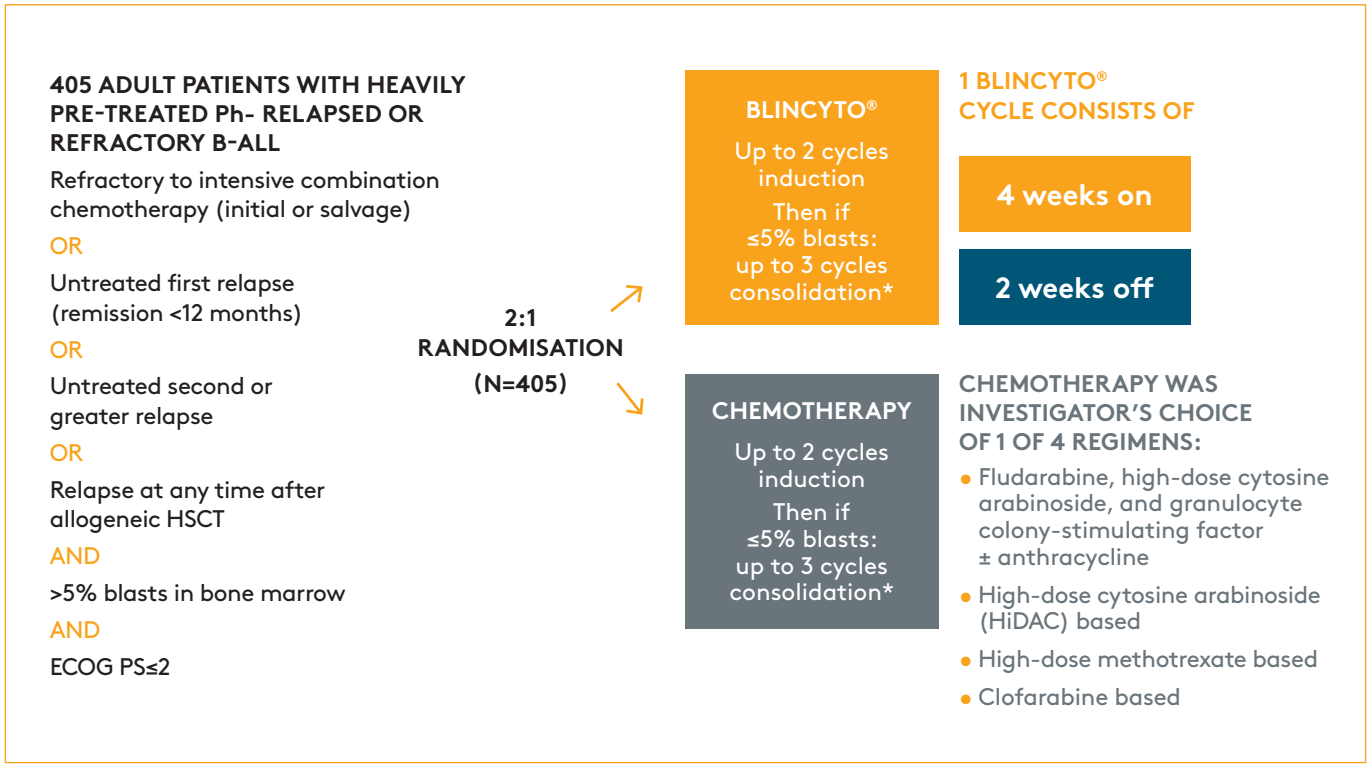
EFFICACY IN Ph- RELAPSED OR REFRACTORY B-ALL

BLINCYTO® WAS STUDIED IN THE INTERNATIONAL, RANDOMISED, OPEN-LABEL, PHASE 3 STUDY (TOWER)[1]

Kantarjian H *et al. N Engl J Med* 2017;376:836–47.



Both study arms were well matched at baseline, in terms of demographic and disease characteristics. BLINCYTO® was given via cIV infusion; dose 9 mcg/day during Week 1 of Cycle 1, and 28 mcg/day thereafter.
*If ≤ 5% blasts in bone marrow after consolidation therapy, patients could continue to receive maintenance therapy.

