# Lymphoid Malignancies
# Integrated Pathology Reporting Guide

Family/Last name

Given name(s)

Date of birth DD – MM – YYYY

Patient identifiers

Date of request DD – MM – YYYY

Accession/Laboratory number

Elements in **black text** are CORE. Elements in **grey text** are NON-CORE.

☐ indicates multi-select values ◯ indicates single select values

SCOPE OF THIS DATASET

## CLINICAL INFORMATION (Note 1)

◯ Information not provided
◯ Information provided

**History of a known or suspected haematological or solid neoplasm and/or reactive disease condition**

◯ Information not provided
◯ No
◯ Yes, *specify*

**Known immune deficiency/dysregulation/cancer predisposition syndrome**

◯ Information not provided
◯ No
◯ Yes, *specify*

**Previous therapy**

◯ Information not provided
◯ No
◯ Yes (select all that apply)

☐ Cancer therapy
☐ Immune therapy
☐ Other, *specify*

**Other clinical information (e.g., B-symptoms, adenopathy/organomegaly, skin changes, travel, occupation/toxic exposures, relevant laboratory and imaging findings), *specify***

## DISEASE STATUS (Note 2)

◯ Not known
◯ Primary diagnosis
◯ Relapsed disease

Date of initial diagnosis DD – MM – YYYY

◯ Refractory disease

Date of initial diagnosis DD – MM – YYYY

## SAMPLING PROCEDURE (select all that apply) (Note 3)

◯ Not specified
☐ Core biopsy
☐ Surgical biopsy (incisional/excisional)
☐ Fine needle aspiration
☐ Other, *specify*

## SPECIMEN(S) SUBMITTED (select all that apply) (Note 4)

◯ Not specified
☐ Lymph node(s), *specify localisation*
☐ Extranodal site(s), *specify*
☐ Bone marrow
☐ Peripheral blood

## TUMOUR SITE (select all that apply) (Note 5)

◯ Not specified
☐ Peripheral blood
☐ Lymph node(s), *specify*
☐ Extranodal site(s), *specify*
☐ Bone marrow
Percent involvement of neoplastic cells %
☐ Other, *specify*

## BLOCK IDENTIFICATION KEY (Note 6)

*(List overleaf or separately with an indication of the nature and origin of all tissue blocks)*

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**FINAL INTEGRATED DIAGNOSIS**[a] (select all that apply) (Note 7)
*(Value list based on the World Health Organization Classification of Haematolymphoid Tumours, 5th Edition (2024))*

- ☐ B-cell lymphoid proliferations and lymphomas
  - ◯ B-cell lymphoma, not further classified
    - ◯ Indolent B-cell lymphoma, not further classified
    - ◯ Aggressive B-cell lymphoma, not further classified
  - ◯ B-lymphoblastic leukaemia/lymphoma
    Entity, *specify*
  - ◯ Preneoplastic and neoplastic small lymphocytic proliferation
    Entity/subtype, *specify*
  - ◯ Splenic B-cell lymphoma and leukaemia
    Entity, *specify*
  - ◯ Lymphoplasmacytic lymphoma
  - ◯ Marginal zone lymphoma
    Entity/subtype, *specify*
  - ◯ Follicular lymphoma
    Entity/subtype, *specify*
  - ◯ Mantle cell lymphoma
    Entity/subtype, *specify*
  - ◯ Diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS)
    Subtype, *specify*
  - ◯ Large B-cell lymphoma (LBCL)
    Entity/subtype, *specify*
  - ◯ Burkitt lymphoma
  - ◯ KSHV/HHV8-associated B-cell lymphoid proliferations and lymphoma
    Entity/subtype, *specify*
  - ◯ Lymphoproliferative disorder and lymphoma associated with immune deficiency and dysregulation
    Entity/subtype, *specify*
  - ◯ Plasma cell neoplasms[b]
- ☐ Hodgkin lymphoma
  - ◯ Classic Hodgkin lymphoma
    Subtype, *specify*
  - ◯ Nodular lymphocyte predominant Hodgkin lymphoma
    Pattern, *specify*
- ☐ T-cell and NK-cell lymphoid proliferations and lymphomas
  - ◯ T-cell and NK-cell lymphoma, not further classified
  - ◯ T-lymphoblastic leukaemia/lymphoma
    Entity, *specify*
  - ◯ Mature T-cell and NK-cell leukaemia
    Entity/subtype, *specify*
  - ◯ Primary cutaneous T-cell lymphoid proliferation and lymphoma
    Entity/subtype, *specify*
  - ◯ Intestinal T-cell and NK-cell lymphoid proliferation and lymphoma
    Entity, *specify*
  - ◯ Hepatosplenic T-cell lymphoma
  - ◯ Anaplastic large cell lymphoma
    Entity, *specify*
  - ◯ Nodal T follicular helper cell lymphoma
    Entity, *specify*
  - ◯ Peripheral T-cell lymphoma, NOS
  - ◯ Epstein-Barr virus (EBV)-positive T-cell and NK-cell lymphoma
    Entity/subtype, *specify*
  - ◯ EBV-positive T-cell and NK-cell lymphoid proliferation and lymphoma of childhood
    Entity/subtype, *specify*
- ☐ Other, *specify*

