Standaardrapport hypofarynx en larynx

Conclusie

Neoadjuvante therapie: Kies een optie.

Tumorlokalisatie[1]:

Hypofarynx: Kies een optie.

Indien andere, specificeer:

Larynx: Kies een optie.

Indien andere, specificeer:

Indien verdere uitbreiding, beschrijf:

Lateraliteit: Kies een optie.

Focaliteit: Kies een optie.

Indien multifocaal, specificeer aantal foci:

Indien niet beoordeeld kan worden, specificeer:

Tumorafmetingen: Kies een optie.

Maximale tumordimensie (in mm):

Indien niet bepaald kan worden, specificeer:

Histologisch tumortype[2]: Kies een optie.

Indien van toepassing, specificeer type:

Differentiatiegraad: Kies een optie.

Indien niet beoordeeld kan worden, specificeer:

[1] Bij tumorlokalisatie moet de locatie van de bulk (hoofdmassa) van de tumor aangeduid worden via het dropdownmenu. Indien er sprake is van uitbreiding buiten de bulk, zoals infiltratie in omliggende structuren, gelieve deze bijkomende informatie duidelijk te vermelden in het vrije tekstveld onderaan.

[2] Bij neoplasmata van kleine speekselklieren moet de optie “speekselkliercarcinoom (specificeer)” gekozen worden. Het histologische subtype kan vervolgens gespecificeerd worden volgens de lijst opgenomen in het standaardrapport “Grote speekselklieren”.

Lokale uitbreiding: Kies een optie.

*Lokale uitbreiding werd aangetoond bij **laryngeale tumor**:*

Invasie van paraglottische ruimte: Kies een optie.

Invasie van pre-epiglottische ruimte: Kies een optie.

Invasie van binnenste cortex van het kraakbeen: Kies een optie.

Invasie van volledige dikte kraakbeen: Kies een optie.

Invasie van weke delen van hals, schildklier, prevertebrale ruimte, arteria carotis of mediastinale structuren: Kies een optie.

Invasie op andere plaats dan hierboven beschreven: Kies een optie.

Indien invasie op andere plaats dan hierboven beschreven, specificeer:

*Lokale uitbreiding werd aangetoond bij **hypofaryngeale tumor**:* Kies een optie.

Indien invasie op andere plaats dan hierboven beschreven, specificeer:

Indien lokale uitbreiding niet beoordeeld kan worden, specificeer:

Lymfovasculaire invasie: Kies een optie.

Indien onderscheid tussen lymfevat- en bloedvatinvasie mogelijk, specificeer: Kies een optie.

Indien niet met zekerheid te bepalen, specificeer:

Perineurale invasie[3]: Kies een optie.

Diameter grootste aangetaste zenuwtak (in mm): Kies een optie.

Indien niet met zekerheid te bepalen, specificeer:

[3] De aan- of afwezigheid van perineurale invasie kan invloed hebben op de behandeling en prognose. Zowel intratumorale en extratumorale invasie wordt beschouwd als een positieve bevinding. Voor meer informatie, zie 'Note 8 – Perineural invasion' onderaan dit document.

Definitieve minimale tumorvrije marge invasief carcinoom (incl. eventuele naresecties en vriescoupes)[4]: Kies een optie.

Definitieve minimale tumorvrije marge (in mm):

Specificeer locatie van minimale marge, indien mogelijk:

Indien niet beoordeeld kan worden, specificeer:

Definitieve minimale vrije marge ernstige dysplasie/in situ carcinoom (incl. eventuele naresecties en vriescoupes)[4] : Kies een optie.

Definitieve minimale vrije marge (in mm):

Specificeer locatie van minimale marge, indien mogelijk:

Indien niet beoordeeld kan worden, specificeer:

pTNM classificatie (UICC TNM 8e editie met errata)[5]: pT

Kies de classificatie die van toepassing is:

Supraglottis: Kies een optie.

Glottis: Kies een optie.

Subglottis: Kies een optie.

Hypofarynx: Kies een optie.

Voorvoegsels:

m (multipele primaire tumoren): Kies een optie.

r (recidief): Kies een optie.

y (na neoadjuvante therapie): Kies een optie.