STUDY ENDPOINTS[1]

Primary	• Overall survival (OS)
Key secondary	• Complete remission (CR) with full haematological recovery within 12 weeks of treatment initiation • CR with full, partial or incomplete haematological recovery (CR/CRh/CRi) within 12 weeks of treatment initiation • Event-free survival (events included relapse after achieving CR/CRh/CRi or death; patients who did not achieve CR/CRh/CRi were assigned an event-free duration of 1 day)

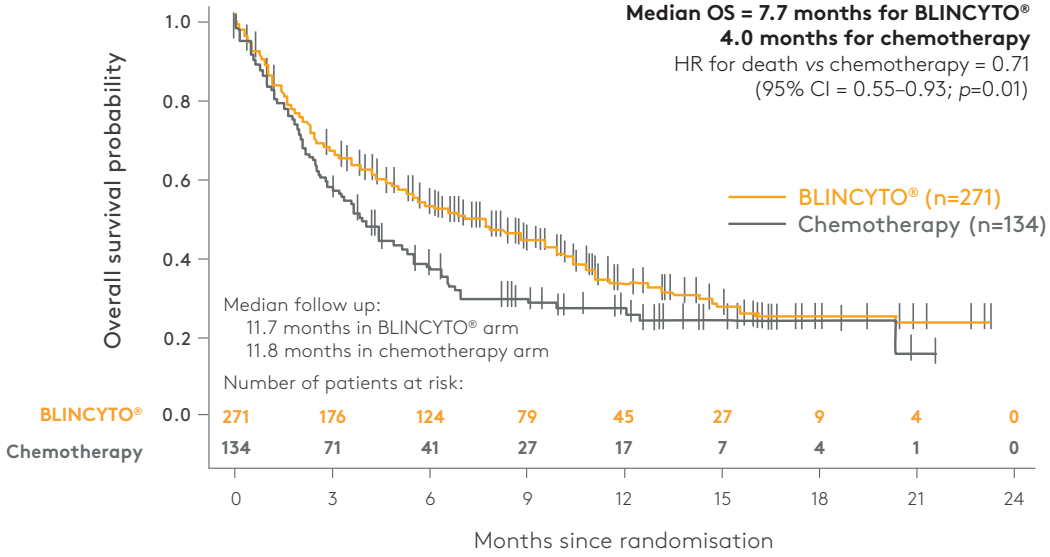
ECOG PS: Eastern Cooperative Oncology Group performance status; **cIV:** continuous intravenous.

Reference: 1. Kantarjian H *et al. N Engl J Med* 2017;376:836–47.

EFFICACY IN Ph- RELAPSED OR REFRACTORY B-ALL

BLINCYTO® ALMOST DOUBLED MEDIAN OVERALL SURVIVAL COMPARED WITH CHEMOTHERAPY (PRIMARY ENDPOINT; ITT)[1]