*Comments*

[a] *Refer to Table 1 for a listing of all Entities and Variants.*

[b] *Refer to the ICCR Plasma cell neoplasms dataset.*

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## INDICATIONS FOR DISEASE TRANSFORMATION (Note 8)

- ◯ Transformed disease confirmed (with proof of clonal identity)
- ◯ Transformed disease suspected (clonal identity not known)

Transformed from, *specify*

Date of initial diagnosis of the low grade lymphoma: DD – MM – YYYY

## IMMUNOPROFILING/PHENOTYPING STUDIES (Note 9)

(select all that apply)

☐ Markers to define lineage and stem cells

CD20
◯ Not performed ◯ Positive ◯ Negative

CD79A
◯ Not performed ◯ Positive ◯ Negative

CD3
◯ Not performed ◯ Positive ◯ Negative

CD2
◯ Not performed ◯ Positive ◯ Negative

*If negative, other markers including*

PAX5
◯ Not performed ◯ Positive ◯ Negative

MPO
◯ Not performed ◯ Positive ◯ Negative

CD68
◯ Not performed ◯ Positive ◯ Negative

C163
◯ Not performed ◯ Positive ◯ Negative

CD34
◯ Not performed ◯ Positive ◯ Negative

TdT
◯ Not performed ◯ Positive ◯ Negative

Additional T or B-cell markers, *specify*

☐ Markers to define activation state

CD30
◯ Not performed ◯ Positive ◯ Negative

AND

Ki-67 proliferation index

% ◯ Not performed

☐ Additional relevant immunoprofiling markers - markers representing essential diagnostic criteria in WHO (refer to Table 2), *specify*

*Comments*

## MOLECULAR GENETIC STUDIES (select all that apply) (Note 10)

☐ Precursor B-cell neoplasms

*BCR::ABL1*
◯ Not performed
◯ Positive ◯ Negative

- ◯ Hyperdiploidy
- ◯ Hypodiploidy
- ◯ Other, *specify karyotype*

Other, *specify*

☐ Mature B-cell neoplasms

MYC rearrangement
◯ Not performed ◯ Positive ◯ Negative

BCL2 rearrangement
◯ Not performed ◯ Positive ◯ Negative

BCL6 rearrangement
◯ Not performed ◯ Positive ◯ Negative

EBER if EBV association is suspected
◯ Not performed ◯ Positive ◯ Negative

Other (refer to Table 3), *specify*

☐ Precursor T-cell neoplasms, *specify*

☐ Mature T-cell and NK-cell neoplasms, *specify*

*Comments*

**Representative blocks for ancillary studies**, *specify those blocks best representing tumour and/or normal tissue for further study*

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# Definitions

**CORE elements**

CORE elements are those which are essential for the clinical management, staging or prognosis of the cancer. These elements will either have evidentiary support at Level P2 or higher (based on the Hierarchy of Research Evidence for Tumour Pathology[1]). In rare circumstances, where level P2 evidence is not available an element may be made a CORE element where there is unanimous agreement in the Dataset Authoring Committee (DAC). An appropriate staging system, e.g., Pathological TNM staging would normally be included as a CORE element.

Molecular and immunohistochemical testing is a growing feature of cancer reporting. However, in many parts of the world this type of testing is limited by the available resources. In order to encourage the global adoption of ancillary tests for patient benefit, International Collaboration on Cancer Reporting (ICCR) includes the most relevant ancillary testing in ICCR Datasets as CORE elements, especially when they are necessary for the diagnosis. Where the technical capability does not yet exist, laboratories may consider temporarily using these data elements as NON-CORE items.

The summation of all CORE elements is considered to be the minimum reporting standard for a specific cancer.

**NON-CORE elements**

NON-CORE elements are those which are unanimously agreed should be included in the dataset but are not supported by level P2 evidence. These elements may be clinically important and recommended as good practice but are not yet validated or regularly used in patient management.

Key information other than that which is essential for clinical management, staging or prognosis of the cancer such as macroscopic observations and interpretation, which are fundamental to the histological diagnosis and conclusion e.g., macroscopic tumour details, may be included as either CORE or NON-CORE elements by consensus of the DAC.

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# Scope

The dataset has been developed for the pathology reporting of precursor and mature lymphoid malignancies involving bone marrow, blood, lymph node, extranodal lymphatic tissue or any other anatomic site.

In development of this dataset, the DAC considered evidence up until June 2026.

The authors of this dataset can be accessed here.

