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Tumours of the Central Nervous System Integrated Final Diagnosis 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 SECTION

INTEGRATED FINAL DIAGNOSIS (Note 1)

◯ Diagnosis not classified elsewhere

HISTOLOGICAL TUMOUR GRADE (Note 2)

◯ Not applicable
◯ CNS World Health Organization (WHO) grade 1
◯ CNS WHO grade 2
◯ CNS WHO grade 3
◯ CNS WHO grade 4
◯ Cannot be determined, *specify*

INTEGRATED FINAL DIAGNOSIS BASED ON (select all that apply) (Note 3)

☐ Histology
☐ Immunohistochemistry
☐ Molecular test

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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 III-2 or above (based on prognostic factors in the National Health and Medical Research Council levels of evidence[1]). In rare circumstances, where level III-2 evidence is not available an element may be made a CORE element where there is unanimous agreement in the Dataset Authoring Committee (DAC).

Non-morphological testing e.g., molecular or 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 III-2 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

This dataset section has been developed for the integrated final diagnosis of benign and malignant primary tumours of the central nervous system (CNS) and its coverings, as well as tumours from those structures of the peripheral nervous system immediately adjacent to the CNS. The CNS dataset applies to both biopsy and resection specimens of adult and paediatric CNS tumours. Haematological lesions that may originate in the brain are included. Most sarcomas are not included and are covered by separate ICCR datasets.[2,3] Secondary tumours of the CNS (for example metastatic tumours from carcinomas, sarcomas or melanomas in other organs) are not covered in this dataset. Tumours of the pituitary gland are included as the majority of these tumours are reported by neuropathologists worldwide.

This dataset section should be used in conjunction with the ICCR dataset sections on ‘Histological assessment of CNS specimens’ and the ‘Molecular information for CNS specimens’, where appropriate.

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The 2nd edition of this dataset incorporates the World Health Organisation (WHO) Classification of Tumours of the CNS, 5th edition (CNS5), 2021.[4] Reports should incorporate these three dataset sections into a single layered report format (see **Note 1 INTEGRATED FINAL DIAGNOSIS**).

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Note 1 – Integrated final diagnosis (Non-core)

All reports should strive to render a diagnosis from the WHO CNS5 Classification,[4] although it is recognised that this may not be possible in all instances (i.e., that more descriptive diagnoses may be needed for tumours that do not meet criteria for WHO CNS5 entities).[4,5]

In many situations, CNS WHO[4] diagnoses 'integrate' histological and molecular information; for these entities, both histological and molecular information is needed. In this context, 'molecular' refers to the detection of molecular alterations in nucleic acids that can be detected at the nucleic acid or protein level. In some scenarios, there may be differences between histological appearance and the WHO CNS5[4] diagnosis (e.g., a diffuse glioma without overt oligodendroglial features but with IDH sequence variant and 1p/19q codeletion).

To capture this nosological heterogeneity and to provide as much clinically relevant information in each report, it is recommended that layered diagnostic formatting be utilized in reports, typically with four layers:

- WHO CNS5 Classification diagnosis (as per this dataset section);
- Histological appearance (as per 'Histological assessment of CNS specimens' dataset section);
- CNS WHO grade (as per 'Histological assessment of CNS specimens' and 'Molecular information for CNS specimens' dataset sections);
- Molecular parameters (as per 'Molecular information for CNS specimens' dataset section).

As mentioned above, for some entities, the WHO CNS5[4] diagnosis may be identical to the histological appearance (e.g., choroid plexus tumours), but for others there may be differences such as the following:

- WHO CNS5 Classification diagnosis: Diffuse astrocytoma, IDH-mutant, CNS WHO grade 4
- Histological appearance: Diffuse glioma
- CNS WHO grade 3
- Molecular parameters:
    - *IDH1* R132H alteration
    - *ATRX* alteration
    - *TP53* alteration
    - 1p/19q retention
    - *CDKN2A/B* homozygous deletion

Table 1. World Health Organization classification and grade of central nervous system tumours.[4]

Descriptor	ICD-O codes[a]	CNS WHO Grade
Gliomas, glioneuronal tumours and neuronal tumours		
Adult-type diffuse gliomas		
Astrocytoma, IDH-mutant	9400/3, 9401/3, 9445/3	2-4

