplastic Anemia. In: Hoffman R, Benz E, Silberstein LE, Heslop HE, Weitz JI, editors. Hematology: basic principles and practice, 6th ed. Orlando: Churchill Livingstone; 2012.

50. Yoshimi A, Kojimi S, Taniguchi S, Hara J, Matsui T, Takahasi Y, et al. Unrelated cord blood transplantation for severe aplastic anemia. Biol Blood Marrow Transplant. 2008 Sep;14(9):1057-63.

51. Zanis-Neto J, Flowers ME, Medeiros CR, Bitencourt MA, Bonfim CM, Setubal DC, et al. Low-dose cyclophosphamide conditioning for haematopoietic cell transplantation from HLA-matched related donors in patients with Fanconi anaemia. Br J Haematol. 2005 Jul;130(1):99-106.