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## Note 1 – Clinical information (Core and Non-core)

Knowledge of history of a known or suspected haematological or solid neoplasm and/or any relevant non-malignant condition is a prerequisite for the pathologist to correctly interpret the histologic findings. The impact of morphological features of e.g., a large cell lymphoma may be entirely different if this is arising *de novo* or if, in case of a precedent/known indolent lymphoma, the question of high grade transformation arises. The former would implicate a different prognosis and the latter should prompt additional investigations regarding clonal identity or divergence of the two neoplasms, again influencing prognosis.[2] Knowledge of a pre-existing non-malignant disease may facilitate the interpretation of a lymphoid proliferation e.g., in extranodal marginal zone lymphoma arising in the background of Sjögren syndrome or Hashimoto thyroiditis.[3] History of a solid (non-haematological) neoplasm that was treated by chemotherapy or immune therapy may impact on the pathogenesis and classification of a lymphoid neoplasm by inferring an iatrogenic immune deficiency/ dysregulation (IDD) context. Information to the pathologist of known IDD/cancer predisposition syndrome is a prerequisite to the correct taxonomic categorisation of the process. Whereas diffuse large B-cell lymphoma (DLBCL) arising *de novo* may be indistinguishable from a large cell lymphoid proliferation arising in the background of IDD, knowledge of the underlying condition will prompt additional investigations for virus associations (Epstein-Barr virus (EBV), HHV8, etc.) and result in a different diagnosis ('DLBCL arising in IDD (specify) with association to EBV').[4]

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## Note 2 – Disease status (Core)

The histological findings in lymphomas often do not allow a distinction between new (second) primary disease and relapsed/refractory disease. Since the latter situation in general heralds an inferior prognosis especially in aggressive lymphomas, and directs clinical decisions, this information is considered core and may prompt additional investigations, e.g., clonal identity of the relapsed tumour with the preceding tumour.[5]

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## Note 3 – Sampling procedure (Core)

It is important that the type and intent of the operative procedure is clearly stated by the clinician, as this impacts the diagnostic accuracy of the pathologic assessment.[6,7]

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## Note 4 – Specimen(s) submitted (Core)

The localisation of the submitted specimen must be clearly indicated. Although a resected lymph node infiltrated by lymphoma can usually be readily distinguished from an extranodal site specimen, this is not the case for core needle biopsies or fine needle aspiration biopsies. Morphologically identical tumours presenting in a lymph node or at an extranodal site may have an entirely different biological background and clinical

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behaviour, such as a nodal DLBCL – not otherwise specified (NOS) and a large B-cell lymphoma (LBCL) arising in an immune-privileged site, e.g., in the central nervous system.[8] Some lymphomas typically or by definition arise in defined locations, such as primary mediastinal LBCL and breast implant-associated anaplastic large cell lymphoma. Moreover, many lymphomas represent organ specific diseases not primarily arising in lymph nodes such as the different types of primary intestinal T-cell lymphomas and primary cutaneous lymphomas.[9]

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## Note 5 – Tumour site (Core)

Knowledge on the extent of disease/involvement provides important prognostic information. Clinical staging (Stages I/II versus Stages III/IV) is prognostic in many types of lymphomas and may determine clinical decisions, including preference for localised versus systemic treatment. Organ-specific lymphomas such as duodenal-type follicular lymphoma, extranodal marginal zone lymphoma or intestinal T-cell lymphoma are often diagnosed in localised/early clinical stage.

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## Note 6 – Block identification key (Non-core)

It is recommended to specify those blocks best representing tumour and/or normal tissue. The origin/ designation of all tissue blocks should be recorded. This information should ideally be documented in the final pathology report and is particularly important should the need for internal or external review arise, in which case a subsequent reviewer would need to know the anatomic sites from which samples were taken for proper assessment and staging purposes. If this information is not included in the final pathology report, it should be available on the laboratory computer system and relayed to the reviewing pathologist. It may be useful to have a digital image of the specimen and record of the origin of the tumour blocks.

Recording the origin/designation of tissue blocks also facilitates retrieval of the appropriate blocks for further immunohistochemical, molecular or research studies.

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## Note 7 – Final integrated diagnosis (Core and Non-core)

The final integrated diagnosis is based on the most recent World Health Organization (WHO) Classification of Haematolymphoid Tumours, 5th edition, 2024 (WHO-HAEM5) (Table 1).[10] Determination of the lymphoma entity/type is based on routine histologic examination, immunohistochemistry and – in some of the entities – molecular studies such as EBER in-situ hybridisation (e.g., in EBV-positive DLBCL) or translocation testing in DLBCL/HGBCL-*MYC/BCL2* (e.g., by FISH). These tests may not be available in all parts of the world. Therefore, an approach is recommended that defines increasing layers of granularity of the diagnosis (refer to Table 1). Using this approach, the minimum diagnostic requirement would be to define the category (B-cell or T-cell lymphoproliferation or lymphoma) followed by indicating the family/class (e.g., follicular lymphoma, mantle cell

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lymphoma). If this is not possible due to insufficient material or testing availability or for other technical reasons, the term 'B-cell lymphoma, not further classified' or 'T-cell lymphoma, not further classified' can be rendered. Within the family/class, the entity according to WHO-HAEM5 should be given (e.g., 'in-situ follicular B-cell neoplasm' or 'classic follicular lymphoma' within the follicular lymphoma family). Subtypes may be given as appropriate.[10] In some cases, more than one diagnosis applies, e.g., both classic follicular lymphoma and DLBCL within one lymph node or extranodal site. The WHO-HAEM5 also includes classification of tumour-like lesions with B-cell or T-cell predominance.[10] Since these are not lymphoid neoplasms, they are beyond the scope of the explanatory notes provided here.[10]