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Descriptor	ICD-O codes[a]	CNS WHO Grade
Oligodendroglioma, IDH-mutant and 1p/19q-codeleted	9450/3, 9451/3	2-3
Glioblastoma, IDH-wildtype	9440/3	4
Paediatric-type diffuse low-grade gliomas		
Diffuse astrocytoma, MYB -or MYBL1-altered	9421/1	1
Angiocentric glioma	9431/1	1
Polymorphous low-grade neuroepithelial tumour of the young	9413/0	1
Diffuse low-grade glioma, MAPK pathway-altered	9421/1	n/a
Paediatric-type diffuse high-grade gliomas		
Diffuse midline glioma, H3 K27-altered	9385/3	4
Diffuse hemispheric glioma, H3 G34-mutant	9385/3	4
Diffuse paediatric-type high-grade glioma, H3 wildtype and IDH-wildtype	9385/3	4
Infant-type hemispheric glioma	9385/3	n/a
Circumscribed astrocytic gliomas		
Pilocytic astrocytoma	9421/1	1
High-grade astrocytoma with piloid features	9421/3	n/a
Pleomorphic xanthoastrocytoma	9424/3	2-3
Subependymal giant cell astrocytoma	9384/1	1
Chordoid glioma	9444/1	2
Astroblastoma, *MN1*-altered	9430/3	n/a
Glioneuronal and neuronal tumours		
Ganglioglioma	9505/1	1
Gangliocytoma	9492/0	1
Desmoplastic infantile ganglioglioma / desmoplastic infantile astrocytoma	9412/1	1
Dysembryoplastic neuroepithelial tumour	9413/0	1
Diffuse glioneuronal tumour with oligodendroglioma-like features and nuclear clusters		n/a
Papillary glioneuronal tumour	9509/1	1
Rosette-forming glioneuronal tumour	9509/1	1
Myxoid glioneuronal tumour	9509/1	1
Diffuse leptomeningeal glioneuronal tumour	9509/3	2-3
Multinodular and vacuolating neuronal tumour	9509/0	1
Dysplastic cerebellar gangliocytoma (Lhermitte-Duclos disease)	9493/0	1
Central neurocytoma	9506/1	2
Extraventricular neurocytoma	9506/1	2
Cerebellar liponeurocytoma	9506/1	2
Ependymal tumours		

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Descriptor	ICD-O codes[a]	CNS WHO Grade
Supratentorial ependymoma	9391/3	2-3
Supratentorial ependymoma, ZFTA fusion-positive	9396/3	2-3
Supratentorial ependymoma, YAP1 fusion-positive	9396/3	2-3
Posterior fossa ependymoma, NOS	9391/3	2-3
Posterior fossa group A (PFA) ependymoma	9396/3	2-3
Posterior fossa group B (PFB) ependymoma	9396/3	2-3
Spinal ependymoma, NOS	9391/3	2-3
Spinal ependymoma, MYCN-amplified	9396/3	n/a
Myxopapillary ependymoma	9394/1	2
Subependymoma	9383/1	1
Choroid plexus tumours		
Choroid plexus papilloma	9390/0	1
Atypical choroid plexus papilloma	9390/1	2
Choroid plexus carcinoma	9390/3	3
Embryonal tumours		
Medulloblastomas, molecularly defined		
Medulloblastoma, WNT-activated	9475/3	4
Medulloblastoma, SHH-activated and *TP53*-wildtype	9471/3	4
Medulloblastoma, SHH-activated and *TP53*-mutant	9476/3	4
Medulloblastoma, non-WNT/non-SHH	9477/3	4
Medulloblastomas, histologically defined		
Medulloblastomas, histologically defined	9470/3	4
Other CNS embryonal tumours		
Atypical teratoid/rhabdoid tumour	9508/3	4
Cribriform neuroepithelial tumour		n/a
Embryonal tumour with multilayered rosettes	9478/3	4
CNS Neuroblastoma, *FOXR2*-activated	9500/3	4
CNS tumour with *BCOR* internal tandem duplication	9500/3	n/a
CNS Embryonal tumour NEC/NOS	9473/3	n/a
Pineal tumours		
Pineocytoma	9361/1	1
Pineal parenchymal tumour of intermediate differentiation	9362/3	2-3
Pineoblastoma	9362/3	4
Papillary tumour of the pineal region	9395/3	2-3
Desmoplastic myxoid tumour of the pineal region, SMARCB1-mutant		n/a
Cranial and paraspinal nerve tumours		
Schwannoma	9560/0	1