[4] De definitie van ' Definitieve minimale tumorvrije marges' is niet gestandaardiseerd, maar een minimale tumorvrije marge van 3-5 mm wordt als 'close' benoemd. De aanwezigheid van ernstige dysplasie/carcinoom in situ in het snedevlak wordt geassocieerd met een verhoogd risico op lokaal recidief en dit moet ook worden geregistreerd. Voor meer informatie, zie 'Note 9 – Margin status' onderaan dit document.

[5] De pathologische stadiëring is gebaseerd op de 'TNM Classification of Malignant Tumours' (8e editie, UICC). Een beschrijving van elke pT-categorie is beschikbaar in 'Note 11 – Pathological staging' onderaan dit document.

Scope

Het protocol is van toepassing op resectie- en biopsiestalen van invasieve epitheliale maligniteiten van de larynx en de hypofarynx, inclusief maligniteiten van het speekselkliertype die voortkomen uit kleine speekselklieren van de larynx en hypofarynx.

Opmerkingen

- Voor resecties van recidieven kan de dataset pragmatisch worden gebruikt, hoewel sommige variabelen mogelijk niet toepasbaar of te beoordelen zijn.
- Mucosaal melanoom, lymfomen en sarcomen worden in aparte datasets behandeld.
- Neuro-endocriene neoplasmen worden in een aparte dataset behandeld.
- Halsdissecties en klierexcisies worden behandeld in een aparte dataset. Deze dataset moet, indien van toepassing, in combinatie worden gebruikt.
- Wanneer er sprake is van meer dan één anatomisch of histologisch verschillende primaire tumor, moet voor elk van deze tumoren een aparte dataset worden ingevuld.

Dataset gebaseerd op

Zidar N, Bal M, Chernock RD, Dahlstrom JE, Perez-Ordonez B, Strojan P, Helliwell T, Thompson LDR (2024). *Carcinomas of the Hypopharynx, Larynx and Trachea Histopathology Reporting Guide. 2nd edition*. International Collaboration on Cancer Reporting; Sydney, Australia. ISBN: 978-1-922324-46-7.

Bijkomende informatie[6]

Note 1 – Tumour site and Tumour laterality

Accurate documentation of the laterality and site of the specimen and tumour avoids errors in the delivery of therapy. The site of the primary tumour is a key determinant in clinicopathological staging systems for hypopharynx and larynx.

For carcinomas that involve more than one site, the principal site of involvement should be recorded and coded; this may not be the site of origin. If required, the involvement of associated sites can be noted to help in further data analysis. Sites and subsites should be recorded according to the UICC nomenclature.[5,18]

Note 2 – Tumour focality

The presence of multiple or multifocal tumours is an important clue to a cancerization or field-effect phenomenon, potentiated by radiotherapy, alcohol, and various forms of tobacco use.[19-23] Multifocality is defined as separate foci of tumour in the same organ, while multicentricity is defined as multiple tumours in separate organs/sites (e.g., hypopharynx, larynx, oral cavity).[24] These designations apply to primary tumours, not metastases, and require histologic confirmation that tumour is present. In some cases, it may not be possible to determine whether there is direct extension or a new primary (hypopharynx and supraglottis).
Similarly, it may not be possible to determine whether a fragmented specimen may contain multifocal tumours. At present, there is no defining distance of intervening, normal, uninvolved mucosa between tumour sites. By inference, using 10 mm of uninvolved mucosa between invasive tumours may be a useful guide to suggest multifocality when there is more than one tumour present. Specimens should be carefully examined both macroscopically and microscopically to determine whether multiple tumours are present, as patients with multiple tumours tend to have a worse overall long-term prognosis.[25,26]

Where more than one anatomically or histologically distinct primary tumours occur, a separate dataset should be completed for each tumour.