**Table 1: 5th edition of the World Health Organization Classification of lymphoid malignancies.[10]**

| Descriptor | ICD-O codes[a] |
|---|---|
| **Precursor B-cell neoplasms** | |
| ***B-lymphoblastic leukaemias/lymphomas*** | |
| B-lymphoblastic leukaemia/lymphoma | 9811/3 |
| B-lymphoblastic leukaemia/lymphoma with high hyperdiploidy | 9815/3 |
| B-lymphoblastic leukaemia/lymphoma with hypodiploidy† | 9816/3 |
| B-lymphoblastic leukaemia/lymphoma with hypodiploidy, near-haploid | 9816/3 |
| B-lymphoblastic leukaemia/lymphoma with hypodiploidy, low hypodiploid | 9816/3 |
| B-lymphoblastic leukaemia/lymphoma with hypodiploidy, high hypodiploid | 9816/3 |
| B-lymphoblastic leukaemia/lymphoma with iAMP21 | 9811/3 |
| B-lymphoblastic leukaemia/lymphoma with *BCR*::*ABL*1 fusion | 9812/3 |
| B-lymphoblastic leukaemia/lymphoma with *BCR*::*ABL1*-like features | 9819/3 |
| B-lymphoblastic leukaemia/lymphoma with *KMT2A* rearrangement | 9813/3 |
| B-lymphoblastic leukaemia/lymphoma with *ETV6*::*RUNX1* fusion | 9814/3 |
| B-lymphoblastic leukaemia/lymphoma with *ETV6*::*RUNX1*-like features | 9814/3 |
| B-lymphoblastic leukaemia/lymphoma with *TCF3*::*PBX1* fusion | 9818/3 |
| B-lymphoblastic leukaemia/lymphoma with *IGH*::*IL3* fusion | 9817/3 |
| B-lymphoblastic leukaemia/lymphoma with *TCF3*::*HLF* fusion | 9818/3 |
| B-lymphoblastic leukaemia/lymphoma with other defined genetic alterations | 9811/3 |
| B-lymphoblastic leukaemia with *DUX4* rearrangement | 9811/3 |
| B-lymphoblastic leukaemia with *MEF2D* rearrangement | 9811/3 |
| B-lymphoblastic leukaemia with *ZNF384* rearrangement | 9811/3 |
| B-lymphoblastic leukaemia with *PAX5alt* | 9811/3 |
| B-lymphoblastic leukaemia with *PAX5* p.P80R | 9811/3 |
| B-lymphoblastic leukaemia with *NUTM1* rearrangement | 9811/3 |
| B-lymphoblastic leukaemia with *MYC* rearrangement† | 9811/3 |
| B-lymphoblastic leukaemia/lymphoma, not otherwise specified (NOS) | 9811/3 |
| **Mature B-cell neoplasms** | |

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| Descriptor | ICD-O codes[a] |
|---|---|
| ***Preneoplastic and neoplastic small lymphocytic proliferations*** | |
| Monoclonal B-cell lymphocytosis, chronic lymphocytic leukaemia type | 9823/1 |
| Monoclonal B-cell lymphocytosis, low count or clonal B-cell expansion (chronic lymphocytic leukaemia/small lymphocytic lymphoma type) | |
| Monoclonal B-cell lymphocytosis, non–chronic lymphocytic leukaemia type | 9591/1 |
| Chronic lymphocytic leukaemia/small lymphocytic lymphoma | 9823/3 |
| ***Splenic B-cell lymphomas and leukaemias*** | |
| Hairy cell leukaemia | 9940/3 |
| Splenic marginal zone lymphoma | 9689/3 |
| Splenic diffuse red pulp small B-cell lymphoma | 9591/3 |
| Splenic B-cell lymphoma/leukaemia with prominent nucleoli† | 9591/3 |
| ***Lymphoplasmacytic lymphoma*** | |
| Lymphoplasmacytic lymphoma | 9671/3 |
| IgM-type lymphoplasmacytic lymphoma/Waldenström macroglobulinaemia† | 9761/3 |
| Non–IgM-type lymphoplasmacytic lymphoma/Waldenström macroglobulinaemia† | 9761/3 |
| ***Marginal zone lymphoma*** | |
| Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue | 9699/3 |
| Immunoproliferative small intestinal disease (alpha heavy chain disease) | 9762/3 |
| Primary cutaneous marginal zone lymphoma† | 9699/3 |
| Primary cutaneous marginal zone lymphoma, heavy chain class-switched form (IgG+, IgA+, or IgE+)† | 9699/3 |
| Primary cutaneous marginal zone lymphoma, non–class-switched form (IgM+)† | 9699/3 |
| Nodal marginal zone lymphoma | 9699/3 |
| Paediatric nodal marginal zone lymphoma | 9699/3 |
| ***Follicular lymphoma*** | |
| In situ follicular B-cell neoplasm† | 9695/1 |
| Follicular lymphoma | 9690/3 |
| Follicular large B-cell lymphoma† | 9698/3 |
| Follicular lymphoma with uncommon features | 9690/3 |
| Paediatric-type follicular lymphoma | 9690/3 |
| Duodenal-type follicular lymphoma | 9695/3 |
| ***Cutaneous follicle centre lymphoma*** | |
| Primary cutaneous follicle centre lymphoma | 9597/3 |
| *Mantle cell lymphoma* | |
| In situ mantle cell neoplasm† | 9673/1 |