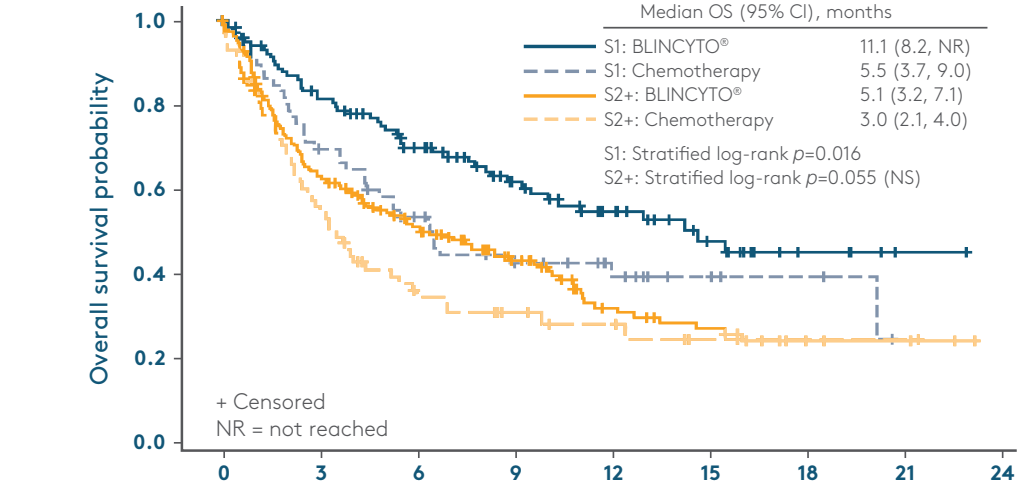
OVERALL SURVIVAL



Adapted from: Kantarjian *et al.* 2017.[1] Caution: Small patient numbers after 15 months.

EARLY USE OF BLINCYTO® (AS FIRST SALVAGE) MORE THAN DOUBLED OVERALL SURVIVAL COMPARED WITH CHEMOTHERAPY[1,2]

OVERALL SURVIVAL AMONG PATIENTS AS FIRST SALVAGE (S1) OR PRIOR (S2+) SALVAGE TREATMENT[2]



No of patients:									
S1: BLINCYTO®	104	80	59	39	26	14	5	1	0
S1: Chemotherapy	63	39	26	18	11	5	3	0	
S2+: BLINCYTO®	167	96	65	40	19	13	4	3	0
S2+: Chemotherapy	71	32	15	9	6	2	1	1	0

Adapted from: Dombret *et al.* 2019.[2] Analysis of salvage status adjudicated separately from prior randomisation status.

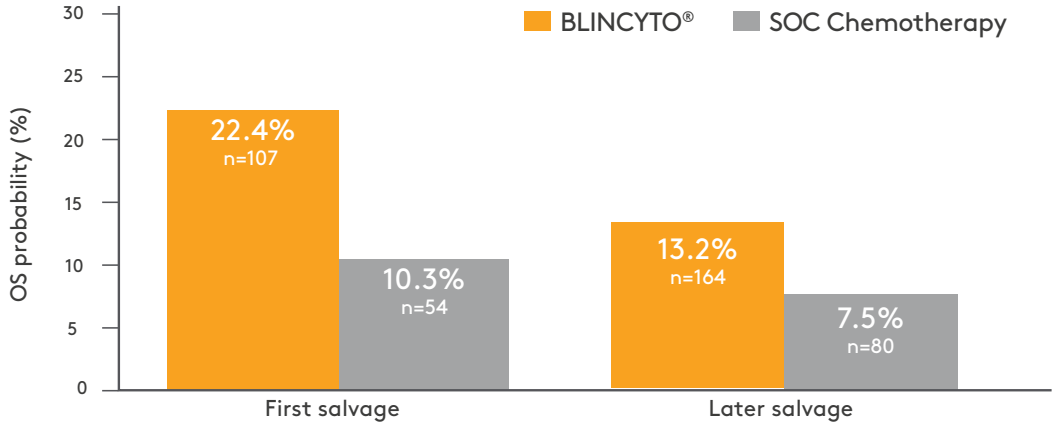
Improved median OS among patients who received BLINCYTO® vs SOC and who had no prior salvage treatment supports early use of BLINCYTO® in adults with Ph– relapsed or refractory B-ALL.[1,2]

ITT: Intent-to-treat; **SOC:** Standard of care; **NS:** not significant.

References: 1. Kantarjian H *et al. N Engl J Med* 2017;376:836–47. **2.** Dombret H *et al. Leuk Lymphoma* 2019;60:2214–22.

EFFICACY IN Ph- RELAPSED OR REFRACTORY B-ALL

PREDICTED 5-YEAR OS VERSUS SOC[1]

