Appendix B UICC staging system for mycosis fungoides and Sezary syndrome

The Union for International Cancer Control (UICC) has endorsed TNM staging of primary cutaneous lymphoma as proposed by the International Society for Cutaneous Lymphomas (ISCL) and the European Organisation of Research and Treatment of Cancer (EORTC).

Table 1. UICC TNM 9 / ISCL/EORTC revision to the staging of MF and SS.

Reproduced from Olsen E *et al*.[31]

TNMB stages	
Skin	
T_1	Limited patches,* papules and/or plaques[+] covering <10% of the skin surface. May further stratify into T_{1a} (patch only) vs T_{1b} (plaque ± patch).
T_2	Patches, papules or plaques covering ≥10% of the skin surface. May further stratify into T_{2a} (patch only) vs T_{2b} (plaque ± patch).
T_3	One or more tumours[++] (≥1cm diameter)
T_4	Confluence of erythema covering ≥80% body surface area
Node	
N_0	No clinically abnormal peripheral lymph nodes[§]; biopsy not required
N_1	Clinically abnormal peripheral lymph nodes; histopathology Dutch grade 1 or NCI LN_{0-2}
N_{1a}	Clone negative[#]
N_{1b}	Clone positive[#]
N_2	Clinically abnormal peripheral lymph nodes; histopathology Dutch grade 2 or NCI LN_3
N_{2a}	Clone negative[#]
N_{2b}	Clone positive[#]
N_3	Clinically abnormal peripheral lymph nodes; histopathology Dutch grades 3-4 or NCI LN_4; clone positive or negative
N_x	Clinically abnormal peripheral lymph nodes; no histologic confirmation
Visceral	
M_0	No visceral organ involvement
M_1	Visceral involvement (must have pathology confirmation[$] and organ involved should be specified)
Blood	

B_0	Absence of significant blood involvement: ≤5% of peripheral blood lymphocytes are atypical (Sezary) cells[&]
B_{0a}	Clone negative[#]
B_{0b}	Clone positive[#]
B_1	Low blood tumour burden: >5% of peripheral blood lymphocytes are atypical (Sezary) cells[&] but does not meet the criteria for B_2
B_{1a}	Clone negative[#]
B_{1b}	Clone positive[#]
B_2	High blood tumour burden: ≥1000/ụl Sezary cells with positive clone[#]

* For skin, patch indicates any size skin lesion without significant elevation or induration. Presence or absence of hypo- or hyperpigmentation, scale, crusting and/or poikiloderma should be noted.

+ For skin, plaque indicates any size skin lesion that is elevated or indurated. Presence or absence of scale, crusting and/or poikiloderma should be noted. Histologic features such as folliculotropism or large-cell transformation (>25% large cells), CD30+ or CD30-, and clinical features such as ulceration are important to document.

++ For skin, tumour indicates at least one 1 cm diameter solid or nodular lesion with evidence of depth and/or vertical growth. Note total number of lesions, total volume of lesions, largest size lesion and region of body involved. Also note if histologic evidence of large-cell transformation has occurred. Phenotyping for CD30 is encouraged.

[§] For node, abnormal peripheral lymph node(s) indicates any palpable peripheral node that on physical examination is firm, irregular, clustered, fixed or 1.5 cm or larger in diameter. Node groups examined on physical examination include cervical, supraclavicular, epitrochlear, axillary and inguinal. Central nodes, which are not generally amenable to pathologic assessment, are not currently considered in the nodal classification unless used to establish N3 histopathologically.

[$] For viscera, spleen and liver may be diagnosed by imaging criteria.

[#] A T-cell clone is defined by PCR or Southern blot analysis of the T-cell receptor gene.

[&] For blood, Sezary cells are defined as lymphocytes with hyperconvoluted cerebriform nuclei. If Sezary cells are not able to be used to determine tumour burden for B2, then one of the following modified ISCL criteria along with a positive clonal rearrangement of the TCR may be used instead: (1) expanded CD4+ or CD3+ cells with CD4/CD8 ratio of 10 or

more, (2) expanded CD4+ cells with abnormal immunophenotype including loss of CD7 or CD26.