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| Descriptor | ICD-O codes[a] |
|---|---|
| Mantle cell lymphoma | 9673/3 |
| Cyclin D1–positive mantle cell lymphoma† | 9673/3 |
| Cyclin D1–negative mantle cell lymphoma† | 9673/3 |
| Leukaemic non-nodal mantle cell lymphoma† | 9673/3 |
| ***Transformations of indolent B-cell lymphomas*** | |
| Refer to indolent lymphoma type | |
| ***Large B-cell lymphomas*** | |
| Diffuse large B-cell lymphoma, NOS | 9680/3 |
| Diffuse large B-cell lymphoma, centroblastic subtype | 9680/3 |
| Diffuse large B-cell lymphoma, immunoblastic subtype | 9684/3 |
| Diffuse large B-cell lymphoma, anaplastic subtype | 9680/3 |
| Diffuse large B-cell lymphoma, germinal-centre B-cell subtype | 9680/3 |
| Diffuse large B-cell lymphoma, activated B-cell subtype | 9680/3 |
| Diffuse large B-cell lymphoma with *MYC* and *BCL6* rearrangements | 9680/3 |
| T-cell/histiocyte–rich large B-cell lymphoma | 9688/3 |
| T-cell/histiocyte–rich large B-cell lymphoma, de novo† | |
| T-cell/histiocyte–rich large B-cell lymphoma, progressed from nodular lymphocyte-predominant Hodgkin lymphoma† | |
| Diffuse large B-cell lymphoma/high-grade B-cell lymphoma with MYC and BCL2 rearrangements (DLBCL/HGBL-MYC/BCL2) | 9680/3 |
| DLBCL/HGBL-*MYC*/*BCL2* without *BCL6* rearrangement | |
| DLBCL/HGBL-*MYC*/*BCL2* with *BCL6* rearrangement | |
| DLBCL/HGBL-*MYC*/*BCL2* (with or without *BCL6* rearrangement) with TdT expression | |
| ALK-positive large B-cell lymphoma | 9737/3 |
| Large B-cell lymphoma with *IRF4* rearrangement | 9698/3 |
| High-grade B-cell lymphoma with 11q aberration | 9687/3 |
| Lymphomatoid granulomatosis, NOS | 9766/1 |
| Lymphomatoid granulomatosis, grade 1 | 9766/1 |
| Lymphomatoid granulomatosis, grade 2 | 9766/1 |
| Lymphomatoid granulomatosis, grade 3 | 9766/3 |
| EBV-positive diffuse large B-cell lymphoma | 9680/3 |
| Diffuse large B-cell lymphoma associated with chronic inflammation | 9680/3 |
| Fibrin-associated large B-cell lymphoma† | 9678/3 |
| Fluid overload–associated large B-cell lymphoma† | 9678/3 |
| Plasmablastic lymphoma | 9735/3 |
| Primary large B-cell lymphoma of immune-privileged sites† | 9680/3 |

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| Descriptor | ICD-O codes[a] |
|---|---|
| Primary large B-cell lymphoma of the CNS | 9680/3 |
| Primary large B-cell lymphoma of the vitreoretina | 9680/3 |
| Primary large B-cell lymphoma of the testis | 9680/3 |
| Primary cutaneous diffuse large B-cell lymphoma, leg type | 9680/3 |
| Intravascular large B-cell lymphoma | 9712/3 |
| Mediastinal large B-cell lymphoma | 9679/3 |
| Mediastinal grey zone lymphoma | 9596/3 |
| High-grade B-cell lymphoma, NOS | 9680/3 |
| High-grade B-cell lymphoma, NOS, with *MYC* and *BCL6* rearrangements | 9680/3 |
| ***Burkitt lymphoma*** | |
| Burkitt lymphoma | 9687/3 |
| *Traditional subtypes:* | |
| Endemic Burkitt lymphoma | 9687/3 |
| Sporadic Burkitt lymphoma | 9687/3 |
| Immunodeficiency-associated Burkitt lymphoma | 9687/3 |
| *Recommended subtypes:* | |
| EBV-associated Burkitt lymphoma† | 9687/3 |
| EBV-negative Burkitt lymphoma† | 9687/3 |
| ***KSHV/HHV8-associated B-cell lymphoid proliferations and lymphomas*** | |
| Primary effusion lymphoma | 9678/3 |
| Extracavitary primary effusion lymphoma† | 9678/3 |
| KSHV/HHV8-positive diffuse large B-cell lymphoma† | 9738/3 |
| KSHV/HHV8-positive germinotropic lymphoproliferative disorder | |
| ***Lymphoid proliferations and lymphomas associated with immune deficiency and dysregulation*** | |
| Hyperplasias arising in immune deficiency/dysregulation | |
| Polymorphic lymphoproliferative disorders arising in immune deficiency/dysregulation | 9971/1 |
| EBV-positive mucocutaneous ulcer | 9680/1 |
| Lymphomas arising in immune deficiency/dysregulation (code as type of lymphoma) | |
| Inborn error of immunity–associated lymphoid proliferations and lymphomas (code as type of lymphoma) | |
| **Hodgkin lymphoma** | |
| Classic Hodgkin lymphoma | 9650/3 |
| Classic Hodgkin lymphoma, nodular sclerosis | 9663/3 |
| Classic Hodgkin lymphoma, mixed cellularity | 9652/3 |

