APPENDIX

Identification of Primary Site *C18.1*

Histopathologic Type

| Code | Description | Code | Description |
|-------|-------------------------------------|------|---|
| 8000* | Neoplasm, malignant | 8140 | Adenocarcinoma |
| 8010* | Carcinoma, NOS | 8154 | Mixed neuroendocrine-non- |
| | | | neuroendocrine neoplasm (MiNEN) |
| 8012* | Large cell carcinoma, NOS | 8213 | Serrated dysplasia, high grade [#] |
| 8210* | Adenocarcinoma in adenomatous polyp | 8243 | Goblet cell adenocarcinoma |
| 8244* | Mixed adenoneuroendocrine carcinoma | 8246 | Neuroendocrine carcinoma (NEC) |
| 8245* | Adenocarcinoid tumor | 8480 | Low grade appendiceal mucinous |
| | | | neoplasm (LAMN) |
| 8255* | Adenocarcinoma with mixed subtypes | 8480 | High grade appendiceal mucinous |
| | | | neoplasm (HAMN) |
| 8440* | Cystadenocarcinoma, NOS | 8480 | Mucinous adenocarcinoma |
| 8481* | Mucin-producing adenocarcinoma | 8490 | Signet ring cell carcinoma/ |
| | | | adenocarcinoma |
| 8013 | Large cell neuroendocrine carcinoma | 8510 | Medullary carcinoma |
| | (NEC) | | |
| 8020 | Undifferentiated carcinoma | 8560 | Adenosquamous carcinoma |
| 8041 | Small cell neuroendocrine carcinoma | 8574 | Adenocarcinoma with neuroendocrine |
| | (NEC) | | differentiation |
| 8070 | Squamous cell carcinoma, NOS | | |

^{*}Histology is not ideal for clinical use in patient care, as it describes an unspecified or outdated diagnosis. Data collectors may use code only if there is not enough information in the medical record to document a more specific diagnosis.

^{*}This diagnosis is appropriate for certain pTis diagnoses.

Definition of Primary Tumor (T)

| T Category | T Criteria |
|------------|--|
| TX | Primary tumor cannot be assessed |
| | No evidence of primary tumor |
| Tis | Carcinoma <i>in situ</i> (intramucosal carcinoma; invasion of the lamina propria or extension into but not through the muscularis mucosae) |
| Tis(LAMN) | Low-grade appendiceal mucinous neoplasm confined to the muscularis propria; Acellular mucin or mucinous epithelium may invade into the muscularis propria T1 and T2 are not applicable to LAMN; Acellular mucin or mucinous epithelium that extends into the subserosa or serosa should be classified as T3 or T4a, respectively |
| T1 | Tumor invades the submucosa (through the muscularis mucosa but not into the muscularis propria) |
| T2 | Tumor invades the muscularis propria |
| Т3 | Tumor invades through the muscularis propria into the subserosa or the mesoappendix |
| T4 | Tumor invades the visceral peritoneum, including the acellular mucin or mucinous epithelium involving the serosa of the appendix or mesoappendix, and/or directly invades adjacent organs or structures |
| T4a | Tumor invades the visceral peritoneum, including acellular mucin or mucinous epithelium involving the serosa of the appendix or serosa of the mesoappendix |
| T4b | Tumor directly invades or adheres to adjacent organs or structures |

Definition of Regional Lymph Node (N)

| N Category | N Criteria |
|------------|---|
| NX | Regional lymph nodes cannot be assessed |
| N0 | No tumor involvement of regional lymph node(s) |
| N1 | Tumor involvement of one to three regional lymph nodes (tumor in lymph node measuring ≥ 0.2 mm) or any number of tumor deposits is present with no tumor involvement in all identifiable lymph nodes |
| N1a | Tumor involvement of one regional lymph node |
| N1b | Tumor involvement of two or three regional lymph nodes |
| N1c | No tumor involvement of regional lymph nodes, but there are tumor deposits in the subserosa or mesentery |
| N2 | Tumor involvement of four or more regional lymph nodes |

Definition of Distant Metastasis (M)

| M Category | M Criteria |
|------------|--|
| cM0 | No distant metastasis |
| cM1 | Distant metastasis |
| cM1c | Metastasis to sites other than peritoneum |
| pM1 | Microscopic confirmation of distant metastasis |
| pM1a | Intraperitoneal acellular mucin, without identifiable tumor cells in the disseminated peritoneal mucinous deposits |
| pM1b | Intraperitoneal metastasis only, including peritoneal mucinous deposits containing tumor cells |
| pM1c | Microscopic confirmation of metastasis to sites other than peritoneum |

Note: For specimens containing acellular mucin without identifiable tumor cells, efforts should be made to obtain additional tissue for thorough histologic examination to evaluate for cellularity.

Prognostic Factors Required for Stage Grouping

| G | G Definition |
|----|---------------------------|
| GX | Grade cannot be assessed |
| G1 | Well differentiated |
| G2 | Moderately differentiated |
| G3 | Poorly differentiated |

Note: In rare cases of discordance in primary and metastatic histological grade, the grade of metastatic disease is utilized for stage group assignment.

AJCC PROGNOSTIC STAGE GROUPS

| When T is | And N is | And M is | And grade is | Then the stage group is |
|------------|----------|----------|--------------|-------------------------|
| Tis | N0 | M0 | Any | 0 |
| Tis (LAMN) | N0 | M0 | Any | 0 |
| T1 | N0 | M0 | Any | I |
| T2 | N0 | M0 | Any | I |
| T3 | N0 | M0 | Any | IIA |
| T4a | N0 | M0 | Any | IIB |
| T4b | N0 | M0 | Any | IIC |
| T1 | N1 | M0 | Any | IIIA |
| T2 | N1 | M0 | Any | IIIA |
| T3 | N1 | M0 | Any | IIIB |
| T4 | N1 | M0 | Any | IIIB |
| Any T | N2 | M0 | Any | IIIC |
| Any T | Any N | M1a | Any | IVA |
| Any T | Any N | M1b | G1 | IVA |
| Any T | Any N | M1b | G2,G3, or GX | IVB |
| Any T | Any N | M1c | Any G | IVC |

References:

ANUS

Identification of Primary Site

C21.0, C21.1 and C21.8

Histopathologic Type

| Code | Description | Code | Description |
|-------|--|------|-------------------------------------|
| 8000* | Neoplasm, malignant | 8085 | Squamous cell carcinoma, HPV- |
| | | | associated |
| 8010* | Carcinoma, NOS | 8086 | Squamous cell carcinoma, HPV- |
| | | | independent |
| 8013 | Large cell neuroendocrine carcinoma | 8090 | Basal cell carcinoma |
| | (NEC) | | |
| 8020 | Undifferentiated carcinoma | 8123 | Basaloid carcinoma |
| 8032 | Spindle cell carcinoma | 8124 | Cloacogenic carcinoma |
| 8033 | Carcinoma with sarcomatoid component | 8140 | Adenocarcinoma |
| 8041 | Small cell neuroendocrine carcinoma | 8154 | Mixed neuroendocrine-non- |
| | (NEC) | | neuroendocrine neoplasm (MiNEN) |
| 8051 | Verrucous carcinoma | 8215 | Adenocarcinoma of anal glands |
| 8070 | Squamous cell carcinoma | 8244 | Mixed adenoneuroendocrine carcinoma |
| | | | (MANEC) |
| 8071 | Squamous cell carcinoma, keratinizing, | 8246 | Neuroendocrine carcinoma (NEC) |
| | NOS | | |
| 8072 | Squamous cell carcinoma, large cell, | 8480 | Mucinous adenocarcinoma |
| | non-keratinizing, NOS | | |
| 8083 | Basaloid squamous cell carcinoma | 8490 | Signet ring cell carcinoma |

^{*}Histology is not ideal for clinical use in patient care, as it describes an unspecified or outdated diagnosis. Data collectors may use code only if there is not enough information in the medical record to document a more specific diagnosis.

Definition of Primary Tumor (T)

| T Category | T Criteria |
|------------|---|
| TX | Primary tumor not assessed |
| T0 | No evidence of primary tumor |
| T1 | Tumor ≤2 cm |
| T2 | Tumor >2 cm but ≤ 5 cm |
| T3 | Tumor >5 cm |
| T4 | Tumor of any size invading adjacent organ(s), such as the vagina, urethra, or bladder |

Definition of Regional Lymph Node (N)

| N Category | N Criteria |
|------------|--|
| NX | Regional lymph nodes cannot be assessed |
| N0 | No tumor involvement of regional lymph node(s) |
| N1 | Tumor involvement of regional lymph node(s) |
| N1a | Tumor involvement of inguinal, mesorectal, superior rectal, internal iliac, or obturator lymph node(s) |
| N1b | Tumor involvement of external iliac lymph node(s) |
| N1c | Tumor involvement of N1b (external iliac) with any N1a node(s) |

Definition of Distant Metastasis (M)

| M Category | M Criteria |
|------------|--|
| сМ0 | No distant metastasis |
| cM1 | Distant metastasis |
| pM1 | Microscopic confirmation of distant metastasis |

AJCC PROGNOSTIC STAGE GROUPS

| When T is | And N is | And M is | Then the stage group is |
|-----------|----------|----------|-------------------------|
| T1 | N0 | M0 | I |
| T2 | N0 | M0 | IIA |
| T1-T2 | N1 | M0 | IIB |
| T3 | N0-N1 | M0 | IIIA |
| T4 | N0 | M0 | IIIB |
| T4 | N1 | M0 | IIIC |
| Any T | Any N | M1 | IV |

References:

BRAIN AND SPINAL CORD

Identification of Primary Site *C71.5 - C71.9*

Histopathologic Type

| Code | Description | Code | Description |
|------|--|------|--|
| 9470 | Medulloblastoma, histologically defined | 9474 | Anaplastic medulloblastoma |
| 9471 | Desmoplastic nodular medulloblastoma | 9475 | Medulloblastoma, WNT-activated |
| 9471 | Medulloblastoma with extensive nodularity | 9476 | Medulloblastoma, SHH-activated and TP53-mutant |
| 9471 | Medulloblastoma, SHH-activated and TP53-wildtype | 9477 | Medulloblastoma, non-WNT/non-SHH |
| 9474 | Large cell medulloblastoma | | |

Definition of primary Tumor (T)

There is no primary tumor (T) category.

Definition of Regional Lymph Node (N)

There is no regional lymph node (N) category.

Definition of Distant Metastasis (M)

The definitions of the M categories for **medulloblastoma** correspond to the Modified Chang system. Both systems are included for comparison.

| M Category (AJCC) | Modified Chang | M Criteria (AJCC) |
|-------------------|-------------------|---|
| cM0 | M 0 | No distant metastasis |
| cM1 | | Distant metastasis |
| cM1b | M2 | Intracranial spread beyond primary site |
| cM1c | M3 | Gross spinal subarachnoid seeding on MRI |
| cM1d | M4 | Metastasis outside CNS (bone marrow, lungs) |
| pM1 | | Microscopic confirmation of distant metastasis |
| pM1a | M1 | Microscopic confirmation of tumor cells present in CSF by cytology |
| pM1b | M2 | Microscopic confirmation of intracranial spread beyond primary site |
| pM1c | M3 | Microscopic confirmation of gross spinal subarachnoid seeding |
| pM1d | M4 | Microscopic confirmation of metastasis outside CNS (bone marrow, lungs) |

AJCC PROGNOSTIC STAGE GROUPS

No prognostic stage grouping is proposed at this time.

References:

APPENDIX

Summary of Changes:

- Per WHO Classification of Tumors 2021 corrigendum localized LAMN and HAMN represent /2 behavior codes, while any appendiceal mucinous neoplasm with extra-appendiceal spread represents a /3 behavior code.
- Goblet cell carcinoid has been replaced by **goblet cell adenocarcinoma** as per WHO classification of tumors.
- Mixed adenoneuroendocrine carcinoma has been replaced with mixed adenocarcinomaneuroendocrine carcinoma as per WHO 2019 terminology; and is considered a form of **mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN)**.

Definition of Distant Metastasis (M) (紅字增修處)

| M Category | M Criteria | |
|------------|---|--|
| cM0 | No distant metastasis | |
| cM1 | Distant metastasis | |
| cM1c | Metastasis to sites other than peritoneum | |
| pM1 | Microscopic confirmation of distant metastasis | |
| pM1a | Intraperitoneal acellular mucin, without identifiable tumor cells in | |
| | the disseminated peritoneal mucinous deposits | |
| pM1b | Intraperitoneal metastasis only, including peritoneal mucinous deposits | |
| | containing tumor cells | |
| pM1c | Microscopic confirmation of metastasis to sites other than peritoneum | |

Note: For specimens containing acellular mucin without identifiable tumor cells, efforts should be made to obtain additional tissue for thorough histologic examination to evaluate for cellularity.

References:

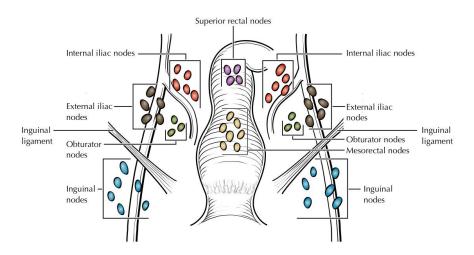
ANUS

Summary of Changes:

• Removal of **Tis** from T category and **Stage group 0** from prognostic stage groups. There are no reliable data on survival after treatment of Tis lesions. There is no routine, standard of care screening system for Tis lesions and reporting of these lesions is not reliable. Thus, in the AJCC Version 9 of the Anus Protocol, **Stage 0 has been removed**.