NCI, US National Cancer Institute; TCR, T-cell receptor; TNMB, tumour, node, metastasis, blood.

Table 2. Histopathological staging of lymph nodes in MF and SS.

Reproduced from Olsen E *et al*.[31]

Updated ISCL/ EORTC classification	**Dutch system[32]**	**NCI-VA classification[33–35]**
N_1	Grade 1: dermatopathic lymphadenopathy (DL)	LN_0: no atypical lymphocytes LN_1: occasional and isolated atypical lymphocytes (not arranged in clusters) LN_2: many atypical lymphocytes or in 3-6 cell clusters
N_2	Grade 2: DL; early involvement by MF (presence of cerebriform nuclei >7.5 ųm)	LN_3: aggregates of atypical lymphocytes; nodal architecture preserved
N_3	Grade 3: partial effacement of LN architecture; many atypical cerebriform mononuclear cells (CMCs) Grade 4: complete effacement	LN_4: partial/complete effacement of nodal architecture by atypical lymphocytes or frankly neoplastic cells

LN, lymph node; NCI-VA, US National Cancer Institute-Veterans Administration.

The Union for International Cancer Control (UICC) does not provide a TNM staging of primary cutaneous lymphomas, but the International Society for Cutaneous Lymphomas (ISCL) and the European Organisation of Research and Treatment of Cancer (EORTC) have proposed the following staging system for primary cutaneous lymphomas other than MF and SS (1368A).

Table 3. UICC TNM 9 / ISCL/ EORTC proposed TNM staging of cutaneous lymphoma other than MF and SS.

Reproduced from Kim YH *et al.*[36]

Classification	
T	
T1	Solitary skin involvement

T1a	A solitary skin lesion <5 cm diameter
T1b	A solitary skin lesion >5 cm diameter
T2	Regional skin involvement: multiple lesions limited to 1 body region or 2 contiguous body regions*
T2a	All-disease encompassing in a <15 cm diameter circular area
T2b	All-disease encompassing in a >15 and <30 cm diameter circular area
T2c	All-disease encompassing in a >30 cm diameter circular area
T3	Generalised skin involvement
T3a	Multiple lesions involving 2 noncontiguous body regions
T3b	Multiple lesions involving ≥3 body regions
N	
N0	No clinical or pathologic lymph node involvement
N1	Involvement of 1 peripheral lymph node region[#] that drains an area of current or prior skin involvement
N2	Involvement of 2 or more peripheral lymph node regions[#] or involvement of any lymph node region that does not drain an area of current or prior skin involvement
N3	Involvement of central lymph nodes
M	
M0	No evidence of extracutaneous non-lymph node disease
M1	Extracutaneous non-lymph node disease present

* Definition of body regions (see Figure 1 of Kim YH *et al.*[33]): Head and neck: inferior border-superior border of clavicles, T1 spinous process. Chest: superior border-superior border of clavicles; inferior border-inferior margin of rib cage; lateral borders-mid-axillary lines, glenohumeral joints (inclusive of axillae). Abdomen/genital: superior border-inferior margin of rib cage; lateral borders-mid-axillary lines. Lower back/buttocks: superior border-inferior margin of rib cage; inferior border-inferior gluteal fold, anterior perineum (inclusive of perineum); lateral borders-mid-axillary lines. Each upper arm: superior borders-glenohumeral joints (exclusive of axillae); inferior borders-ulnar/radial-humeral (elbow) joint. Each lower fossae. Each lower leg/foot: superior borders-mid-patellae, mid popliteal fossae.

[#] Definition of lymph node regions is consistent with the Ann Arbor system: Peripheral sites: antecubital, cervical, supraclavicular, axillary, inguinal-femoral, and popliteal. Central sites: mediastinal, pulmonary hilar, para-aortic, iliac.