

Paediatric cancer stage guidelines for the Belgian general cancer registration, incidence year 2018

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Abbreviations

BCR	Belgian Cancer Registry
CNS	Central nervous system
CSF	Cerebrospinal fluid
С	Clinical
FIGO	International Federation of Gynecology and Obstetrics
ICD-0 3	International Classification of Diseases for Oncology, 3th edition
IDRF	Imaging-defined risk factor
INRGSS	International Neuroblastoma Risk Group Staging System
IRSS	International Retinoblastoma Staging System
Μ	Distant metastasis
Ν	Regional lymph node metastasis
р	Pathological
т	Extent of primary tumour
UICC	Union for International Cancer Control
WBCR	Web-based cancer registration
У	Classification after initial multimodality treatment



1 Aim of the document

The Belgian Cancer Registry recommends to include the Tiered staging system described in the chapter "Paediatric Tumours" of the TNM booklet, 8th edition¹ into their general cancer registration. This staging system is based on the Toronto Paediatric Cancer Stage Guidelines, which were determined on the consensus meeting held in 2014².

This document indicates and explains all the guidelines used for this registration.

2 Scope of application

- Those guidelines have to be applied by all paediatric hemato-oncology centres of Belgium for the registration of all children **aged 0-14 years at diagnosis**.
- Only for the data of incidence year 2018, so **starting from incidence date January 1**st !!! An update of this manual will be made for the data of the incidence year 2019.

3 Indications

3.1 For the guidelines

- For the 13 types of tumours that are discussed in this manual :
 - We will notify in the beginning of each chapter if the TNM is applicable for the cancer group, and if so, the pages of the TNM 8th edition where you can find the information about this TNM.
 - You also have to fill out the paediatric cancer stage
- Unless otherwise stated, we will use the Tier 2 classification. There are, however, 4 exceptions for this incidence year, for which you only have to register the Tier 1 classification. This concerns :
 - o Acute lymphoblastic leukaemia
 - Non-Hodgkin's lymphoma
 - Wilms' tumours
 - Soft tissue sarcoma other than rhabdomyosarcoma

3.2 For the registration

- If applicable, fill out the TNM classification for all kind of tumours.
- Fill out the paediatric cancer stage in the **Other Classification variable** (Figure 1).
- For each cancer group, the stage overview is given for your information. It is also indicated in red which stage information should be registered by the Oncological Care Programs.

¹ TNM Classification of Malignant Tumours, Eighth Edition. Edited by Brierley JD, Gospodarowicz MK and Wittekind C, 2017 Union for International Cancer Control (UICC). Published by John Wiley & Sons, Ltd. p.247-53. ² Gupta S *et al.* Paediatric cancer stage in population-based cancer registries: the Toronto consensus principles and guidelines. Lancet Oncol. 2016 Apr;17(4):e163-72.





Figure 1: Dutch (A) and French (B) version of the variables cTNM, pTNM and Other classification as they appear in the general web-based cancer registration (WBCR) of a new cancer diagnosis.

4 Paediatric Cancer Staging : guidelines

4.1 Leukaemia

- 4.1.1 Acute lymphoblastic leukaemia (ICD-O 3: 9811→ 9818, 9835, 9837, 9727)
 - > **TNM classification** : not applicable.
 - Paediatric cancer stage : use the Tier 1 classification which is based on the central nervous system involvement.

Stage	Explanation	Registration
CNS negative	No clinical sign* of the CNS	Other classification: Other →
	involvement and n <mark>o de</mark> tectab <mark>le</mark>	Stage: CNS-
	leukaemia cells in t <mark>he C</mark> SF	
CNS positive	Clinical signs* of C <mark>NS in</mark> volvement or	Other classification: Other →
	presence of leukae <mark>mia</mark> cells <mark>in th</mark> e CSF	Stage: CNS+

CSF: cerebrospinal fluid.