Of note, direct invasion of the rectal wall, perianal skin, subcutaneous tissue or the anal sphincter muscles is <u>not classified as T4</u>.

• **Obturator nodal regions** were added to the list of regional nodes. N1a is revised as metastasis in inguinal, mesorectal, **superior rectal**, internal iliac, or **obturator** lymph nodes.



AJCC PROGNOSTIC STAGE GROUPS (紅字增修處)

| When T is | And N is | And M is | Then the stage group is |
|-----------|----------|---------------|-------------------------|
| Tis | NO | M0 | 0 |
| T1 | N0 | M0 | I |
| T2 | N0 | M0 | IIA |
| T1 | N1 | M0 | HIA IIB |
| T2 | N1 | M0 | HIA IIB |
| T3 | N0 | M0 | HB IIIA |
| T3 | N1 | M0 | HIC IIIA |
| T4 | N0 | M0 | IIIB |
| T4 | N1 | M0 | IIIC |
| Any T | Any N | M1 | IV |

References:

BRAIN AND SPINAL CORD

Summary of Changes:

• An M category is not pertinent to most CNS neoplasms because of the inherent biology that favors local recurrence and regional spread, rather than metastasis outside the CNS. In some instances, spread within the CNS or outside the CNS does alter treatment plans, and this issue has been addressed in the current 9th version for **medulloblastoma** (AJCC M category for staging).

Definition of Distant Metastasis (M) for Medulloblastoma (紅字增修處)

| M Category | Modified Chang | M Criteria (AJCC) |
|------------|----------------|---|
| cM0 | M0 | No distant metastasis |
| cM1 | | Distant metastasis |
| cM1b | M2 | Intracranial spread beyond primary site |
| cM1c | M3 | Gross spinal subarachnoid seeding on MRI |
| cM1d | M4 | Metastasis outside CNS (bone marrow, lungs) |
| pM1 | | Microscopic confirmation of distant metastasis |
| pM1a | M1 | Microscopic confirmation of tumor cells present in CSF by cytology |
| pM1b | M2 | Microscopic confirmation of intracranial spread beyond primary site |
| pM1c | M3 | Microscopic confirmation of gross spinal subarachnoid seeding |
| _ | | Microscopic confirmation of metastasis outside CNS (bone |
| pM1d | M4 | marrow, lungs) |

AJCC Prognostic Stage Groups

No prognostic stage grouping is proposed at this time.

References:

附件一. AJCC Version 9 TNM 與 stage 編碼對應表、及比對第 9 版與第 8 版差異處

Neuroendocrine Tumors of the Stomach

Identification of Primary Site C16.0, C16.1, C16.2, C16.3, C16.4, C16.5, C16.6, C16.8, and C16.9

Histopathologic Type

| Code | Description | | |
|------|--|--|--|
| 8240 | Neuroendocrine tumor, NOS | | |
| 8240 | Neuroendocrine tumor, grade 1 | | |
| 8249 | Neuroendocrine tumor, grade 2 | | |
| 8249 | Neuroendocrine tumor, grade 3 | | |
| 8153 | Gastrin-producing (G-cell) neuroendocrine tumor | | |
| 8241 | Serotonin-producing enterochromaffin-cell (EC-cell) neuroendocrine tumor | | |
| 8242 | Histamine-producing enterochromaffin-like-cell (ECL-cell) neuroendocrine tumor | | |
| 8156 | Somatostatinoma, NOS (D-cell neuroendocrine tumor) | | |

Grade

| G | G Definition |
|----|--|
| GX | Grade cannot be assessed |
| G1 | Mitotic count (per 2 mm ²)* < 2 and Ki-67 index (%)** < 3 |
| G2 | Mitotic count (per 2 mm ²)* = 2-20 or Ki-67 index (%)** = 3-20 |
| G3 | Mitotic count (per 2 mm ²)* > 20 or Ki-67 index (%)** > 20 |

^{*2} mm² equals 10 high-power fields at 40x magnification and an ocular field diameter of 0.5 mm; the number of high-power field for 10 mm² is different using microscopes with different field diameter; at least 10 mm² must be evaluated in areas of highest mitotic density.

The final grade is determined by whichever (mitotic count and Ki-67 index) places the tumor in higher grade category.

^{**}MIB1 antibody; % of 500-2000 cells in areas of highest nuclear labeling.

Definition of Primary Tumor (T)

| T Category | T Criteria |
|------------|---|
| TX | Primary tumor cannot be assessed |
| ТО | No evidence of primary tumor |
| T1 | Tumor invades the mucosa or submucosa, and ≤ 1 cm in greatest dimension |
| T2 | Tumor invades the muscularis propria or > 1 cm in greatest dimension |
| Т3 | Tumor invades through the muscularis propria into subserosal tissue without penetration of overlying serosa |
| T4 | Tumor invades visceral peritoneum (serosa) or other organs or adjacent structures |

Note: Multiple tumors should be designated as such (the largest tumor should be used to assign T category):

- Use T(#); c.g., pT3(4) N0 M0, or
- Use the m suffix, T(m); e.g., pT3(m) N0 M0

Definition of Regional Lymph Node (N)

| N Category | N Criteria |
|------------|--|
| NX | Regional lymph nodes cannot be assessed |
| N0 | No tumor involvement of regional lymph node(s) |
| N1 | Tumor involvement of regional lymph node(s) |

Definition of Distant Metastasis (M)

| M Category | M Criteria |
|------------|--|
| cM0 | No distant metastasis |
| cM1 | Distant metastasis |
| cM1a | Metastasis confined to liver |
| cM1b | Metastases in at least one extrahepatic site (e.g., lung, ovary, nonregional lymph node, peritoneum, bone) |
| cM1c | Both hepatic and extrahepatic metastases |
| pM1 | Microscopic confirmation of distant metastasis |
| pM1a | Microscopic confirmation of metastasis confined to liver |
| pM1b | Microscopic confirmation of metastases in at least one extrahepatic site (e.g., lung, |
| | ovary, nonregional lymph node, peritoneum, bone) |
| pM1c | Microscopic confirmation of both hepatic and extrahepatic metastases |

AJCC Prognostic Stage Groups

| When T is | And N is | And M is | Then the stage group is |
|-----------|----------|----------|-------------------------|
| T1 | NX, NO | M0 | ı |
| T2, T3 | NO | M0 | II |
| T4 | NO | M0 | III |
| Any T | N1 | M0 | III |
| Any T | Any N | M1 | IV |

References:

Neuroendocrine Tumors of the Duodenum and Ampulla of

<u>Vater</u>

Cancers Staged Using This Staging System

This staging system applies only to **well-differentiated neuroendocrine tumors** of the duodenum and ampulla of Vater (**NET G1, G2, and G3**).