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| Descriptor | ICD-O codes[a] |
|---|---|
| Classic Hodgkin lymphoma, lymphocyte-rich | 9651/3 |
| Classic Hodgkin lymphoma, lymphocyte-depleted | 9653/3 |
| Nodular lymphocyte-predominant Hodgkin lymphoma | 9659/3 |
| **Precursor T-cell neoplasms** | |
| ***T-lymphoblastic leukaemia/lymphoma*** | |
| T-lymphoblastic leukaemia/lymphoma, NOS | 9837/3 |
| Early T-precursor lymphoblastic leukaemia/lymphoma | 9837/3 |
| **Mature T-cell and NK-cell neoplasms** | |
| ***Mature T-cell and NK-cell leukaemias*** | |
| T-prolymphocytic leukaemia | 9834/3 |
| T-large granular lymphocytic leukaemia | 9831/3 |
| NK-large granular lymphocytic leukaemia | 9831/3 |
| Adult T-cell leukaemia/lymphoma | 9827/3 |
| Smouldering adult T-cell leukaemia/lymphoma† | 9827/3 |
| Chronic adult T-cell leukaemia/lymphoma† | 9827/3 |
| Lymphoma adult T-cell leukaemia/lymphoma | 9827/3 |
| Acute adult T-cell leukaemia/lymphoma† | 9827/3 |
| Sézary syndrome | 9701/3 |
| Aggressive NK-cell leukaemia | 9948/3 |
| ***Primary cutaneous T-cell lymphoid proliferations and lymphomas*** | |
| Primary cutaneous CD4-positive small or medium T-cell lymphoproliferative disorder | 9709/1 |
| Primary cutaneous acral CD8-positive T-cell lymphoproliferative disorder† | 9709/3 |
| Mycosis fungoides | 9700/3 |
| Folliculotropic mycosis fungoides | 9700/3 |
| Pagetoid reticulosis | 9700/3 |
| Granulomatous slack skin disease | 9700/3 |
| Primary cutaneous CD30-positive T-cell lymphoproliferative disorder, lymphomatoid papulosis | 9718/1 |
| Primary mucosal CD30-positive T-cell lymphoproliferative disorder | 9718/1 |
| Lymphomatoid papulosis subtypes A, B, C, D, E | 9718/1 |
| Lymphomatoid papulosis with *DUSP22* locus rearrangement | 9718/1 |
| Primary cutaneous CD30-positive T-cell lymphoproliferative disorder, primary cutaneous anaplastic large cell lymphoma | 9718/3 |
| Subcutaneous panniculitis-like T-cell lymphoma | 9708/3 |
| Primary cutaneous gamma-delta T-cell lymphoma | 9726/3 |

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| Descriptor | ICD-O codes[a] |
|---|---|
| Primary cutaneous CD8-positive aggressive epidermotropic cytotoxic T-cell lymphoma | 9709/3 |
| Primary cutaneous peripheral T-cell lymphoma, NOS | 9709/3 |
| ***Intestinal T-cell and NK-cell lymphoid proliferations and lymphomas*** | |
| Indolent T-cell lymphoma of the gastrointestinal tract | 9702/1 |
| Indolent NK-cell lymphoproliferative disorder of the gastrointestinal tract† | 9702/1 |
| Enteropathy-associated T-cell lymphoma | 9717/3 |
| Monomorphic epitheliotropic intestinal T-cell lymphoma | 9717/3 |
| Intestinal T-cell lymphoma, NOS | 9717/3 |
| ***Hepatosplenic T-cell lymphoma*** | |
| Hepatosplenic T-cell lymphoma | 9716/3 |
| ***Anaplastic large cell lymphoma*** | |
| ALK-positive anaplastic large cell lymphoma | 9714/3 |
| ALK-negative anaplastic large cell lymphoma | 9715/3 |
| Breast implant–associated anaplastic large cell lymphoma | 9715/3 |
| ***Nodal T follicular helper cell lymphoma*** | |
| Nodal T follicular helper cell lymphoma, angioimmunoblastic type† | 9705/3 |
| Nodal T follicular helper cell lymphoma, follicular type | 9702/3 |
| Nodal T follicular helper cell lymphoma, NOS | 9702/3 |
| ***Other peripheral T-cell lymphomas*** | |
| Peripheral T-cell lymphoma, NOS | 9702/3 |
| ***EBV-positive T-cell and NK-cell lymphomas*** | |
| EBV-positive nodal T- and NK-cell lymphoma† | 9702/3 |
| Extranodal NK/T-cell lymphoma† | 9719/3 |
| ***EBV-positive T-cell and NK-cell lymphoid proliferations and lymphomas of childhood*** | |
| Severe mosquito bite allergy | |
| Hydroa vacciniforme lymphoproliferative disorder | 9725/1 |
| Systemic chronic active EBV-positive disease† | 9725/1 |
| Systemic EBV-positive T-cell lymphoma of childhood | 9724/3 |

[a] These morphology codes are from the International Classification of Diseases for Oncology, third edition, second revision (ICD-O-3.2).[11] Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour: /2 for carcinoma in situ and grade lll intraepithelial neoplasia; /3 for malignant tumours, primary site; and /6 for malignant tumours, metastatic site. Behaviour code /6 is not generally used by cancer registries.