* Clinical signs of central nervous system (CNS) involvement includes cranial nerve palsy, signs of meningeal disease and a non-haemorrhagic CNS mass or chloroma².



4.2 Lymphoma

4.2.1 Hodgkin's Lymphoma (ICD-O 3: 9650→9653, 9659, 9663)

- > **TNM classification** : not applicable.
- Paediatric cancer stage : use the Tier 2 classification which is determined according to the Lugano classification, an updated version of the Ann Arbor (see TNM 8th edition page 235 for more information)¹.

Stage	Explanation	Registration
Lugano stage I A/B	Involvement of a single lymph node	Other classification: Other →
	region or localised involvement of a	Stage: Lugano IA or Lugano IB *
	single extralymphatic organ or site	
Lugano stage II A/B	Involvement of two or more lymph	Other classification: Other →
	node regions on the <u>same</u> side of the	Stage: Lugano IIA or
	diaphragm, or localised involvement of	Lugano IIB *
	a single extralymphatic organ or site	
	and its regional lymph node(s) with or	
	without involvement of other	
	contiguous lymph node regions on the	
	same side of the diaphragm	
Lugano Bulky stage II	Stage II disease with a single nodal	Other classification: Other →
	mass greater than 10cm in maximum	Stage: Lugano Bulky IIA or
	dimension or greater than a third of	Lugano Bulky IIB *
	the thoracic diameter as assessed on	
	CT.	
Lugano stage III A/B	Involvement of lymph node regions on	Other classification: Other →
	both sides of the diaphragm, which	Stage: Lugano IIIA or
	may also be accompanied by	Lugano IIIB *
	involvement of the spleen	
Lugano stage IV A/B	Disseminated (multifocal) involvement	Other classification: Other →
	of one or more extralymphatic organs,	Stage: Lugano IVA or
	with or without associated lymph node	Lugano IVB *
	involvement, or non-contiguous	
	extralymphatic organ involvement	
	with involvement o <mark>f ly</mark> mph n <mark>ode</mark>	
	regions on the sam <mark>e or</mark> both s <mark>ides</mark> of	
	the diaphragm	

* A and B classification:

Each stage should be divided into A and B according to the absence (A) or presence (B) of defined general symptoms, which include:

- Unexplained weight loss of more than 10% of the usual body weight in the 6 months prior to first attendance
- Unexplained fever with temperature above 38°C
- Night sweats (e.g. those that require change of bedclothes)



4.2.2 Non-Hodgkin's Lymphoma (ICD-O 3: 9591, 967_→969_)

- > **TNM classification** : not applicable.
- Paediatric cancer stage : use the Tier 1 classification which is based on the central nervous system and bone marrow involvement.

Stage	Explanation	Registration
Limited disease	No involvement of the bone marrow	Other classification: Other →
	or CNS	Stage: Limited
Advanced disease	Involvement of the bone marrow	Other classification: Other →
	and/or CNS	Stage: Advanced

4.3 Nervous system tumours

- 4.3.1 Ependymoma^{*} & Medulloblastoma^{**} (and other CNS embryonal tumours^{***}) (ICD-O 3: * 9383,9391→9394; ** 9470→9472, 9474, 9490; *** 9473, 9500→9504, 9508)
 - > **TNM classification** : not applicable.
 - Paediatric cancer stage : use the Tier 2 classification which is classified according to the Mstage.

Stage	Explanation	Registration
M0	Absence of visible disease beyond the	Other classification: Other →
	primary tumour on imaging (MRI brain	Stage: MO
	and spine) and absence of tumour cells	
	in the cerebrospinal fluid	
M1	Tumour cells in the cerebrospinal fluid	Other classification: Other →
		Stage: M1
M2	Visible metastases in the brain	Other classification: Other \rightarrow
		Stage: M2
M3	Visible metastases in the spine or	Other classification: Other →
	cervicomedullary (junction)	Stage: M3
M4	Metastases outside of the central	Other classification: Other →
	nervous system	Stage: M4

4.3.2 Neuroblastoma (ICD-O 3: 9490, 9500)

- > TNM classification : not applicable.
- Paediatric cancer stage : use the Tier 2 classification which is made according to the International Neuroblastoma Risk Groupe Staging System (INRGSS), a clinical classification system that is determined prior to any treatment, including surgery.