Cancers NOT Staged Using This Staging System

- Carcinomas of the ampulla of Vater, including neuroendocrine carcinoma (NEC) and mixed adenocarcinoma-neuroendocrine carcinoma should be staged according to the classification for ampulla of Vater.
- Carcinomas of the duodenum, including neuroendocrine carcinoma (NEC) and mixed adenocarcinoma-neuroendocrine carcinoma should be staged according to the classification for small intestine.
- **Neuroendocrine tumors of the small intestine including jejunum and ileum** should be staged according to the classification for **neuroendocrine tumors of the jejunum and ileum**.

Identification of Primary Site CI7.0, and C24.1

Histopathologic Type

| Code | Description |
|------|--|
| 8240 | Neuroendocrine tumor, NOS |
| 8240 | Neuroendocrine tumor, grade 1 |
| 8249 | Neuroendocrine tumor, grade 2 |
| 8249 | Neuroendocrine tumor, grade 3 |
| 8153 | Gastrinoma (G-cell neuroendocrine tumor) |
| 8156 | Somatostatinoma, NOS (D-cell neuroendocrine tumor) |
| 8241 | Enterochromaffin-cell (EC-cell) neuroendocrine tumor |
| 8683 | Composite gangliocytoma/neuroma and neuroendocrine tumor |

Grade

| G | G Definition |
|----|--|
| GX | Grade cannot be assessed |
| G1 | Mitotic count (per 2 mm ²)* < 2 and Ki-67 index (%)** < 3 |
| G2 | Mitotic count (per 2 mm ²)* = 2-20 or Ki-67 index (%)** = 3-20 |
| G3 | Mitotic count (per 2 mm ²)* > 20 or Ki-67 index (%)** > 20 |

^{*2} mm² equals 10 high-power fields at 40x magnification and an ocular field diameter of 0.5 mm; the number of high-power field for 10 mm² is different using microscopes with different field diameter; at least 10 mm² must be evaluated in areas of highest mitotic density.

The final grade is determined by whichever (mitotic count and Ki-67 index) places the tumor in higher grade category.

Definition of Primary Tumor (T)

| T Category | T Criteria |
|------------|--|
| TX | Primary tumor cannot be assessed |
| T1 | Tumor invades the mucosa or submucosa only, and is ≤ 1 c m in greatest dimension (duodenal tumors); Tumor ≤ 1 cm in greatest dimension and confined within the sphincter of Oddi (ampullary tumors) |
| Т2 | Tumor invades the muscularis propria or is > I cm in greatest dimension (duodenal tumors); Tumor invades through sphincter into duodenal submucosa or muscularis propria, or is > I cm in greatest dimension (ampullary tumors) |
| T3 | Tumor invades the pancreas or peripancreatic adipose tissue |
| T4 | Tumor invades the visceral peritoneum (serosa) or other organs |
| | |

Note: Multiple tumors should be designated as such (the largest tumor should be used to assign T category):

- Use T(#); c.g., pT3(4) N0 M0, or
- Use the m suffix, T(m); e.g., pT3(m) N0 M0

Definition of Regional Lymph Nodes (N)

| N Category | N Criteria |
|------------|--|
| NX | Regional lymph nodes cannot be assessed |
| N0 | No tumor involvement of regional lymph node(s) |
| N1 | Tumor involvement of regional lymph node(s) |

^{**}MIB1 antibody; % of 500-2000 cells in areas of highest nuclear labeling.

Definition of Distant Metastasis (M)

| M Category | M Criteria | |
|------------|---|--|
| cM0 | No distant metastasis | |
| cM1 | Distant metastasis | |
| cM1a | Metastasis confined to liver | |
| cM1b | Metastases in at least one extrahepatic site (e.g., lung, ovary, nonregional lymph | |
| | node, peritoneum, bone) | |
| cM1c | Both hepatic and extrahepatic metastases | |
| pM1 | Microscopic confirmation of distant metastasis | |
| pM1a | Microscopic confirmation of metastasis confined to liver | |
| pM1b | Microscopic confirmation of metastases in at least one extrahepatic site (e.g., lung, | |
| | ovary, nonregional lymph node, peritoneum, bone) | |
| pM1c | Microscopic confirmation of both hepatic and extrahepatic metastases | |

AJCC Prognostic Stage Groups

| 1 2 2 1 1 2 0 1 2 1 2 1 2 1 2 1 2 1 2 1 | | | |
|---|----------|----------|-------------------------|
| When T is | And N is | And M is | Then the stage group is |
| T1 | NX, NO | M0 | ı |
| T2, T3 | N0 | M0 | II |
| T4 | N0 | M0 | III |
| Any T | N1 | M0 | III |
| Any T | Any N | M1 | IV |

References:

Neuroendocrine Tumors of the Jejunum and Ileum

Cancers Staged Using This Staging System

This staging system applies only to **well-differentiated neuroendocrine tumors** of the jejunum and ileum (**NET G1, G2, and G3**).

Cancers NOT Staged Using This Staging System

- Carcinomas of the jejunum and ileum, including neuroendocrine carcinoma (NEC) and mixed adenocarcinoma-neuroendocrine carcinoma should be staged according to the classification for small intestine.
- **Neuroendocrine tumors of the duodenum (CI7.0) and ampulla of Vater (C24.1)** should be staged according to the classification for **neuroendocrine tumors of the duodenum and ampulla of Vater.**

Identification of Primary Site C17.1, C17.2, C17.8, and C17.9

Histopathologic Type

| Code | Description |
|------|--|
| 8240 | Neuroendocrine tumor, NOS |
| 8240 | Neuroendocrine tumor, grade 1 |
| 8249 | Neuroendocrine tumor, grade 2 |
| 8249 | Neuroendocrine tumor, grade 3 |
| 8241 | Enterochromaffin-cell (EC-cell) neuroendocrine tumor |

Grade

| G | G Definition |
|----|--|
| GX | Grade cannot be assessed |
| G1 | Mitotic count (per 2 mm ²)* < 2 and Ki-67 index (%)** < 3 |
| G2 | Mitotic count (per 2 mm ²)* = 2-20 or Ki-67 index (%)** = 3-20 |
| G3 | Mitotic count (per 2 mm ²)* > 20 or Ki-67 index (%)** > 20 |

^{*2} mm² equals 10 high-power fields at 40x magnification and an ocular field diameter of 0.5 mm; the number of high-power field for 10 mm² is different using microscopes with different field diameter; at least 10 mm² must be evaluated in areas of highest mitotic density.

