Supplementary Table 2. Postmarketing Safety Issues for Indications with Accelerated Approval vs. Regular Approval

Postmarketing Safety Issues for Indications with Accelerated Approval				
Product	**Indication**	**Study Design**	**Basis for Approval**	**Major Post Marketing Safety Issues**
ibritumomab tiuxetan (ZEVALIN®)	Relapsed or refractory low-grade, follicular, or transformed B-cell non-Hodgkin's lymphoma, including rituximab-refractory follicular non-Hodgkin's lymphoma	Single arm	ORR*	Severe mucomuctaneous reactions
pralatrexate (FOLOTYN®)	Treatment of patients with relapsed or refractory peripheral T-cell lymphoma	Single arm	ORR	Dermatologic reactions, mucositis, tumor lysis syndrome
imatinib (GLEEVEC®)	Treatment of patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST)	Single arm	ORR	Dermatologic reactions
dasatinib (SPRYCEL®)	Treatment of adults with chronic, accelerated, or myeloid or lymphoid blast phase chronic myeloid leukemia with resistance or intolerance to prior therapy including imatinib	Single arm	ORR	Cardiac dysfunction

gemtuzumab ozogamicin (MYLOTARG®)	Treatment of patients with CD33 positive acute myeloid leukemia in first relapse who are 60 years of age or older and who are not considered candidates for other cytotoxic chemotherapy	Single arm	ORR	Hypersensitivity reactions + hepatic veno-occlusive to boxed warning
Temzolamide (TEMODAR®)	Treatment of adult patients with refractory anaplastic astrocytoma who have experienced disease progression on a drug regimen containing a nitrosourea and procarbazine	Single arm	ORR	Allergic reactions, dermatologic reactions, hepatotoxicity, occasional pulmonary toxicity and aplastic anemia
Romidepsin (ISTODAX®)	Treatment of cutaneous T-cell lymphoma (CTCL) in patients who have received at least one prior systemic therapy	Single arm	ORR	Tumor lysis syndrome
everolimus (AFINITOR®)	Treatment of patients with subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis (TS) who require therapeutic intervention but are not candidates for curative surgical resection.	Single arm	ORR	Renal failure
Lenalidomide (REVLIMID®)	For use in combination with dexamethasone for the treatment of	Randomized	TTP†	Tumor lysis syndrome, dermatologic reactions

	multiple myeloma patients who have received at least one prior therapy.			
Postmarketing Safety Issues for Indications with Regular Approval				
Product	**Indication**	**Study Design**	**Basis for Approval**	**Major Post Marketing Safety Issues**
rituximab (RITUXAN®)	Treatment of patients with relapsed or refractory low-grade or follicular, CD20 positive, B-cell non-Hodgkin's lymphoma	Single arm	ORR	Progressive multi-focal leukoencephalopathy, reactivation of Hep B virus and progression of Kaposi's sarcoma
dasatinib (SPRYCEL®)	Treatment of adults with Philadelphia chromosome-positive acute lymphoblastic leukemia with resistance or intolerance to prior therapy	Single arm	ORR	Cardiac dysfunction
bendamustine hydrochloride (TREANDA®)	Treatment of patients with chronic lymphocytic leukemia	Randomized	ORR	Local extravasation reactions, toxic epidermal necrolysis and Steven Johnson syndrome
sunitinib Malate (SUTENT®)	GIST after disease progression on or intolerance to imatinib (Gleevac®)	Randomized	TTP	Prolonged QT, hypothyroidism

bortezomib (VELCADE®)	Treatment of multiple myeloma patients who have received at least one prior therapy	Randomized	TTP	Hepatic impairment
imatinib (GLEEVEC®)	Treatment of adult patients with relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL).	Single arm	ORR	Tumor lysis syndrome, growth retardation in children & hypothyroidism
mitoxantrone (NOVANTRONE®)	In combination with Ara-C for the treatment of adult acute non-lymphocytic leukemia (ANLL)	Single arm	ORR	Secondary AML‡

Abbreviations: *ORR= Overall response rate (complete response rate + partial response rate). †TTP- Time to progression, ‡AML- Acute myeloid leukemia