Note 3 – Tumour dimensions

Tumour dimension is an important component in pathologic staging of the tumours of hypopharynx (core element). The macroscopic diameter (in millimetres) should be used unless the histological extent is greater than macroscopically apparent, in which case the microscopic dimension is used. As for other tissues, measurements are made pragmatically, acknowledging distortion of tissues by fixation and processing.[18,27]

Tumour dimension is not important in pathologic staging of the tumours of larynx (non-core).[18,27]

[6] Bijkomende informatie ('notes') overgenomen en aangepast vanuit
Zidar N, Bal M, Chernock RD, Dahlstrom JE, Perez-Ordonez B, Strojan P, Helliwell T, Thompson LDR (2024). Carcinomas of the Hypopharynx, Larynx and Trachea Histopathology Reporting Guide. 2nd edition. International Collaboration on Cancer Reporting; Sydney, Australia. ISBN: 978-1-922324-46-7.

Note 4 – Histological tumour type

All tumours of the hypopharynx, larynx and trachea should be given a type based on the most recent edition of the WHO Classification of Head and Neck Tumours, 5th edition, 2024 (Table 1).[5]

Histopathological type is important for cancer registration and prognosis, with strength of evidence varying for different types. Verrucous and papillary carcinomas tend to have a good prognosis while, adenosquamous carcinomas have a worse prognosis than conventional and spindle cell carcinomas. For most of the subtypes of SCC, surgery with adequate margins is the main treatment. In some malignancies, such as large cell NECs, a combination of irradiation and chemotherapy is indicated.[5,28-30]

Epithelial neuroendocrine neoplasms are classified as NETs, NECs and mixed neuroendocrine-non-neuroendocrine neoplasms (MiNEN).

Neuroendocrine tumours (NET) are separated into grades (1, 2, and 3) based on mitotic rate and Ki-67 proliferation index, but these criteria are not yet fully developed for each of the anatomic sites in the head and neck. At present, the general cutoffs are: grade 1: <2 mitoses/2 mm^2 and <2% Ki-67 proliferation index; grade 2: ≥2-10 mitoses/2 mm^2 and 2-20% Ki-67 proliferation index; and grade 3: >10 mitoses/2mm^2 and
>20% Ki-67 proliferation index.[31,32]

Further, NECs are separated into small cell NEC and large cell NEC, showing tumour necrosis, >10 mitoses/ 2 mm^2 and >20% Ki-67 proliferation index,[31,33-35] with universal Rb1 loss and common p53 overexpression.[36]

Mixed neuroendocrine-non-neuroendocrine neoplasms (MiNEN) usually consist of a poorly differentiated NEC component and a SCC or adenocarcinoma component. Immunohistochemically confirmed and morphologically distinct tumour components should be recognised and reported irrespective of their extent.

For salivary-type tumour arising from mucosal glands, please refer to the ICCR Carcinomas of the major salivary glands dataset for descriptors and ICD-O codes.[2]

Table 1: World Health Organization classification of tumours of the hypopharynx, larynx and trachea.[5]

Descriptor	**ICD-O codes[a]**
Malignant surface epithelial tumours	
Conventional squamous cell carcinoma	8070/3
Verrucous squamous cell carcinoma	8051/3
Basaloid squamous cell carcinoma	8083/3
Papillary squamous cell carcinoma	8052/3
Spindle cell squamous carcinoma	8074/3
Adenosquamous carcinoma	8560/3
Lymphoepithelial carcinoma	8082/3
Epithelial neuroendocrine neoplasms	
Small cell neuroendocrine carcinoma	8041/3

Large cell neuroendocrine carcinoma	8013/3
Carcinoma mixed with small cell neuroendocrine carcinoma[b]	8045/3
Carcinoma mixed with large cell neuroendocrine carcinoma[b]	8013/3

[a] These morphology codes are from the International Classification of Diseases for Oncology, third edition, second revision (ICD-0-3.2).[37] Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour;

/2 for carcinoma in situ and grade Ill 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.

[b] This terminology is synonymous with the ICD-O terminology of combined small/large cell neuroendocrine carcinomas.

