TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: Imatinib

INDICATION: Acute lymphoblastic leukemia, Philadelphia chromosome positive, newly diagnosed, as part of combination therapy [pediatric]

COMPENDIA TRANSPARENCY REQUIREMENTS	
1	Provide criteria used to evaluate/prioritize the request (therapy)
2	Disclose evidentiary materials reviewed or considered
3	Provide names of individuals who have substantively participated in the review or disposition of the request and disclose their potential direct or indirect conflicts of interest
4	Provide meeting minutes and records of votes for disposition of the request (therapy)

EVALUATION/PRIORITIZATION CRITERIA: **A, C, L, P, S**
*to meet requirement 1

CODE	EVALUATION/PRIORITIZATION CRITERIA
A	Treatment represents an established standard of care or significant **advance** over current therapies
C	**Cancer** or cancer-related condition
E	Quantity and robustness of **evidence** for use support consideration
L	**Limited** alternative therapies exist for condition of interest
P	**Pediatric** condition
R	**Rare** disease
S	**Serious**, life-threatening condition

Note: a combination of codes may be applied to fully reflect points of consideration [eg, therapy may represent an advance in the treatment of a life-threatening condition with limited treatment alternatives (ASL)]

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EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Schultz,K.R., et al: Improved early event-free survival with imatinib in Philadelphia chromosome-positive acute lymphoblastic leukemia: a children's oncology group study. J Clin Oncol Nov 01, 2009; Vol 27, Issue 31; pp. 5175-5181.	Study methodology comments: This was a randomized, open-label, comparative trial that should be interpreted with caution. The patients were stratified in to small cohorts and a power analysis focused on detecting differences was not conducted. Additional weaknesses included 1) open-label design without the use of independent reviewers; and 2) possible selection bias since patients were not recruited in a random or consecutive manner. Strengths were 1) presented eligibility criteria; 2) had a control group; 3) defined primary outcome; 4) compared baseline characteristics of groups; 5) examined the effect of risk factors on outcomes; and 6) conducted sample size calculations to increase precision of confidence intervals	S
Badell I, Munoz A, Estella J, et al: Long-term results of two consecutive trials in childhood acute lymphoblastic leukaemia performed by the Spanish Cooperative Group for Childhood Acute Lymphoblastic leukemia group (SHOP) from 1989 to 1998. Clin Trans Oncol 2008;10(2):117-124.		S
Rives,S., et al: Intermediate dose of imatinib in combination with chemotherapy followed by allogeneic stem cell transplantation improves early outcome in paediatric Philadelphia chromosome-positive acute lymphoblastic leukaemia (ALL): results of the Spanish Cooperative Group SHOP studies ALL-94, ALL-99 and ALL-2005. Br J Haematol Sep 2011; Vol 154, Issue 5; pp. 600-611.	Study methodology comments: Patients who participated in three studies of similar chemotherapy protocols were analyzed. Patients in the SHOP-94 and SHOP-99 studies did not receive imatinib (historical control group) and thus were compared to patients in the SHOP-2005 study who did receive imatinib. Strengths of the study were 1) had a control group; 2) defined response; and 3) compared baseline characteristics of groups. Weaknesses were 1) did not present eligibility criteria; 2) open-label design without the use of independent reviewers; 3) did not examine the effect of confounds on outcomes; 4) did not present 95% confidence intervals; and 5) no power analysis.	S

Champagne,M.A., et al: Imatinib mesylate (STI571) for treatment of children with Philadelphia chromosome-positive leukemia: results from a Children's Oncology Group phase 1 study. Blood Nov 01, 2004; Vol 104, Issue 9; pp. 2655-2660.		2
Fagioli,F., et al: Allogeneic Hematopoietic Stem Cell Transplantation for Philadelphia-Positive Acute Lymphoblastic Leukemia in Children and Adolescents: A Retrospective Multicenter Study of the Italian Association of Pediatric Hematology and Oncology (AIEOP). Biol Blood Marrow Transplant Oct 20, 2011; Vol E Pub, p. E Pub		2
Burke,M.J., et al: Allo-hematopoietic cell transplantation for Ph chromosome-positive ALL: impact of imatinib on relapse and survival. Bone Marrow Transplant Jan 2009; Vol 43, Issue 2; pp. 107-113		
Ribera,J.M., et al: Concurrent intensive chemotherapy and imatinib before and after stem cell transplantation in newly diagnosed Philadelphia chromosome-positive acute lymphoblastic leukemia. Final results of the CSTIBES02 trial. Haematologica Jan 2010; Vol 95, Issue 1; pp. 87-95.		1