The final grade is determined by whichever (mitotic count and Ki-67 index) places the tumor in higher grade category.

^{**}MIB1 antibody; % of 500-2000 cells in areas of highest nuclear labeling.

Definition of Primary Tumor (T)

| T Category | T Criteria |
|------------|---|
| TX | Primary tumor cannot be assessed |
| T0 | No evidence of primary tumor |
| T1 | Tumor invades the mucosa or submucosa, and ≤ 1cm in greatest dimension |
| T2 | Tumor invades the muscularis propria or > 1 cm in greatest dimension with invasion of the mucosa or submucosa |
| Т3 | Tumor invades through the muscularis propria into subserosal tissue without penetration of overlying serosa |
| T4 | Tumor invades the visceral peritoneum (serosa), or other organs or adjacent structures |

Note: Multiple tumors should be designated as such (the largest tumor should be used to assign T category):

- Use T(#); c.g., pT3(4) N0 M0, or
- Use the m suffix, T(m); e.g., pT3(m) N0 M0

Definition of Regional Lymph Node (N)

| N Category | N Criteria |
|------------|---|
| NX | Regional lymph nodes cannot be assessed |
| N0 | No tumor involvement of regional lymph node(s) |
| N1 | Tumor involvement of less than 12 regional lymph nodes |
| N2 | Tumor involvement of large mesenteric masses (> 2 cm) and/or extensive nodal deposits (12 or greater), especially those that encase the superior mesenteric vessels <i>Note</i> : Mesenteric masses ≤ 2 cm should be stated in the pathology report as being present and collected by registrars but do not affect stage. |

Definition of Distant Metastasis (M)

| M Category | M Criteria |
|------------|---|
| cM0 | No distant metastasis |
| cM1 | Distant metastasis |
| cM1a | Metastasis confined to liver |
| cM1b | Metastases in at least one extrahepatic site (e.g., lung, ovary, nonregional lymph |
| | node, peritoneum, bone) |
| cM1c | Both hepatic and extrahepatic metastases |
| pM1 | Microscopic confirmation of distant metastasis |
| pM1a | Microscopic confirmation of metastasis confined to liver |
| pM1b | Microscopic confirmation of metastases in at least one extrahepatic site (e.g., lung, |
| | ovary, nonregional lymph node, peritoneum, bone) |
| pM1c | Microscopic confirmation of both hepatic and extrahepatic metastases |

AJCC Prognostic Stage Groups

| When T is | And N is | And M is | Then the stage group is |
|-----------|----------|----------|-------------------------|
| T1 | N0 | M0 | 1 |
| T2, T3 | N0 | M0 | II |
| T4 | N0 | M0 | Ш |
| Any T | N1, N2 | M0 | III |
| Any T | Any N | M1 | IV |

References:

Neuroendocrine Tumors of the Appendix

Cancers Staged Using This Staging System

This staging system applies only to **well-differentiated neuroendocrine tumors** of the appendix (**NET G1, G2, and G3**).

Cancers NOT Staged Using This Staging System

High-grade neuroendocrine carcinoma (NEC), Goblet cell adenocarcinoma and mixed adenocarcinoma-NET/NEC should be staged according to the classification for appendix.

Identification of Primary Site

C18.1

Histopathologic Type

| Code | Description |
|------|--|
| 8240 | Neuroendocrine tumor, NOS |
| 8240 | Neuroendocrine tumor, grade 1 |
| 8249 | Neuroendocrine tumor, grade 2 |
| 8249 | Neuroendocrine tumor, grade 3 |
| 8152 | L-cell neuroendocrine tumor |
| 8152 | Glucagon-like peptide producing neuroendocrine tumor |
| 8152 | PP/PPY-producing tumor |
| 8241 | Enterochromaffin-cell (EC-cell) neuroendocrine tumor |
| 8241 | Serotonin-producing neuroendocrine tumor |

Grade (G)

| G | G Definition |
|----|--|
| GX | Grade cannot be assessed |
| G1 | Mitotic count (per 2 mm ²)* < 2 and Ki-67 index (%)** < 3 |
| G2 | Mitotic count (per 2 mm ²)* = 2-20 or Ki-67 index (%)** = 3-20 |
| G3 | Mitotic count (per 2 mm ²)* > 20 or Ki-67 index (%)** > 20 |

^{*2} mm² equals 10 high-power fields at 40x magnification and an ocular field diameter of 0.5 mm; the number of high-power field for 10 mm² is different using microscopes with different field diameter; at least 10 mm² must be evaluated in areas of highest mitotic density.

The final grade is determined by whichever (mitotic count and Ki-67 index) places the tumor in higher grade category.

^{**}MIB1 antibody; % of 500-2000 cells in areas of highest nuclear labeling.

Definition of Primary Tumor (T) (Note T)

| T Category | T Criteria |
|------------|---|
| TX | Primary tumor cannot be assessed |
| T0 | No evidence of primary tumor |
| T1 | Tumor \leq 2 cm in greatest dimension |
| T2 | Tumor > 2 cm but \leq 4 cm in greatest dimension |
| Т3 | Tumor > 4 cm in greatest dimension, or with subserosal invasion, or involvement of the mesoappendix |
| T4 | Tumor perforates the peritoneum, or directly invades other adjacent organs or structures (excluding direct mural extension to adjacent subserosa of adjacent bowel), e.g., abdominal wall and skeletal muscle |

Note: Multiple tumors should be designated as such (the largest tumor should be used to assign T category):

- Use T(#); e.g., pT3(4) N0 M0, or
- Use the m suffix, T(m); e.g., pT3(m) N0 M0

Definition of Regional Lymph Node (N) (Note N)

| N Category | N Criteria |
|------------|--|
| NX | Regional lymph nodes cannot be assessed |
| N0 | No tumor involvement of regional lymph node(s) |
| N1 | Tumor involvement of regional lymph nodes(s) |

Definition of Distant Metastasis (M) (Note M)

| M Category | M Criteria | | |
|------------|--|--|--|
| сМ0 | No distant metastasis | | |
| cM1 | Distant metastasis | | |
| cM1a | Metastasis confined to liver | | |
| cM1b | Metastases in at least one extrahepatic site (e.g., lung, ovary, nonregional lymph node, peritoneum, bone) | | |
| cM1c | Both hepatic and extrahepatic metastases | | |
| pM1 | Microscopic confirmation of distant metastasis | | |
| pM1a | Microscopic confirmation of metastasis confined to liver | | |
| pM1b | Microscopic confirmation of metastasis in at least one extrahepatic site (e.g., lung, ovary, nonregional lymph node, peritoneum, bone) | | |
| pM1c | Microscopic confirmation of both hepatic and extrahepatic metastasis | | |

AJCC Prognostic Stage Groups

| When T is | And N is | And M is | Then the stage group is |
|-----------|----------|----------|-------------------------|
| T1 | NX, NO | M0 | 1 |
| T2 | NX, NO | M0 | II |
| T3 | N0 | M0 | II |
| T4 | N0 | M0 | III |
| Any T | N1 | M0 | III |
| Any T | Any N | M1 | IV |

References:

Neuroendocrin Tumors of the Colon and Rectum

Cancers Staged Using This Staging System

This staging system applies only to **well-differentiated neuroendocrine tumors** of the colon and rectum (**NET G1, G2, and G3**).