† Labels marked with a dagger have undergone a change in terminology of a previous code.

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## Note 8 – Indications for disease transformation (Non-core)

High grade transformation in indolent lymphomas, e.g., Richter transformation in chronic lymphocytic leukaemia (CLL) or a diagnosis of DLBCL or high grade B-cell lymphoma (HGBCL) in the background of follicular lymphoma usually heralds a change in the disease course and more aggressive disease. However, transformed DLBCL or HGBCL cannot be distinguished by morphology from their *de novo* counterparts. If an aggressive lymphoma type is diagnosed in the setting of known indolent lymphoma, information on the clonal relationship with the preceding low grade lymphoma should be sought. Where necessary, investigation concerning the clonal evolution pattern – linear versus divergent – should be considered. Clonally unrelated secondary neoplasms in patients with indolent lymphomas may have different biological features and a different – usually better – prognosis than clonally related transformations.[5,12,13]

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## Note 9 – Immunoprofiling/phenotyping studies (Core and Non-core)

All immunostaining tests that contributed to the diagnosis should be documented. To this end, the committee discussed that immunohistochemical studies may be performed in several tiers, first using general/standard markers forcell lineage/category determination (B-cell, T-cell, myeloid, histiocytic/dendritic) then proceeding to more family/class- or entity-specific markers depending on local established procedures. The marker panels listed in Table 2 follow the criteria of essential and/or desirable diagnostic criteria as listed in WHO-HAEM5.[10] Staining for Ki-67 is a helpful adjunct in the assessment of indolent or aggressive disease, and the level of Ki-67 expression is listed as a prognostic and/or predictive marker in many entities as are various other immunohistochemical markers (mutant p53 over-expression or null-phenotype in many entities, or MYC/BCL2 double expression in DLBCL).

**Table 2: Immunoprofiling/phenotyping markers**

| **Suspect disease/disease category** (to which all pre-test information is in favour of) | **Recommended supporting immunohistochemical markers (non-core)** |
|---|---|
| Chronic lymphocytic leukaemia (CLL)/small lymphocytic lymphoma (SLL) | CD5, CD23 |
| Splenic B-cell lymphoma/leukaemia | ANXA1, CD103, CyclinD1, CD25, CD200/CD80 (flow cytometry) |
| Lymphoplasmacytic lymphoma (LPL) | MUM1, kappa, lambda, IgM |
| Marginal zone lymphoma (MZL) | CD5, CD10, CD23, Cyclin D1, BCL6, SOX11 (mainly to exclude other entities) |
| Follicular lymphoma (FL) | CD10, BCL6, BCL2 |

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| Mantle cell lymphoma (MCL) | CyclinD1, SOX11 |
| Diffuse large B-cell lymphoma (DLBCL) | CD10, BCL6, MUM1 (Hans classifier)<br>BCL2, MYC (double expresser status) |
| Specific entities of large B-cell lymphoma (LBCL) | CD10, BCL6, MUM1, TdT (HGBCL/DLBCL-*MYC/BCL2*)<br>CD138, MUM1, ALK (ALK-positive LBCL)<br>CD10, BCL6, IRF4/MUM1 (LBCL with *IRF4* rearrangement)<br>CD10, BCL6, BCL2, MYC (HGBCL-11q)<br>CD138, MUM1, EBER, EBV-LMP1, EBNA2 (various LBCL entities associated with Epstein-Barr virus (EBV))<br>CD10, BCL6, MUM1 (IP-DLBCL)<br>BCL2, MUM1, IgM (PCLBCL-LT)<br>CD30, CD23, MAL, PDL1/2 (PMBCL) |
| Burkitt lymphoma | EBER, CD10, BCL6, BCL2, MYC, LMO2 (a marker of exclusion) |
| High grade B-cell lymphoma (HGBCL), not otherwise specified (NOS) | CD10, BCL6, BCL2, MUM1 (Hans classifier), TdT, CD34, CyclinD1 (markers of exclusion) |
| KSHV/HHV8-associated B-cell lymphoproliferative disorder (LPD)/lymphomas | HHV8, EBER, CD30, CD138, MUM1, IgM (lambda) |
| LPD/lymphomas associated with immune deficiency/dysregulation (IDD) | EBER, EBV-LMP1, EBNA2, others according to subtype |
| Classic Hodgkin lymphoma | CD30, CD15, PAX5, CD20, EBER, EBV-LMP1, CD3, MUM1 |
| Nodular lymphocyte predominant Hodgkin lymphoma | CD20, CD30, CD3, BCL6, OCT2, PD1, CD21 |
| Plasma cell neoplasms | CD38, CD138, MUM1, kappa, lambda |
| T-cell and NK-cell LPDs and lymphomas | Variable (as recommended by WHO-HAEM5[10]):<br>TdT (T-LBL/ALL)<br>TCL1 (T-PLL)<br>CD3, CD4, CD5, CD7, CD8, TCRαβ, TCRγδ<br>PD1, ICOS1, CXCL13, CD10, BCL6 (nTFHL)<br>CD30, Perforin, TIA1, Granzyme B, ALK (anaplastic large cell lymphoma)<br>CD2, CD5, CD56, Perforin, Granzyme B, TIA1 (NK/T and NK LPDs/ lymphomas) |