Stage	Explanation	Registration
INRGSS - localised L1	Localised tumour confined to one body compartment, neck, chest, abdomen or pelvis, and with the absence of imaging-defined risk factors (IDRFs)*. An isolated finding of intraspinal tumour extension that does not fulfil the criteria for an IDRF* is consistent with stage L1.	Other classification: Other → Stage: INRGSS L1
INRGSS - locoregional L2	Locoregional tumours with the presence of one or more IDRFs*. The tumour may be ipsilateral continuous within body compartments (ie, a left-sided abdominal tumour with left-sided chest involvement should be considered stage L2). However, a clearly left sided abdominal tumour with right-sided chest (or vice versa) involvement is defined as metastatic disease.	Other classification: Other → Stage: INRGSS L2
INRGSS - metastatic M	Distant metastatic disease (ie, not contiguous with the primary tumour) except as defined for stage MS. Non regional (distant) lymph node involvement is metastatic disease. However, an upper abdominal tumour with enlarged lower mediastinal nodes or a pelvic tumour with inguinal lymph node involvement is considered locoregional disease. Ascites and/or pleural effusion, even with malignant cells, do not constitute metastatic disease unless they are remote from the body compartment of the primary tumour.	Other classification: Other → Stage: INRGSS M
INRGSS - MS disease	Metastatic disease confined to skin, liver and/or bone marrow in children < 18 months of age (547 days). MIBG scintigraphy must be negative in bone and bone marrow.	Other classification: Other → Stage: INRGSS MS

* For more information regarding IDRFs, see Table 1.



Table 1: Imaging-defined risk factors (IDRFs) in neuroblastic tumours

Table 1. Image-Defined Risk Factors in Neuroblastic Tumors
Ipsilateral tumor extension within two body compartments
Neck-chest, chest-abdomen, abdomen-pelvis
Neck
Tumor encasing carotid and/or vertebral artery and/or internal jugular vein
Tumor extending to base of skull
Tumor compressing the trachea
Cervico-thoracic junction
Tumor encasing brachial plexus roots
Tumor encasing subclavian vessels and/or vertebral and/or carotid artery
Tumor compressing the trachea
Thorax
Tumor encasing the aorta and/or major branches
Tumor compressing the trachea and/or principal bronchi
Lower mediastinal tumor, infiltrating the costo-vertebral junction between T9 and T12
Thoraco-abdominal
Tumor encasing the aorta and/or vena cava
Abdomen/pelvis
Tumor infiltrating the porta hepatis and/or the hepatoduodenal ligament
Tumor encasing branches of the superior mesenteric artery at the mesenteric root
Tumor encasing the origin of the coeliac axis, and/or of the superior mesenteric artery
Tumor invading one or both renal pedicles
Turnor encasing the aorta and/or vena cava
Tumor encasing the iliac vessels
Pelvic tumor crossing the sciatic notch
Intraspinal tumor extension whatever the location provided that:
More than one third of the spinal canal in the axial plane is invaded and/ or the perimedullary leptomeningeal spaces are not visible and/or the spinal cord signal is abnormal
Infiltration of adjacent organs/structures
Pericardium, diaphragm, kidney, liver, duodeno-pancreatic block, and mesentery
Conditions to be recorded, but not considered IDRFs
Multifocal primary tumors
Pleural effusion, with or without malignant cells
Ascites, with or without malignant cells
Abbreviation: IDRFs, image-defined risk factors.

Adopted from Monclair et al., 2009.³

³ Monclair T *et al.* The International Neuroblastoma Risk Group (INRG) staging system: an INRG Task Force report. J Clin Oncol 2009; 27: 298–303.