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Descriptor	ICD-O codes[a]	CNS WHO Grade
Neurofibroma	9540/0	1
Perineurioma	9571/0	1
Hybrid nerve sheath tumour	9563/0	1
Malignant melanotic nerve sheath tumour	9540/3	n/a
Malignant peripheral nerve sheath tumour	9540/3	n/a
Cauda equina neuroendocrine tumour (previously paraganglioma)	8693/3	1
Meningioma		
Meningioma	9530/0	1-3
Mesenchymal, non-meningothelial tumours involving the CNS		
Fibroblastic and myofibroblastic tumours		
Solitary fibrous tumour	8815/1	1-3
Vascular tumours		
Hemangiomas and vascular malformations	9121/0, 9131/0, 9123/0	n/a
Haemangioblastoma	9161/1	1
Skeletal muscle tumours		
Rhabdomyosarcoma	8910/3	n/a
Tumours of uncertain differentiation		
Intracranial mesenchymal tumour, *FET::CREB* fusion-positive		n/a
CIC-rearranged sarcoma	9367/3	4
Primary intracranial sarcoma, *DICER1*-mutant	9480/3	n/a
Ewing sarcoma	9364/3	4
Chondrogenic tumours		
Mesenchymal chondrosarcoma	9240/3	n/a
Chondrosarcoma	9220/3	1-3
Notochordal tumours		
Chordoma	9370/3	n/a
Melanocytic tumours		
Diffuse meningeal melanocytic neoplasms		
Meningeal melanocytosis	8728/0	n/a
Meningeal melanomatosis	8728/3	n/a
Circumscribed meningeal melanocytic neoplasms		
Meningeal melanocytosis	8728/1	n/a
Meningeal melanomatosis	8720/3	n/a
Tumours of the sellar region		
Adamantinomatous craniopharyngioma	9351/1	1
Papillary craniopharyngioma	9352/1	1

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Descriptor	ICD-O codes[a]	CNS WHO Grade
Pituicytoma, granular cell tumour of the sellar region, and spindle cell oncocytoma	9432/1, 9582/0, 8290/0	n/a
Pituitary adenoma / pituitary neuroendocrine tumour	8272/3	n/a
Pituitary blastoma	8273/3	n/a
Genetic tumour syndromes involving the CNS		
Neurofibromatosis type 1		
Neurofibromatosis type 2		
Schwannomatosis		
Von Hippel-Lindau syndrome		
Tuberous sclerosis		
Li-Fraumeni syndrome		
Cowden syndrome		
Constitutional mismatch repair deficiency syndrome		
Familial adenomatous polyposis 1		
Naevoid basal cell carcinoma syndrome		
Rhabdoid tumour predisposition syndrome		
Carney complex		
DICER1 syndrome		
Familial paraganglioma syndromes		
Melanoma-astrocytoma syndrome		
Familial retinoblastoma		
BAP1 tumour predisposition syndrome		
Fanconi anaemia		
ELP1-medulloblastoma syndrome		

[a] These morphology codes are from the International Classification of Diseases for Oncology, Third Edition, second revision (ICD-O-3.2).[5] Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours, primary site; and /6 for malignant tumours, metastatic site. Subtype labels are indented. Incorporates all relevant changes from the 5th edition Corrigenda, November 2022.[6]
n/a – CNS WHO grade is not included in the tumour definition.