Note 5 – Histological tumour grade

Although human papillomavirus (HPV)-associated carcinomas arising in the oropharynx are not graded (see ICCR Carcinomas of the oropharynx and nasopharynx dataset[38]), there is insufficient evidence to justify this approach in the hypopharynx and larynx. The recommendation is that HPV assessment should not be performed except for basaloid, lymphoepithelial, and papillary carcinomas. The conventional grading system for classical SCCs should be used for all tumours at these sites.[5,39-44]

Grading is based on the degree of resemblance of the carcinoma to the normal epithelium and follows the descriptions in the WHO Classification.[5] The most aggressive area is graded as well, moderately, or poorly differentiated. This system is widely used and prognostically useful, even though it suffers from inter- observer variability and sampling problems. While most SCCs will be well or moderately differentiated, it is important for prognostication to separate tumours based on differentiation. Where a tumour has a varied appearance, then the highest grade (poorest differentiation) is recorded as a core data item, while the predominant pattern may be recorded as non-core data.

Squamous cell carcinoma (SCC) subtypes (such as verrucous, basaloid, adenosquamous and spindle cell) are considered to have intrinsic biological potential and are not graded.

Still, several grading systems for each tumour type are available, with differing merits, and as such, recording which system has been applied is more clinically meaningfully (use ‘specify’ to state the system used), with the ICCR deferring to the WHO Classification current edition for grading guidance and preference.[5]

For the grading of salivary-type tumour arising from mucosal glands, please refer to the ICCR Carcinomas of the major salivary glands dataset for descriptors.[2]

Note 6 – Extent of invasion

In the larynx, the invasion of tissue compartments deep to the mucosa is important for staging. The important tissues for staging purposes are the paraglottic space, the pre-epiglottic space and the

thyroid and cricoid cartilages. One of the points of distinction between T3 and T4a carcinomas is whether cartilage invasion involves the inner cortex (partial) or outer cortex (full thickness). Further, involvement of the adjacent soft tissues, oesophagus, trachea, encasement of the carotid artery, and/or involvement of the mediastinum, are seen in advanced disease and are prognostically significant.[5,18,27,55]

In the hypopharnyx, the extent of invasion is important, too. The involvement oesophagus, thyroid/cricoid cartilage, hyoid bone, thyroid gland, central compartment soft tissue (prelaryngeal strap muscle, subcutanous fat), prevertebral fascia, carotid structures and mediastinal structures are important for staging and prognostically significant.[5]

Note 7 – Lymphovascular invasion

Reports on the prognostic value of lymphovascular invasion in laryngeal and hypopharyngeal carcinomas are variable, but some studies suggest that it is an independent indicator of poor outcome.[56-60] The consensus of the DAC was that lymphovascular invasion should be a core element.

Lymphovascular invasion is recognised by the presence of tumour cells within an endothelial-lined space and should be distinguished from retraction artefact.

Small vessel invasion includes invasion of the lymphatics, capillaries or post-capillary venules. As it is often difficult to distinguish among the types of small vessels, their invasion by tumour cells is reported as lymphovascular invasion.

Recognition of lymphovascular invasion may be difficult and subjective and can be improved by using immunohistochemistry (e.g., D2-40, CD61) and histochemical stains (e.g., elastic staining to identify venous elastic lamina) but this is not recommended in routine work. Specifically, CD61 is a marker of activation of the fibrinogen cascade, and its presence in a linear fashion on platelets in a space confirms fibrin is present, and thus genuine vascular/endothelial destruction.[61]

Cases that are still equivocal after taking additional steps may be reported as ‘indeterminate’ for lymphovascular invasion, but this designation should be sparingly used and it is useful to provide the reason in a comment in the report.

Note 8 – Perineural invasion

The presence or absence of perineural invasion should be recorded, regardless of the size of the nerve. Invasion of the perineural plane is a predictor of local recurrence and nodal metastasis and may prompt consideration of adjuvant chemoradiotherapy.[44,45,58,62-68]

The perineural plane is a potential space between the bundles of axons and the perineurium; the presence of carcinoma around a nerve (external to the perineurium) is not regarded as perineural invasion. There is currently insufficient evidence to separate it into extratumoural and intratumoural invasion though some studies suggest that extratumoural perineural invasion is more important.[63] For this dataset, either intratumoural or extratumoural invasion is regarded as a positive finding.