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4.4 Ophthalmic, renal and hepatic tumours

4.4.1 Retinoblastoma (ICD-O 3: 9510→9514)

- TNM classification : has to be registered (for more information about this TNM, see TNM 8th edition, p.226-229)¹.
- Paediatric cancer stage : use the Tier 2 classification which is made according to the International Retinoblastoma Staging System (IRSS), a pathological classification system determined after enucleation.
- > In case of bilateral disease, two registrations should be performed.

Stage	Explanation	Registration
IRSS stage 0	The tumour is confined to the globe,	Other classification: Other →
	enucleation has not been performed	Stage: IRSS 0
IRSS stage I	Enucleation with negative margins (R0)	Other classification: Other →
		Stage: IRSS I
IRSS stage II	Enucleation with microscopic residual	Other classification: Other →
	disease (R1)	Stage: IRSS II
IRSS stage III	Involvement of the orbit and/or	Other classification: Other →
	metastases to regional lymph nodes	Stage: IRSS III
IRSS stage IV	Metastatic disease	Other classification: Other →
		Stage: IRSS IV

R: residual tumour.

4.4.2 Nephroblastoma/Wilms' tumour (ICD-O 3: 8959, 8960)

- > **TNM classification** : not applicable.
- Paediatric cancer stage : use the Tier 1 classification which indicates if the tumour is metastatic or not.
- > In case of bilateral disease, two registrations should be performed.

Stage	Explanation	Registration
Localized	Tumour confined to the area of origin	Other classification: Other →
		Stage: Localized
Metastatic	Distant metastases present at diagnosis	Other classification: Other →
		Stage: Metastatic



4.5 Hepatoblastoma (ICD-O 3: 8970)

- > **TNM classification** : not applicable.
- Paediatric cancer stage : use the Tier 2 classification which indicates if the tumour is metastatic or not.

Stage	Explanation	Registration
Localized	Tumour confined to the liver, including	Other classification: Other →
	regional lymph nodes	Stage: Localized
Metastatic	Distant metastases present	Other classification: Other →
		Stage: Metastatic

4.6 Bone and soft tissue tumours

- 4.6.1 Osteosarcoma^{*} & Ewing's Sarcoma^{**} (considered together as Bone tumours) (ICD-O 3: * 9180→9187, 9191→9195,9200; ** 9364)
 - TNM classification : has to be registered, except for surface/juxtacortical osteosarcoma for which the TNM is not applicable (for more information about this TNM, see TNM 8th edition, p.120-123)¹.
 - Paediatric cancer stage : use the Tier 2 classification which indicates if the tumour is metastatic or not.

Stage	Explanation	Registration
Localized	Tumour confined to area of origin,	Other classification: Other →
	including regional lymph nodes	Stage: Localized
Metastatic	Distant metastases present	Other classification: Other →
		Stage: Metastatic

Note that "skip lesions", "skip metastases" or "seeding" in the same bone as the primary tumour are considered localized and not metastatic; if in a different bone to the primary tumour these are considered metastatic.



4.6.2 Rhabdomyosarcoma (ICD-O 3: 8900→8905,8910,8912,8920,8921)

- TNM classification : has to be registered. Be careful, the paediatric TNM options are different from the adult options (for more information about this TNM, see TNM 8th edition, p.248)¹.
- Paediatric cancer stage : use the Tier 2 classification which incorporates this paediatric TNM classification with the anatomical site of the tumour.

Stage	Explanation	Registration
Stage I	Any T; Any N; M0; Favourable site*	Other classification: Other →
		Stage: Toronto I
Stage II	T1a, T2a; N0; M0; Unfavourable site**	Other classification: Other →
		Stage: Toronto II
Stage III	T1a, T2a; N1; M0; Unfavourable site**	Other classification: Other →
	T1b, T2b; Any N; M0; Unfavourable site**	Stage: Toronto III
Stage IV	Any T; Any N; M1; Any site	Other classification: Other →
		Stage: Toronto IV

* Favourable anatomic sites: Orbit, head and neck (excluding parameningeal tumours) and genito-urinary sites (excluding bladder and prostate tumours).