Chen,H., et al: Administration of imatinib in the first 90 days after allogeneic hematopoietic cell transplantation in patients with Philadelphia chromosome-positive acute lymphoblastic leukemia. Chin Med J (Engl) Jan 2011; Vol 124, Issue 2; pp. 246-252.		1
Wassmann,B., et al: Early molecular response to posttransplantation imatinib determines outcome in MRD+ Philadelphia-positive acute lymphoblastic leukemia (Ph+ ALL). Blood Jul 15, 2005; Vol 106, Issue 2; pp. 458-463		1
Lee,K.H., et al: Clinical effect of imatinib added to intensive combination chemotherapy for newly diagnosed Philadelphia chromosome-positive acute lymphoblastic leukemia. Leukemia Sep 2005; Vol 19, Issue 9; pp. 1509-1516		1
Thomas,D.A., et al: Treatment of Philadelphia chromosome-positive acute lymphocytic leukemia with hyper-CVAD and imatinib mesylate. Blood Jun 15, 2004; Vol 103, Issue 12; pp. 4396-4407.		1
Lahaye,T., et al: Response and resistance in 300 patients with BCR-ABL-positive leukemias treated with imatinib in a single center: a 4.5-year follow-up. Cancer Apr 15, 2005; Vol 103, Issue 8; pp. 1659-1669.		3

Carpenter,P.A., et al: Prophylactic administration of imatinib after hematopoietic cell transplantation for high-risk Philadelphia chromosome-positive leukemia. Blood Apr 01, 2007; Vol 109, Issue 7; pp. 2791-2793		1
Wassmann,B., et al: Therapy with imatinib mesylate (Glivec) preceding allogeneic stem cell transplantation (SCT) in relapsed or refractory Philadelphia-positive acute lymphoblastic leukemia (Ph+ALL). Leukemia Dec 2002; Vol 16, Issue 12; pp. 2358-2365.		1
Cioch,M.B. and Dmoszynska,A.: Imatinib therapy of Ph positive acute lymphoblastic leukaemia - 2 Case reports. Reports of Practical Oncology and Radiotherapy 2005; Vol 10, Issue 2; pp. 103-106.		3
Fuster,J.L., et al: Imatinib mesylate in combination with chemotherapy in four children with de novo and advanced stage Philadelphia chromosome-positive acute lymphoblastic leukemia. Haematologica-the Hematology Journal Dec 2007; Vol 92, Issue 12; pp. 1723-1724.		4

Rives,S., et al: Intermediate Dose of Imatinib In Combination with Chemotherapy Followed by Allogeneic Stem Cell Transplantation (SCT) Improves Early Outcome In Childhood Philadelphia Chromosome-Positive (Ph plus) Acute Lymphoblastic Leukemia (ALL). Results of the Spanish Cooperative Group SHOP/SEHOP Studies SHOP 94, SHOP 99 and SHOP 05. Blood Nov 19, 2010; Vol 116, Issue 21; pp. 1331-1332	Abstract	3
Schultz,K.R., et al: Minimal toxicity of imatinib mesylate in combination with intensive chemotherapy for Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL) in children: A report of the Children's Oncology Group (COG) AALL0031 protocol for very high risk ALL. Blood Nov 16, 2006; Vol 108, Issue 11; pp. 87A-87A.	Abstract	3

Literature evaluation codes: S = Literature selected; 1 = Literature rejected = Topic not suitable for scope of content; 2 = Literature rejected = Does not add clinically significant new information; 3 = Literature rejected = Methodology flawed/Methodology limited and unacceptable; 4 = Other (review article, letter, commentary, or editorial)

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CONTRIBUTORS:
*to meet requirement 3

PACKET PREPARATION	DISCLOSURES	EXPERT REVIEW	DISCLOSURES
Margi Schiefelbein, PA	None	Edward P. Balaban, DO	None
Stacy LaClaire, PharmD	None	Thomas McNeil Beck, MD	None
Felicia Gelsey, MS	None	James E. Liebmann, MD	None
		Jeffrey A. Bubis, DO	None
		John M. Valgus, PharmD	None

ASSIGNMENT OF RATINGS:
*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	---	---		B
Edward P. Balaban, DO	Evidence favors efficacy	Class IIa - Recommended, In Most Cases	It would be important to have more data to confirm, however the results are so provocative (with little adverse effect), that it seems reasonable to factor in this drug in the treatment of this population that tends to have a poor prognosis	N/A
Thomas McNeil Beck, MD	Evidence favors efficacy	Class IIa - Recommended, In Most Cases	Strong evidence of efficacy- moderate toxicity.	N/A
James E. Liebmann, MD	Effective	Class I - Recommended	I do not believe a prospective, randomized trial of Imatinib in Ph+ ALL can or should be done. The drug is already FDA-approved for recurrent Ph+ ALL. The results of the European and US trials are similar and believable. Imatinib is an active drug and adds very little toxicity in the treatment of this disease.	N/A
Jeffrey A. Bubis, DO	Effective	Class I - Recommended	Increased event free survival and overall survival over treatment without it.	N/A

John M. Valgus, PharmD	Evidence favors efficacy	Class IIa - Recommended, In Most Cases	Two large trials suggest efficacy and safety when compared to historical controls. No randomized data currently available. Data in adult population also positive.	N/A