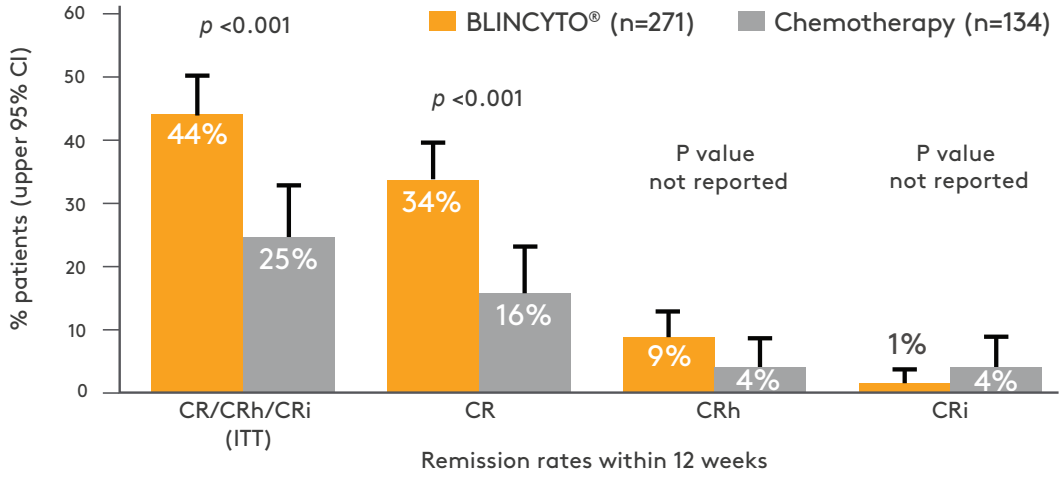


In an analysis† estimating long-term survival outcomes in the TOWER trial, patients treated with BLINCYTO® had a higher probability of 5-year OS versus SOC, regardless of use in first or later salvage (P values not reported).

†A partitioned survival model with a lifetime (50-year) time horizon was used to estimate expected life-years and quality-adjusted life-years gained for BLINCYTO® versus SOC in subgroups of patients who had not previously received salvage therapy versus those who had received at least one prior line of salvage therapy (i.e. early versus late treatment).

Adapted from Severin *et al.* 2018.[1]

REMISSION RATES WITHIN 12 WEEKS OF TREATMENT INITIATION (SECONDARY ENDPOINTS)[2]



Adapted from: Kantarjian *et al.* 2017.[2]

Among patients who achieved CR/CRh/CRi:[2]

- The median duration of remission in the BLINCYTO® arm was 7.3 months (95% CI, 5.8–9.9) versus 4.6 months (95% CI, 1.8–19.0) with chemotherapy
- 76% of patients in the BLINCYTO® group achieved MRD negativity versus 48% with chemotherapy (treatment difference: 28%; 95% CI, 9–47).

CR: Complete remission (≤ 5% bone marrow blasts and no evidence of disease), with full haematologic recovery (platelets >100,000/mcL and absolute neutrophil count [ANC] >1,000/mcL). **CRh:** CR, with partial haematologic recovery (platelets >50,000/mcL, ANC >500/mcL). **CRi:** CR, with incomplete haematologic recovery (platelets >100,000/mcL or ANC >1,000/mcL). **ITT:** Intention-to-treat population. **MRD:** Minimal residual disease ($<10^{-4}$ bone marrow blasts).