** Unfavourable anatomic sites: Bladder, prostate, extremity, cranial, parameningeal, trunk, retro-peritoneum and all other sites not noted as favourable.

TNM clinical classification for Rhabdomyosarcoma:

T - Primary tumour

- TX Primary tumour cannot be assessed
- T0 No evidence of primary tumour
- T1 Confined to a single anatomic site
- T1a Tumour 5 cm or less in greatest dimension
- T1b Tumour more than 5 cm in greatest dimension
- T2 Extension beyond anatomic site
- T2a Tumour 5 cm or less in greatest dimension
- T2b Tumour more than 5 cm in greatest dimension

N - Regional Lymph Nodes

- NX Regional lymph nodes cannot be assessed
- NO No regional lymph node metastasis
- N1 Regional lymph node metastasis

M - Distant Metastasis

- M0 No distant metastasis
- M1 Distant metastasis



4.6.3 Soft Tissue Sarcoma other than Rhabdomyosarcoma

- TNM classification : has to be registered if applicable. This will depend on the histological type and anatomical site of the tumour (for more information about this TNM, see TNM 8th edition, p.124-126)¹.
- Paediatric cancer stage : use the Tier 1 classification which indicates if the tumour is metastatic or not.

Stage	Explanation	Registration
Localized	Tumour confined to the area of origin,	Other classification: Other →
	including regional lymph nodes	Stage: Localized
Metastatic	Distant metastases present	Other classification: Other →
		Stage: Metastatic

4.7 Reproductive system tumours

4.7.1 **Ovarian tumour (ICD-O 3: C56.9)**

- TNM classification : has to be registered if applicable. This will depend on the histological type of the tumour (for more information about this TNM, see TNM 8th edition, p.179-183)¹.
- Paediatric cancer stage : use the Tier 2 classification which corresponds to the International Federation of Gynecology and Obstetrics stage (FIGO).

Stage	Explanation	Registration
FIGO stage I	Tumour confined to the ovaries (one	Other classification: Figo →
	or both)	Stage: I
FIGO stage II	Tumour extension to pelvis without	Other classification: Figo →
	extension to peritoneum outside the	Stage: II
	pelvis nor to retroperitoneal lymph	
	nodes	
FIGO stage III	Tumour extension to peritoneum	Other classification: Figo \rightarrow
	outside the pelvis and/or	Stage: III
	retroperitoneal lymph nodes	
FIGO stage IV	Distant metastases present (excludes	Other classification: Figo →
	peritoneal metasta <mark>ses)</mark>	Stage: IV

The FIGO staging subclassifications described in the TNM 8th edition, p.179-183¹ can be further specified during registration (A-C, Ali, Alii), but are not required.



4.7.2 Testicular tumour (ICD-O 3: C62.0, C62.1, C62.9)

- TNM classification : has to be registered (for more information about this TNM, see TNM 8th edition, p.195-198)¹.
- Paediatric cancer stage : use the Tier 2 classification which is made according to the TNM classification.
- In case of bilateral disease, two registrations should be performed.

Stage	Explanation	Registration
Stage I	Any T; N0; M0	Other classification: Other →
		Stage: Toronto I
Stage II	Any T; N1, N2, N3; M0	Other classification: Other →
		Stage: Toronto II
Stage III	Any T; Any N; M1	Other classification: Other →
		Stage: Toronto III

TNM clinical classification for Testis Tumour:

T - Primary Tumour

Except for pTis and pT4, where radical orchiectomy is not always necessary for classification purposes, the extent of the primary tumour is classified after radical orchiectomy; see pT. In other circumstances, TX is used if no radical orchiectomy has been performed.