Note 9 – Margin status

A positive margin is usually defined by the presence of an invasive carcinoma or carcinoma in situ at margins. It is recommended that the distance from in situ or invasive carcinoma to the closest

margin is measured and reported in mm, if assessable. Margin status is a predictor of local recurrence and may require consideration of adjuvant therapy.[69-75]

The definition of a 'close margin' varies between published series, typically being regarded as between 3 and 5 mm.[76] For laser resections of glottic carcinomas even 1 mm may be adequate due to the thermal damage and shrinkage of tissue at the margin.[69,76-79]

Note 10 – Ancillary studies

For neuroendocrine neoplasms core elements are neuroendocrine markers, epithelial markers, and Ki-67 proliferation index. The diagnosis of neuroendocrine neoplasms (specifically NETs and NECs) must be confirmed immunohistochemically, with positive reaction for neuroendocrine markers (synaptophysin, chromogranin, INSM1) and for epithelial markers (pancytokeratin, cytokeratin). Furthermore, a proliferation index as determined by Ki-67 immunohistochemical analysis is recommended for grading all NETs, helping to confirm NECs, and p53 and Rb1 may be helpful in the distinction between NET and NEC, especially G3 NET from NEC.[32,80,36]

The majority of SCCs are diagnosed on the basis of morphology. Immunohistochemistry must be used only in case of poorly differentiated SCC to confirm the diagnosis (e.g., p40, CK 5/6, p63). If necessary, other malignant tumours such as melanoma and lymphomas must be excluded by the use of the appropriate immunohistochemistry. Special stains for mucin and FISH for *MAML2* rearrangement may help to diagnose mucoepidermoid carcinoma.

The literature recognises that a very few HPV-associated carcinomas may occur in the hypopharynx and larynx, but prognostic relevance is uncertain.[81] There is some evidence suggesting that HPV-associated hypopharyngeal and laryngeal carcinoma may have a better prognosis.[82-84] HPV testing may be performed, particularly in cases with basaloid, papillary, lymphoepithelial or warty morphology.[5,82,85] p16INK4a immunohistochemistry as a surrogate marker for HPV-associated carcinoma may be less reliable in the larynx than in the oropharynx.[86]

Programmed cell death-ligand 1 (PD-L1) expression has been used as predictive biomarker for checkpoint inhibitor therapy since the anti-programmed cell death-1 receptor (PD-1) antibodies, nivolumab and pembrolizumab, have been approved for the treatment of patients with recurrent and/or unresectable metastatic head and neck SCC.[87,88] It is currently advised to use antibody 22C3 and to calculate a combined positive score (CPS), defined as the number of PD-L1-positive cells (tumour cells, lymphocytes, and macrophages) divided by the total number of tumour cells × 100. PD-L1 expression is associated with an increased objective response rates in patients with CPS ≥1, with a better response with CPS ≥20.89,90 However, the lack of response in some PD-L1 positive patients clearly indicates that other factors are involved in the resistance to treatment with check-point inhibitors.[91]

Note 11 – Pathological staging

By UICC/AJCC convention,[18,27] the designation 'T' refers to a primary tumour that has not been previously treated. The symbol 'p' refers to the pathologic classification of the stage, as opposed to the clinical classification, and is based on gross and microscopic examination. pT entails a resection of the primary tumour adequate to evaluate the highest pT category, pN entails removal of nodes adequate to validate lymph node metastasis, and pM implies microscopic examination of distant lesions. There is no pathologic M0 category as this designation requires clinical evaluation and imaging. Clinical classification (cTNM) is usually carried out by the evaluating clinician before

treatment during initial evaluation of the patient or when pathologic classification is not possible.

Pathological staging is usually performed after surgical resection of the primary tumour and depends on documentation of the anatomic extent of disease, whether or not the primary tumour has been completely removed. If a biopsied tumour is not resected for any reason (e.g., when technically unfeasible) and if the highest T and N categories or the M1 category of the tumour can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied even though total removal of the primary cancer was not performed.