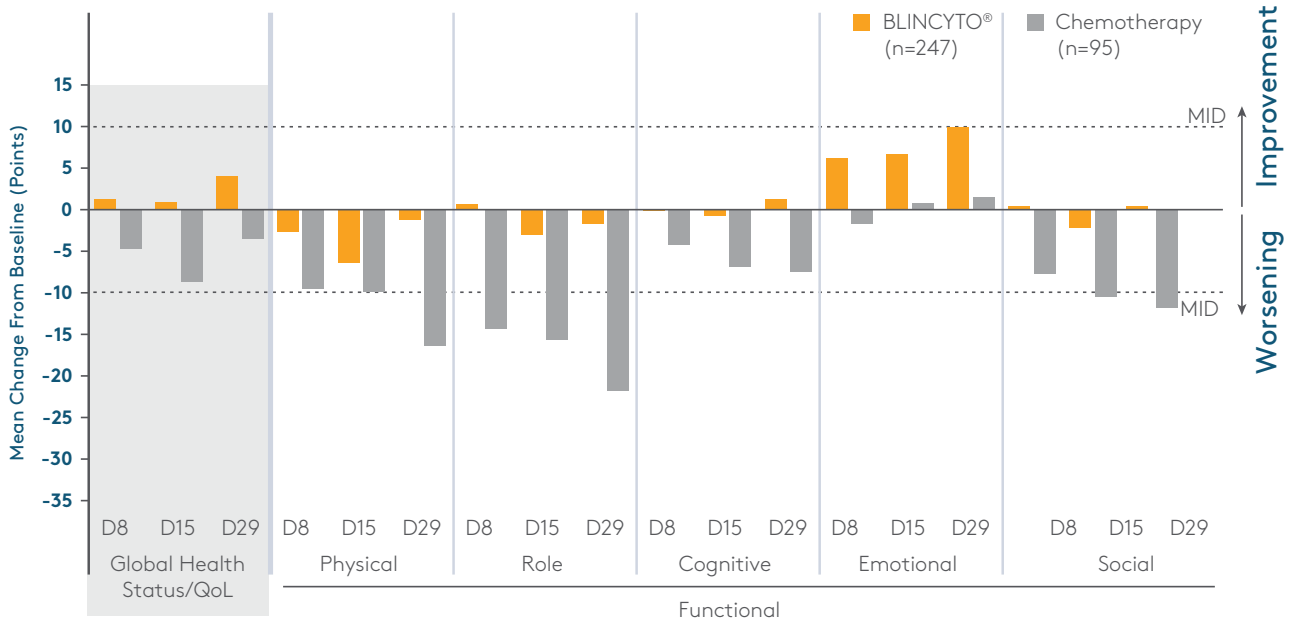
References: 1. Severin F, *et al.* Poster presented at: 23rd Annual Meeting of the European Hematology Association; June 14-17, 2018; Stockholm, Sweden. Abstract #PS1427. **2.** Kantarjian H *et al. N Engl J Med* 2017;376:836–47.

EFFICACY IN Ph- RELAPSED OR REFRACTORY B-ALL

PATIENTS RECEIVING BLINCYTO® REPORTED BETTER POST-TREATMENT HRQoL THAN THOSE RECEIVING CHEMOTHERAPY ACROSS ALL QLQ-C30 SUBSCALES*[1]

*Based on descriptive mean change from baseline.

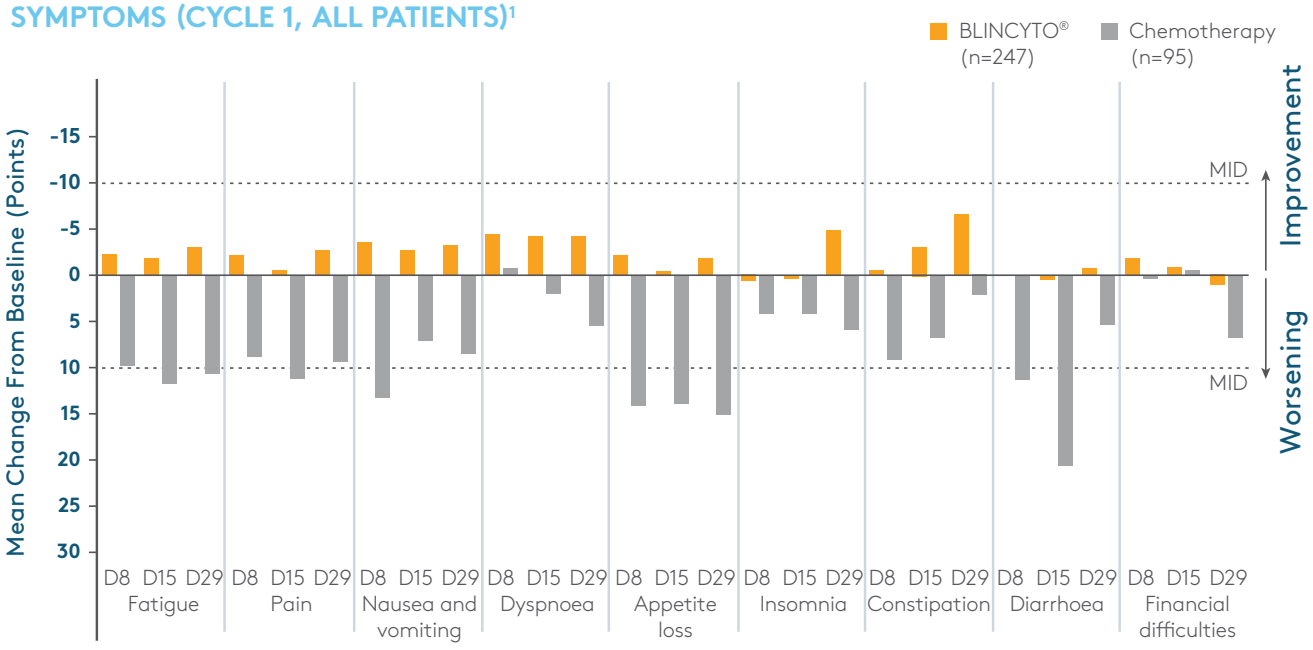
GLOBAL HEALTH STATUS AND FUNCTIONAL SCALE (CYCLE 1, ALL PATIENTS)[1]