Cancers NOT Staged Using This Staging System

Poorly differentiated neuroendocrine carcinoma (NEC) and mixed neuroendocrine non-neuroendocrine (MiNEN) neoplasms should be staged according to the classification for colon and rectum.

Identification of Primary Site C18.0, C18.2-C18.9, C19.9, and C20.9

Histopathologic Type

| Code | Description |
|------|--|
| 8240 | Neuroendocrine tumor, NOS |
| 8240 | Neuroendocrine tumor, grade 1 |
| 8249 | Neuroendocrine tumor, grade 2 |
| 8249 | Neuroendocrine tumor, grade 3 |
| 8152 | L-cell neuroendocrine tumor |
| 8152 | Glucagon-like peptide-producing neuroendocrine tumor |
| 8152 | PP/PYY-producing neuroendocrine tumor |
| 8241 | Enterochromaffin-cell (EC-cell) neuroendocrine tumor |
| 8241 | Serotonin-producing neuroendocrine tumor |

Grade (G)

| G | G Definition | |
|----|---|--|
| GX | Grade cannot be assessed | |
| G1 | Mitotic count (per 2 mm²)* < 2 and Ki-67 index (%)** < 3 | |
| G2 | Mitotic count (per 2 mm²)* = 2-20 or Ki-67 index (%)** = 3-20 | |
| G3 | Mitotic count (per 2 mm²)* > 20 or Ki-67 index (%)** > 20 | |

^{*2} mm² equals 10 high-power fields at 40x magnification and an ocular field diameter of 0.5 mm; the number of high-power field for 10 mm² is different using microscopes with different field diameter; at least 10 mm² must be evaluated in areas of highest mitotic density.

The final grade is determined by whichever (mitotic count and Ki-67 index) places the tumor in higher grade category.

^{**}MIB1 antibody; % of 500-2000 cells in areas of highest nuclear labeling.

Definition of Primary Tumor (T)

| T Category | T Criteria |
|------------|--|
| TX | Primary tumor cannot be assessed |
| T0 | No evidence of primary tumor |
| T1 | Tumor invades the mucosa or submucosa, and ≤ 2 cm in greatest dimension |
| T1a | Tumor <1 cm in greatest dimension |
| T1b | Tumor > I cm but ≤2 cm in greatest dimension |
| T2 | Tumor invades the musct1laris propria, or is > 2 cm in greatest dimension with invasion of the mucosa or submucosa |
| Т3 | Tumor invades through the muscularis propria into subserosal tissue without penetration of overlying serosa |
| T4 | Tumor invades the visceral peritoneum (serosa), or other organs or adjacent structt1res |

Note: Multiple tumors should be designated as such (the largest tumor should be used to assign T category):

- Use T(#); e.g., pT3(4) N0 M0, or
- Use the m suffix, T(m); e.g., pT3(m) N0 M0

Definition of Regional Lymph Node (N)

| N Category | N Criteria |
|------------|--|
| NX | Regional lymph nodes cannot be assessed |
| NO | No tumor involvement of regional lymph node(s) |
| N1 | Tumor involvement of regional lymph node(s) |

Definition of Distant Metastasis (M)

| M Category | M Criteria |
|------------|---|
| cM0 | No distant metastasis |
| cM1 | Distant metastasis |
| cM1a | Metastasis confined to liver |
| cM1b | Metastases in at least one extrahepatic site (e.g., lung, ovary, nonregional lymph node, peritonet1m, bone) |
| cM1c | Both hepatic and extrahepatic metastases |
| pM1 | Microscopic confirmation of distant metastasis |
| pM1a | Microscopic confirmation of metastasis confined to liver |
| pM1b | Microscopic confirmation of metastases in at least one extrahepatic site (e.g., lung, ovary, nonregional lymph node, peritonet1m, bone) |
| pM1c | Microscopic confirmation of both hepatic and extrahepatic metastases |

AJCC Prognostic Stage Groups

| When T is | And N is | And M is | Then the stage group is |
|-----------|----------|----------|-------------------------|
| T1 | NX, NO | M0 | 1 |
| T2 | N0 | M0 | IIA |
| T3 | N0 | M0 | IIB |
| T4 | N0 | M0 | IIIA |
| Any T | N1 | M0 | IIIB |
| Any T | Any N | M1 | IV |

References:

Neuroendocrine Tumors of the Pancreas

Cancers Staged Using This Staging System

This staging system applies only to **well-differentiated neuroendocrine tumors** of the pancreas (**NET G1, G2, and G3**).

Cancers NOT Staged Using This Staging System

- Carcinomas of the pancreas, including **poorly differentiated neuroendocrine carcinoma (NEC) and mixed neuroendocrine non-neuroendocrine (MiNEN) neoplasms** should be staged according to the classification for **exocrine pancreas**.
- Well-differentiated neuroendocrine tumors of the duodenum (CI7.0) or ampulla of Vater (C24.I)
 should be staged according to the classification for neuroendocrine tumors of the duodenum and
 ampulla of Vater.

Identification of Primary Site

C25.0 C25.1 C25.2 C25.4 C25.7 C25.8, and C25.9

Histopathologic Type

| Code | Description |
|------|--|
| 8240 | Neuroendocrine tumor, NOS |
| 8240 | Neuroendocrine tumor, grade 1 |
| 8249 | Neuroendocrine tumor, grade 2 |
| 8249 | Neuroendocrine tumor, grade 3 |
| 8150 | Pancreatic neuroendocrine tumor, non-functioning |
| 8151 | Insulinoma |
| 8152 | Glucagonoma |
| 8153 | Gastrinoma |
| 8155 | VIPoma |
| 8156 | Somatostatinoma |
| 8158 | ACTH-producing neuroendocrine tumor |
| 8241 | Serotonin-producing neuroendocrine tumor |
| 8272 | GH-producing neuroendocrine tumor |

This list includes histology codes and preferred terms from the WHO Classification of Tumours and the International Classification of Diseases for Oncology (ICD-0). Most of the terms in this list represent malignant behavior.