Primary tumour (pT)

Primary tumour: Supraglottis

T1 Tumour limited to one subsite of supraglottis with normal vocal cord mobility

T2 Tumour invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis (e.g., mucosa of base of tongue, vallecula, medial wall of piriform sinus) without fixation of the larynx

T3 Tumour limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, pre-epiglottic space, paraglottic space, and/or inner cortex of thyroid cartilage

T4a Tumour invades through the thyroid cartilage and/or invades tissues beyond the larynx, e.g., trachea, soft tissues of neck including deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), strap muscles, thyroid, or oesophagus

T4b Tumour invades prevertebral space, encases carotid artery, or mediastinal structures

Primary tumour: Glottis

T1 Tumour limited to the vocal cord(s) (may involve anterior or posterior commissure) with normal mobility

- T1a Tumour limited to one vocal cord
- T1b Tumour involves both vocal cords

T2 Tumour extends to supraglottis and/or subglottis and/or with impaired vocal cord mobility

T3 Tumour limited to the larynx with vocal cord fixation and/or invades paraglottic space, and/or inner cortex of the thyroid cartilage

T4a Tumour invades through the outer cortex of the thyroid cartilage and/or invades tissues beyond the larynx, e.g., trachea, soft tissues of neck including deep/extrinsic muscle of the tongue (genioglossus, hyoglossus, palatoglossus and styloglossus), strap muscles, thyroid, oesophagus

T4b Tumour invades prevertebral space, encases carotid artery, or mediastinal structures

Primary tumour: Subglottis

T1 Tumour limited to subglottis

T2 Tumour extends to vocal cord(s) with normal or impaired mobility

T3 Tumour limited to larynx with vocal cord fixation

T4a Tumour invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx, e.g.,

trachea, soft tissues of neck including deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus and styloglossus), strap muscles, thyroid, oesophagus

T4b Tumour invades prevertebral space, encases carotid artery, or mediastinal structures

Note that the UICC and AJCC staging differs for T3/T4a subglottic carcinomas.[18,27] In the AJCC system, T3 carcinomas include those limited to larynx with vocal cord fixation and/or invasion of paraglottic space and/or inner cortex of the thyroid cartilage.[27]

Primary tumour: Hypopharynx

T1 Tumour limited to one subsite of hypopharynx and/or 2 cm or less in greatest dimension

T2 Tumour invades more than one subsite of hypopharynx or an adj acent site, or measures more than 2 cm but not more than 4 cm in greatest dimension, without fixation of hemilarynx

T3 Tumour more than 4cm in greatest dimension, or with fixation of hemilarynx or extension to oesophageal mucosa

T4a Tumour invades any of the following: thyroid/cricoid cartilage, hyoid bone, thyroid gland, oesophagus, central compartment soft tissue

T4b Tumour invades prevertebral fascia, encases carotid artery, or invades mediastinal structures

Larynx

Normal (T1) or impaired (T2) vocal cord mobility and vocal cord fixation (T3) may only be determined clinically.

TNM Descriptors

For identification of special cases of TNM or pTNM classifications, the 'm' suffix and 'y' and 'r' prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

The 'm' suffix indicates the presence of multiple primary tumours in a single site and is recorded in parentheses: pT(m)NM.

The 'y' prefix indicates those cases in which classification is performed during or following initial multimodality therapy (i.e., neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation therapy). The cTNM or pTNM category is identified by a 'y' prefix. The ycTNM or ypTNM categorises the extent of tumour actually present at the time of that examination. The 'y' categorisation is not an estimate of tumour prior to multimodality therapy (i.e., before initiation of neoadjuvant therapy).

The 'r' prefix indicates a recurrent tumour when staged after a documented disease-free interval, and is identified by the 'r' prefix: rTNM.

For the pN classification of regional lymph nodes, see ICCR Nodal excisions and neck dissection specimens dataset.[92]

Reporting of pathological staging categories (pT, pN, pM) is based on the evidence available to the

pathologist at the time of reporting. As indicated in UICC TNM8 and AJCC TNM8,[18,27] the final stage grouping
of a patient's tumour is based on a combination of pathological staging and other clinical and imaging information.

Pathological staging should not be reported if the submitted specimen is insufficient for definitive staging, especially with biopsy samples (core needle, incisional or excisional). Staging is based on the submitted resection, and even if there is grossly residual disease or there is tumour at the margin, pT staging should only be reported on findings in the resection specimen and/or at operation.[18,27]

The reference document TNM Supplement: A commentary on uniform use, 5th Edition (C Wittekind et al. editors) may be of assistance when staging.[93]

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