Adapted from: Topp *et al.* 2018.
EORTC QLQ-C30 Analysis Set.

P values not provided.

SYMPTOMS (CYCLE 1, ALL PATIENTS)[1]



Adapted from: Topp *et al.* 2018.
EORTC QLQ-C30 Analysis Set

P values not provided.

"Differences in HRQL favoring blinatumomab vs chemotherapy were observable as early as 8 days after treatment initiation."[1]

HRQL: health-related quality of life; **HRQoL:** health-related quality of life; **D:** day; **EORTC QLQ-C30:** European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; **GHS:** global health status; **MID:** minimally important difference.

Reference: 1. Topp MS *et al. Blood* 2018;131:2906–14.

SAFETY IN Ph– RELAPSED OR REFRACTORY B-ALL

BLINCYTO®: CHEMOTHERAPY-FREE IMMUNOTHERAPY WITH A MANAGEABLE TOLERABILITY PROFILE[1]

Event, no. (%)	BLINCYTO® (n = 267)	Chemotherapy (n = 109)
Any adverse event	263 (99)	108 (99)
Event leading to premature discontinuation of trial treatment	33 (12)	9 (8)
Serious adverse event	165 (62)	49 (45)
Fatal serious adverse event	51 (19)	19 (17)
Any adverse event grade ≥3	231 (87)	100 (92)
Grade ≥3 adverse events of interest reported in ≥3% of patients in either group		
Neutropenia	101 (38)	63 (58)
Infection	91 (34)	57 (52)
Elevated liver enzyme	34 (13)	16 (15)
Neurological event	25 (9)	9 (8)
Cytokine release syndrome	13 (5)	0 (0)
Infusion reaction	9 (3)	1 (1)
Lymphopenia	4 (1)	4 (4)
Any decrease in platelet count	17 (6)	13 (12)
Any decrease in white cell count	14 (5)	6 (6)

Data are summarised for all patients who received at least one dose of trial treatment.
Adpated from Kantarjian *et al.* 2017.

After adjusting for treatment exposure, the rate of serious adverse events in the BLINCYTO® arm was 349.4 per 100 patient-years, compared with 641.9 per 100 patient-years in the chemotherapy arm (p-value not reported).[1]

Reference: 1. Kantarjian H *et al. N Engl J Med* 2017;376:836–47.

BLINCYTO®
(blinatumomab)

For more information on BLINCYTO® or to report any adverse events or product complaints involving BLINCYTO® please contact Australia Medical Information on 1800 803 638

PBS Information: Section 100 listed. Authority required.
Refer to PBS Schedule for full Authority listing.

***WARNING*:** *The following have occurred in patients receiving BLINCYTO®:*
• Cytokine Release Syndrome, which may be life-threatening or fatal • Neurological toxicities, which may be severe, life-threatening, or fatal • Reactivation of JC viral infection
Interrupt or discontinue BLINCYTO® as recommended if any of these adverse events occur
(See Section 4.4 Special warnings and precautions for use and Section 4.2 Dose and method of administration).

