IBM Watson Health™

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 6/27/2019

PACKET: 1903

DRUG: Ponatinib Hydrochloride

USE: Philadelphia chromosome-positive acute lymphoblastic leukemia; Newly diagnosed, in combination with chemotherapy

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: C, R, L, 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)]

EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Jabbour,E., Short,N.J., Ravandi,F., et al: Combination of hyper-CVAD with ponatinib as first-line therapy for patients with Philadelphia chromosome-positive acute lymphoblastic leukaemia: long-term follow-up of a single-centre, phase 2 study. Lancet Haematol Dec 2018; Vol 5, Issue 12; pp. e618-e627.	This was an open-label, single-arm phase II clinical trial that assessed ponatinib in patients with previously untreated Philadelphia-chromosome-positive ALL. There was low risk of bias associated with selection of cohorts and assessment of outcomes. Data was gathered prospectively for objective outcomes. All subjects were included in the analyses. One caveat of the study is that it lacked a control group.	S
Jabbour,E., Kantarjian,H., Ravandi,F., et al: Combination of hyper-CVAD with ponatinib as first-line therapy for patients with Philadelphia chromosome-positive acute lymphoblastic leukaemia: a single-centre, phase 2 study. Lancet Oncol Nov 2015; Vol 16, Issue 15; pp. 1547-1555.		2
Short,N.J., Kantarjian,H., Pui,C.H., et al: SOHO state of the art update and next questions: Philadelphia chromosome-positive acute lymphoblastic leukemia. Clin Lymphoma Myeloma Leuk Jul 2018; Vol 18, Issue 7; pp. 439-446.		4

Hoelzer,D., Bassan,R., Dombret,H., et al: Acute lymphoblastic leukaemia in adult patients: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann.Oncol Sep 2016; Vol 27, Issue suppl 5; pp. v69-v82.		1

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)

CONTRIBUTORS:

*to meet requirement 3

PACKET PREPARATION	DISCLOSURES	EXPERT REVIEW	DISCLOSURES
Megan Smith	None		
Stacy LaClaire, PharmD	None		
Catherine Sabatos, PharmD	None		
		John D Roberts	None
		Jeffrey Klein	None
		Richard LoCicero	Incyte Corporation Local PI for REVEAL. Study is a multicenter, non-interventional, non-randomized, prospective, observational study in an adult population for patients who have been diagnosed with clinically overt PV and are being followed in either community or academic medical centers in the US who will be enrolled over a 12-month period and observed for 36 months.

ASSIGNMENT OF RATINGS:
*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
IBM MICROMEDEX	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases		B
John Roberts	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	Imatinib, a first generation tyrosine kinase inhibitor targeting the bcr-abl translocation, in combination with chemotherapy is the accepted standard treatment of Philadelphia chromosome positive acute lymphoblastic leukemia in adults. In single arm studies ponatinib, a next generation TKI, in combination with chemotherapy showed effectiveness similar to previous studies of imatinib in combination with chemotherapy. The combination was safe and reasonably tolerated. Nilotinib has a different side effect profile than imatinib. There are theoretical reasons both to prefer and not prefer ponatinib. Some have suggested that chemotherapy should be adjusted to be less dose intense when given with a TKI.	
Richard LoCicero	Effective	Class IIa: Recommended, in Most Cases	A phase II trial has established the effectiveness of ponatinib in combination with chemotherapy in Ph+ALL. No unexpected toxicities were noted.	
Jeffrey Klein	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	The use of Ponatinib in newly diagnosed ALL Philadelphia chromosome postive patients along with other chemotherapy demonstrated a “good event free survival.” Further studies are needed to evaluate the advantage of Ponatinib over other similar products in its class. The incidence of more serious adverse effects needs to be considered as well.	