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## Note 10 – Molecular genetic studies (Core and Non-core)

According to the essential diagnostic criteria listed in WHO-HAEM5, molecular genetic studies are mandatory for the diagnosis of certain entities defined by the presence of a molecular aberration (as examples *BCR*::*ABL1* fusion or ploidy assessment in precursor B-cell neoplasms, *IRF4* status in *IRF4*-rearranged large B-cell lymphoma (*IRF4*r LBCL), *MYC* and *BCL2* rearrangements in DLBCL/HGBCL-*MYC*/*BCL2*, or EBER assessment in EBV-positive DLBCL).[10] In some genetically defined entities, well-established surrogate immunohistochemical markers are available, such as ALK staining in ALK-positive anaplastic large cell lymphoma or ALK-positive large B-cell lymphoma; while in others, immunohistochemistry may be suggestive of the diagnosis if molecular testing is not available, such as IRF4/MUM1 staining in *IRF4*r LBCL or MYC immunohistochemistry in Burkitt lymphoma. It should be noted that in case of absence of a molecular assay or a validated surrogate marker, a definite diagnosis at the entity level is not accepted. Table 3 lists molecular markers that either define the entity or that are helpful in characterising (molecular) subtypes. While the field of molecular markers in lymphoid disease is increasingly expanding,[14] the use of more sophisticated marker constellations to add more granularity to for example, the molecular classification of DLBCL[15-17] is currently not advised due to a lack of consensus regarding different algorithms and/or platforms.

**Table 3: Molecular analyses**

| **Suspect disease/disease category** (to which all pre-test information is in favour of) | **Recommended supportive molecular investigations (non-core)** |
|---|---|
| B-cell lymphoma/ lymphoproliferation | B-cell receptor rearrangement |
| Chronic lymphocytic leukaemia (CLL)/small lymphocytic lymphoma (SLL) | FISH 11q, 17p, *TP53* mutation, trisomy 12(+12), somatic hypermutation in select cases |
| Splenic B-cell lymphoma/leukaemia | *BRAF*, *MAP2K1*, *KLF2*, *NOTCH2* mutations |
| Lymphoplasmacytic lymphoma (LPL) | *MYD88 L265P*, *CXCR4* mutations |
| Marginal zone lymphoma (MZL) | t(11;18)(q21;q21)/*BIRC3*::*MALT1* fusion (in gastric mucosa-associated lymphoid tissue (MALT) lymphoma); other MALT lymphoma-associated translocation or mutation (various sites) |
| Follicular lymphoma (FL) | *BCL2* rearrangement |
| Mantle cell lymphoma (MCL) | *CCND1* rearrangement |
| Diffuse large B-cell lymphoma (DLBCL) | Cell-of-origin (COO) classification<br>*MYC*, *BCL2*, *BCL6* rearrangement |

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|---|---|
| DLBCL/high grade B-cell lymphoma (HGBCL), not otherwise specified (NOS) | No concurrent *MYC* and *BCL2* rearrangement; 11q aberration negative |
| Primary mediastinal large B-cell lymphoma (PMBCL) | *CIITA* and *PDL1/2 (9p24.1) SOCS1 JAK/STAT6 CIITA*, *B2M*, *TNFAIP3* |
| Specific entities of large B-cell lymphoma (LBCL) | *MYC*, *IG*::*MYC*, *BCL2*, *BCL6* rearrangements (HGBCL/DLBCL-*MYC/BCL2*)<br>*IGH*::*IRF4* (LBCL with *IRF4* rearrangement)<br>11q FISH (HGBCL-11q)<br>*MYC* rearrangement, EBER (plasmablastic lymphoma (PBL)) |
| Burkitt lymphoma | *IG*::*MYC* fusion, no concurrent *BCL2 and BCL6* rearrangements |
| T-cell and NK-cell lymphoproliferative disorders (LPDs) and lymphomas | Variable (as recommended by WHO-HAEM5[10]):<br>T-cell receptor rearrangement<br>t(14;14); inv14 (T-PLL)<br>*ALK, DUSP22* and TP63 rearrangements (anaplastic large cell lymphoma)<br>EBER (ENKTL, EBV positive nodal T and NK lymphomas)<br>*DNMT3A, TET2, RHOA, IDH2* mutations (nTFHL)<br>EBER (ENKTL, EBV-positive nodal T- and NK lymphoma)<br>*SETD2; JAK/STAT (STAT5B, JAK3)* mutations (monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL))<br>*JAK/STAT (JAK1, STAT3)* mutations (enteropathy-associated T-cell lymphoma (EATL)) |

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