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Table 2. World Health Organization classification of haematological tumours involving the central nervous system.[7]

Descriptor	ICD-O codes[a]
Lymphomas	
Lymphomas with predominant primary CNS presentation	
Primary large B-cell lymphoma of the CNS	9680/3

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Descriptor	ICD-O codes[a]
Lymphomas arising in immune deficiency/dysregulation	
Lymphomatoid granulomatosis	9766/1, 9766/3
Intravascular large B-cell lymphoma	9712/3
Extranodal NK/T-cell lymphoma	9712/3
Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (EMZL) of the dura	9699/3
Lymphoplasmacytic lymphoma (Bing-Neel syndrome)	9671/3
Other rare lymphomas with predominant primary CNS presentation	
Other indolent B-cell lymphomas of the CNS	9690/3, 9823/3
Other aggressive B-cell lymphomas	9687/3
Peripheral T-cell lymphoma, NOS	9702/3
ALK-negative and ALK-positive anaplastic large cell lymphoma	9715/3, 9714/3
Histiocytic tumours	
Erdheim-Chester disease	9749/3
Rosai-Dorfman disease	9749/3
Juvenile xanthogranuloma	9749/1
Langerhans cell histiocytosis	9751/1
Histiocytic sarcoma	9755/3
ALK-positive histiocytosis	9750/3

[a] These morphology codes are from the International Classification of Diseases for Oncology, Third Edition, second revision (ICD-O-3.2).[5] Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours, primary site; and /6 for malignant tumours, metastatic site. Subtype labels are indented.

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In the event that all diagnostic information is present but the tumour still does not meet criteria for a tumour type defined by the 2021 WHO Classification,[4] a 'descriptive' or 'not elsewhere classified' (NEC) diagnosis can be issued, which draws attention to the unusual nature of the lesion. Such designations are distinct from 'not otherwise specified' (NOS) diagnoses, which are cases in which necessary diagnostic information is not available.[8]

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Note 2 – Tumour grade (Core)

In as many pathology reports of CNS neoplasms as possible, the diagnosis should include a grade based on the WHO CNS5 Classification (see Table 1).[4,9] As for other organ systems, different grades of a diagnostic entity do not have a separate entry in the WHO CNS5 Classification anymore but are grouped under the respective diagnostic tumour type.

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The scale of CNS WHO grades from 1 to 4 reflects the natural histories of various tumour types, rather than their shifting prognoses with changes in therapeutic practice over time.[10]

- Generally speaking, a CNS WHO grade 1 tumour is considered benign and potentially curable by surgery, although in unfavourable locations, such tumours may still create significant morbidity. Note that this approach is different from that of many other tumour types in other parts of the body, for which a grade 1 designation would reflect a low grade malignancy. For this reason, CNS tumour grades are termed 'CNS WHO grades' rather than simply 'WHO grades'.
- Central nervous system WHO grade 2 tumours typically are slowly growing tumours that often recur and are associated with significant mortality, albeit with survival times of many years in most cases.
- Central nervous system WHO grade 3 tumours are rapidly growing malignancies with typical survivals of only a few years if treated with surgery alone.
- Central nervous system WHO grade 4 neoplasms are highly aggressive malignancies with rapid mortality (typically in less than 2 years after diagnosis) in the absence of therapies beyond surgery (e.g., glioblastomas and embryonal neoplasms).

Progression from lower-grade malignancy to higher-grade forms occurs in some CNS neoplasms, most commonly the IDH-mutant diffuse gliomas, and to a lesser extent in the meningiomas.

For some tumours, assigning a CNS WHO grade could cause more confusion than clarification for clinical colleagues (e.g., when the exact tumour subtype remains unclear or the when the prognostic impact of the grade is unclear); in such cases, it preferable to omit the CNS WHO grade from the final diagnosis (Table 1). Also, for some more recently defined tumour types, a CNS WHO grade has not been assigned because a definite understanding of that tumour's natural history is not yet available in the literature. Bone, soft tissue and haematological neoplasms occurring within the neural axis are mostly classified and graded using the same criteria as in other parts of the body, although the CNS grading scheme for solitary fibrous tumours differs from its soft tissue counterpart.

Tumour histology and grade are strong predictors of clinical behaviour for different CNS tumours, including diffusely infiltrating astrocytomas and meningiomas. Table 1 lists the grading criteria for these common CNS tumour types.

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Note 3 – Integrated diagnosis based on (Core)

The final integrated diagnosis is a core element and may be based on the following information:

- histological
- immunohistochemistry
- molecular tests

Histopathology reports optimally include an integrated assessment of all available information in a layered diagnostic format.

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