REFER TO FULL PRODUCT INFORMATION BEFORE PRESCRIBING; AVAILABLE FROM AMGEN AUSTRALIA PTY LTD, PH: 1800 803 638 OR AT WWW.AMGEN.COM.AU/BLINCYTO.PI

For more information about BLINCYTO® or to report an adverse event or product complaints about BLINCYTO®, please contact Amgen Medical Information on 1800 803 638.

BLINCYTO® Minimum Product Information: Indication: treatment of relapsed or refractory (R/R) B-cell precursor acute lymphoblastic leukaemia (ALL); treatment of minimal residual disease (MRD) positive ALL in patients in complete haematological remission. **Contraindications:** hypersensitivity to blinatumomab, CHO-derived proteins or any excipient. **Precautions:** neurologic events; increased risk for serious infections; cytokine release syndrome; infusion reactions; tumour lysis syndrome, pancreatitis. Management of these adverse reactions may require interruption or discontinuation of treatment. Neutropenia and febrile neutropenia; elevated liver enzymes; leukoencephalopathy; medication errors – strictly follow preparation and administration instructions. Pregnancy Category: C. Use contraception during and for 48 hours after treatment. Discontinue breast-feeding during and for at least 48 hours after treatment. Do not use recommended adult fixed dose in paediatric patients. No data in patients aged less than 28 days. **Interactions:** low potential of clinically meaningful drug interaction with BLINCYTO® mediated cytokine elevation. Vaccination with live viral vaccines not recommended 2 weeks prior to or during treatment, and until recovery of B lymphocytes to normal range following last treatment cycle. **Adverse Reactions:** Common: infections, pyrexia, infusion-related reactions, headache, anaemia, febrile neutropenia, neutropenia, thrombocytopenia, oedema, increased liver enzymes, fatigue, nausea, tremor, hypokalaemia, diarrhoea, chills. See also Precautions for serious adverse reactions. **Dosage & Administration:** R/R ALL: Single cycle is 4 weeks continuous intravenous (cIV) infusion then 2 week treatment free interval. *For patients greater than or equal to 45 kg (fixed dose)*: Cycle 1 – starting dose 9 micrograms/day for days 1-7, then 28 micrograms/day for days 8-28. All other cycles 28 micrograms/day for 4 weeks. For patients less than 45 kg (body surface area based dose): Cycle 1 – starting dose 5 micrograms/m^2/day for days 1-7 (do not exceed 9 micrograms/day), then 15 micrograms/m^2/day (do not exceed 28 micrograms/day); all other cycles, 15 micrograms/m^2/day (do not exceed 28 micrograms/day). For maintenance, 28 day cIV infusion, then 56 days treatment free. Hospitalise at least first 9 days of Cycle 1 and first 2 days of Cycle 2. Supervision or hospitalisation for other cycle starts and reinitiation. Adults: premedicate with 20 mg IV dexamethasone prior to initiation of each cycle. Intrathecal chemotherapy prophylaxis recommended before and during therapy. Treat with dexamethasone (≤ 24 mg/day) if high tumour burden. Paediatrics: premedicate with dexamethasone 10 mg/m2 (not to exceed 20 mg) oral or IV 6 to 12 hours prior to start of BLINCYTO® (Cycle 1 day 1), followed by premedication with dexamethasone 5 mg/m^2 oral or IV within 30 minutes of start of BLINCYTO® (Cycle 1 day 1). **MRD+ ALL:** 28 day cIV infusion then 14 days treatment free, for up to 4 cycles; premedicate with prednisone 100 mg IV or equivalent 1 hour prior to start of BLINCYTO® each cycle; hospitalise first 3 days Cycle 1 and first 2 days Cycle 2, supervise/hospital for subsequent cycle starts and reinitiation – see full PI. R/R & MRD+ ALL – Interrupt BLINCYTO® if grade 3 neurological events, Cytokine Release Syndrome or other clinically relevant adverse reactions occur see full PI.

BLINCYTO®
(blinatumomab)

AMGEN®