Grade (G)

| G | G Definition |
|----|--|
| GX | Grade cannot be assessed |
| G1 | Mitotic count (per 2 mm ²)* $<$ 2 and Ki-67 index (%)** $<$ 3 |
| G2 | Mitotic count (per 2 mm ²)* = 2-20 or Ki-67 index (%)** = 3-20 |
| G3 | Mitotic count (per 2 mm ²)* > 20 or Ki-67 index (%)** > 20 |

^{*2} mm² equals 10 high-power fields at 40x magnification and an ocular field diameter of 0.5 mm; the number of high-power field for 10 mm² is different using microscopes with different field diameter; at least 10 mm² must be evaluated in areas of highest mitotic density.

The final grade is determined by whichever (mitotic count and Ki-67 index) places the tumor in higher grade category.

Definition of Primary Tumor (T)

| T Category | T Criteria |
|------------|--|
| TX | Tumor cannot be assessed |
| T1 | Tumor limited to the pancreas*, \leq 2 cm in greatest dimension |
| T2 | Tumor limited to the pancreas*, > 2 cm but \leq 4 cm in greatest dimension |
| Т3 | Tumor limited to the pancreas*, > 4 cm in greatest dimension; or tumor invading the duodenum, ampulla of Vater, or common bile duct |
| Т4 | Tumor invading adjacent organs (stomach, spleen, colon, adrenal gland) or the wall of large vessels (celiac axis, superior mesenteric artery/vein, splenic artery/vein, gastroduodenal artery/vein, portal vein) |

^{*}Limited to the pancreas means there is no invasion of adjacent organs (stomach, spleen, colon, adrenal gland) or the wall of large vessels (celiac axis or the superior mesenteric artery). Extension of tumor into peripancreatic adipose tissue is NOT a basis for staging.

Note: Multiple tumors should be designated as such (the largest tumor should be used to assign T category):

- Use T(#); e.g., pT3(4) N0 M0, or
- Use the m suffix, T(m); e.g., pT3(m) N0 M0

Definition of Regional Lymph Node (N)

| N Category | N Criteria |
|------------|--|
| NX | Regional lymph nodes cannot be assessed |
| N0 | No tumor involvement of regional lymph node(s) |
| N1 | Tumor involvement of regional lymph node(s) |

^{**}MIB1 antibody; % of 500-2000 cells in areas of highest nuclear labeling.

Definition of Distant Metastasis (M)

| M Category | M Criteria | | |
|------------|---|--|--|
| cM0 | No distant metastasis | | |
| cM1 | Distant metastasis | | |
| cM1a | Metastasis confined to liver | | |
| cM1b | Metastases in at least one extrahepatic site (e.g., lung, ovary, nonregional lymph | | |
| | node, peritoneum, bone) | | |
| cM1c | Both hepatic and extrahepatic metastases | | |
| pM1 | Microscopic confirmation of distant metastasis | | |
| pM1a | Microscopic confirmation of metastasis confined to liver | | |
| pM1b | Microscopic confirmation of metastases in at least one extrahepatic site (e.g., lung, | | |
| | ovary, nonregional lymph node, peritoneum, bone) | | |
| pM1c | Microscopic confirmation of both hepatic and extrahepatic metastases | | |

AJCC Prognostic Stage Groups

| , nee : 10811001110 011100 | | | | |
|----------------------------|----------|----------|-------------------------|--|
| When T is | And N is | And M is | Then the stage group is | |
| T1 | N0 | M0 | 1 | |
| T2, T3 | N0 | M0 | II | |
| T4 | N0 | M0 | III | |
| Any T | N1 | M0 | III | |
| Any T | Any N | M1 | IV | |

References:

<u>Vulva</u>

Identification of Primary Site C51.0, C51.1, C51.2, C51.8 and C51.9

Histopathologic Type

| Code | Description | | |
|-------------------|--|--|--|
| 8085 | Squamous cell carcinoma, HPV-associated | | |
| 8086 | Squamous cell carcinoma, HPV-independent | | |
| 8070 | Squamous cell carcinoma, NOS | | |
| 8090 | Basal cell carcinoma, NOS | | |
| 9020 | Phyllodes tumor, malignant | | |
| 8500 | Adenocarcinoma of anogenital mammary-like glands | | |
| 8200 | Adenoid cystic carcinoma | | |
| 8020 | Carcinoma, poorly differentiated, NOS | | |
| 8560 | Adenosquamous carcinoma | | |
| 8240 | Neuroendocrine tumor, NOS | | |
| 8249 | Neuroendocrine tumor, grade 2 | | |
| 8041 | Small cell neuroendocrine carcinoma | | |
| 8982 | Myoepithelial carcinoma | | |
| 8562 | Epithelial-myoepithelial carcinoma | | |
| 8542 | Paget disease, extramammary | | |
| 8400 | Sweat gland adenocarcinoma | | |
| 8401 | Apocrine adenocarcinoma | | |
| 8413 | Eccrine adenocarcinoma | | |
| 8409 | Porocarcinoma, NOS | | |
| 8144 | Adenocarcinoma, intestinal type | | |
| 9064 | Germ cell tumor, NOS | | |
| 9071 | Yolk sac tumor, NOS | | |
| 8000 [*] | Neoplasm, malignant | | |
| 8010* | Carcinoma, NOS | | |
| 8140* | Adenocarcinoma, NOS | | |
| 8051* | Squamous cell carcinoma, verrucous | | |
| 8054* | Squamous cell carcinoma, warty | | |
| 8071* | Squamous cell carcinoma, keratinizing | | |
| 8072* | Squamous cell carcinoma, non-keratinizing | | |
| 8076* | Squamous cell carcinoma, micro invasive | | |
| 8083* | Squamous cell carcinoma, basaloid | | |
| 8097* | Basal cell carcinoma, nodular | | |

Definition of Primary Tumor (T)

| T Category | FIGO Stage | T Criteria | |
|------------|---------------|---|--|
| TX | | Primary tumor cannot be assessed | |
| Т0 | | No evidence of primary tumor | |
| T1 | 1 | Tumor confined to the vulva | |
| T1a | IA | Tumor size <= 2 cm in greatest dimension and stromal invasion <=1 mm Note: Depth of invasion is measured from the basement membrane of the deepest adjacent tumor-free rete ridge to the deepest point of invasion. | |
| T1b | IB | Tumor size> 2 cm in greatest dimension or stromal invasion > 1 mm Note: Depth of invasion is measured from the basement membrane of the deepest adjacent tumor-free rete ridge to the deepest point of invasion. | |
| T2 | II | Tumor of any size with extension to lower 1/3 of urethra, lower 1/3 of vagina, or anus | |
| Т3 | IIIA | Tumor of any size with disease extension to upper 2/3 of urethra, upper 2/3 of vagina, bladder mucosa, rectal mucosa | |
| T4 | IVA | Tumor fixed to pelvic bone | |