N - Regional Lymph Nodes

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Metastases to single or multiple lymph nodes, each ≤2 cm in greatest dimension
- N2 Metastases to single or multiple lymph nodes, >2 cm but ≤5 cm in greatest dimension
- N3 Metastases with a lymph node mass >5 cm in greatest dimension

M - Distant Metastasis

- M0 No distant metastasis
- M1 Distant metastasis
- M1a Non-regional lymph node(s) or lung metastasis
- M1b Distant metastasis other than to non-regional lymph nodes and lung

pTNM pathological classification for Testis Tumour:

pT - Primary tumour

- pTX Primary tumour cannot be assessed (see T Primary Tumour)
- pT0 No evidence of primary tumour (e.g. histological scar in tes<mark>tis)</mark>
- pTis Intratubular germ cell neoplasia (carcinoma *in situ*)
- pT1 Tumour limited to testis and epididymis without vascular/lymphatic invasion; tumour may invade tunica albuginea but not tunica vaginalis
- pT2 Tumour limited to testis and epididymis with vascular/lymphatic invasion, or tumour extending through tunica albuginea with involvement of tunica vaginalis
- pT3 Tumour invades spermatic cord with or without vascular/lymphatic invasion



pT4 Tumour invades scrotum with or without vascular/lymphatic invasion

pN - Regional Lymph Nodes

- pNX Regional lymph nodes cannot be assessed
- pN0 No regional lymph node metastasis
- pN1 Metastases to single or maximum 5 lymph nodes, each ≤2 cm in greatest dimension
- pN2 Metastases to single or maximum 5 lymph nodes, >2 cm but ≤5 cm in greatest dimension; or evidence of extranodal extension of tumour
- pN3 Metastases with a lymph node mass >5 cm in greatest dimension

pM - Distant Metastasis

- pM1 Distant metastasis microscopically confirmed
- pM1a Non-regional lymph node(s) or lung metastasis
- pM1b Distant metastasis other than to non-regional lymph nodes and lung





5 Paediatric Cancer Staging : Summary

- > If applicable, fill out the TNM classification for all kind of tumours.
- > In the table below, you can find a summary of the tiered paediatric cancer staging.
- > All the cancer staging systems asked for the incidence year 2018 are highlighted in yellow.

	Tier 1 staging system	Tier 2 staging system
ALL	CNS neg/ pos	CNS 1/ 2/ 3
Hodgkin's lymphoma	Lugano stage I/ II/ III/ IV A/ B	Lugano stage I/ II/ III/ IV A/ B
Non-Hodgkin lymphoma	Limited/Advanced	St Jude/Murphy stage I/ II/ III/ IV
Ependymoma	M0/ M+	M0/ 1/ 2/ 3/ 4
Medulloblastoma and other CNS embryonal tumours	M0 or localised/ M+ or metastatic	M0/ 1/ 2/ 3/ 4
Neuroblastoma	Localised/ Locoregional/ Metastatic/ INRGSS - MS disease	INRGSS - Localised L1/ Locoregional L2/ Metastatic M/ MS disease
Retinoblastoma	Localised (intraocular) / Regional (orbital or regional lymph nodes) / Distant (extra-orbital)	IRSS stage 0/ I/ II/ III/ IV
Wilms' tumour	Localised/ Metastatic	NWTSG or SIOP stage I/ II/ III/ IV
Hepatoblastoma	Localised/ Metastatic	Localised/ Metastatic
Osteosarcoma	Localised/ Metastatic	Localised/ Metastatic
Ewing's sarcoma	Localised/ Metastatic	Localised/ Metastatic
Rhabdomyosarcoma	Localised/ Metastatic	TNM stage I/ II/ III/ IV
Non-rhabdomyosarcoma soft-tissue sarcomas	Localised/ Metastatic	TNM stage I/ II/ III/ IV
Ovarian	Localised/ Regional/ Metastatic	FIGO stage I/ II/ III/ IV
Testicular	Localised/ Regional/ Metastatic	TNM stage I/ II/ III