Definition of Regional Lymph Node (N)

| N Category | FIGO Stage | N Criteria | |
|------------|---------------|--|--|
| NX | | Regional lymph nodes cannot be assessed | |
| N0 | | No regional lymph node metastasis | |
| N0(i+) | | Isolated tumor cells in regional lymph node(s) <= 0.2 mm, or single cells or clusters of cells <= 200 cells in a single lymph node cross-section | |
| N1 | Ш | Tumor involvement of non-fixed, non-ulcerated regional lymph nodes | |
| N1mi | IIIA | Tumor involvement > 0.2 mm but <= 2.0 mm in diameter of regional lymph nodes | |
| N1a | IIIA | Tumor involvement > 2.0 mm but <= 5mm of regional lymph nodes | |
| N1b | IIIB | Tumor involvement > 5 mm of regional lymph nodes | |
| N1c | IIIC | Tumor involvement of regional lymph nodes with extranodal extension (ENE) | |
| N2 | IVA | Tumor involvement of fixed or ulcerated regional lymph nodes | |

^{*} Histology is not ideal for clinical use in patient care, as it describes an unspecified or outdated diagnosis. Data collectors may use this code only if there is not enough information in the medical record to document a more specific diagnosis.

Definition of Distant Metastasis (M)

| M Category | FIGO Stage | M Criteria |
|------------|---------------|--|
| cM0 | | No distant metastasis |
| cM1 | IVB | Distant metastasis |
| pM1 | IVB | Microscopic confirmation of distant metastasis |

AJCC Prognostic Stage Groups

| When T is | And N is | And M is | Then the stage group is |
|-----------|-----------|----------|-------------------------|
| T1 | N0 | MO | 1 |
| T1a | N0 | MO | IA |
| T1b | N0 | MO | IB |
| T2 | N0 | MO | II |
| TX-T3 | N1 | MO | III |
| T3 | N0 | MO | IIIA |
| TX-T3 | N1mi, N1a | MO | IIIA |
| TX-T3 | N1b | MO | IIIB |
| TX-T3 | N1c | M0 | IIIC |
| T4 | Any N | MO | IVA |
| Any T | N2 | MO | IVA |
| Any T | Any N | M1 | IVB |

References:

Neuroendocrine Tumors of the Stomach

Summary of Changes:

- Histopathologic type updated according to the WHO Classification of Tumors, 5th Ed.
- New section on modalities and imaging used for diagnosis and staging.
- New table describing diagnostic workup.
- New table describing pathological staging with endoscopic resection highlighted as a surgical specimen.
- TINXMO has been added to stage I.
- Removed chromogranin A and added types of gastric neuroendocrine tumor.
- Non-tumor factors have been added.
- Clinical history of proton pump inhibitor use has been added.

Definition of Primary Tumor (T) (紅字增修處)

| T Category | T Criteria | | |
|------------|---|--|--|
| TX | Primary tumor cannot be assessed | | |
| ТО | No evidence of primary tumor | | |
| T1 | Tumor invades the lamina propria mucosa or submucosa, and ≤ 1 cm in greatest dimension | | |
| T2 | Tumor invades the muscularis propria or > 1 cm in greatest dimension | | |
| Т3 | Tumor invades through the muscularis propria into subserosal tissue without penetration of overlying serosa | | |
| T4 | Tumor invades visceral peritoneum (serosa) or other organs or adjacent structures | | |

Note: Multiple tumors should be designated as such (the largest tumor should be used to assign T category):

- Use T(#); c.g., pT3(4) N0 M0, or
- Use the m suffix, T(m); e.g., pT3(m) N0 M0

Definition of Distant Metastasis (M) (紅字增修處)

| M Category | M Criteria | | | |
|------------|--|--|--|--|
| cM0 | No distant metastasis | | | |
| cM1 | Distant metastasis | | | |
| cM1a | Metastasis confined to liver | | | |
| cM1b | Metastases in at least one extrahepatic site (e.g., lung, ovary, nonregional lymph | | | |
| | node, peritoneum, bone) | | | |
| cM1c | Both hepatic and extrahepatic metastases | | | |
| pM1 | Microscopic confirmation of distant metastasis | | | |
| pM1a | Microscopic confirmation of metastasis confined to liver | | | |
| pM1b | Microscopic confirmation of metastases in at least one extrahepatic site (e.g., | | | |
| | lung, ovary, nonregional lymph node, peritoneum, bone) | | | |
| pM1c | Microscopic confirmation of both hepatic and extrahepatic metastases | | | |

AJCC Prognostic Stage Groups (紅字增修處)

| When T is | And N is | And M is | Then the stage group is |
|-----------|----------|----------|-------------------------|
| T1 | NX, NO | M0 | I |
| T2, T3 | N0 | M0 | II |
| T4 | N0 | M0 | III |
| Any T | N1 | M0 | III |
| Any T | Any N | M1 | IV |

References:

Neuroendocrine Tumors of the Duodenum and Ampulla of

Vater

Summary of Changes:

- Histopathologic type updated according to the WHO Classification of Tumors, 5th Ed.
- New section on modalities and imaging used for diagnosis and staging highlight endoscopic management for small duodenal NETs.
- New section highlights endoscopic resection.
- TINXMO has been added to stage I to reflect lesions undergoing endoscopic resection.
- Associated genetic syndrome and chromogranin A have been removed.
- Non-tumor factors have been added.

Definition of Primary Tumor (T) (紅字增修處)

| T Category | T Criteria |
|------------|--|
| TX | Primary tumor cannot be assessed |
| T1 | Tumor invades the mucosa or submucosa only and is≦1 c m in greatest dimension (duodenal tumors); |
| | Tumor≤ I cm in greatest dimension and confined within the sphincter of Oddi (ampullary tumors) |
| T2 | Tumor invades the muscularis propria or is > I cm in greatest dimension (duodenal tumors); |
| | Tumor invades through sphincter into duodenal submucosa or muscularis propria, |
| | or is > I cm in greatest dimension (ampullary tumors) |
| T3 | Tumor invades the pancreas or peripancreatic adipose tissue |
| T4 | Tumor invades the visceral peritoneum (serosa) or other organs |

Note: Multiple tumors should be designated as such (the largest tumor should be used to assign T category):

- Use T(#); c.g., pT3(4) N0 M0, or
- Use the m suffix, T(m); e.g., pT3(m) N0 M0

Definition of Distant Metastasis (M) (紅字增修處)

| M Category | M Criteria |
|------------|--|
| cM0 | No distant metastasis |
| cM1 | Distant metastasis |
| cM1a | Metastasis confined to liver |
| cM1b | Metastases in at least one extrahepatic site (e.g., lung, ovary, nonregional lymph node, peritoneum, bone) |
| cM1c | Both hepatic and extrahepatic metastases |
| pM1 | Microscopic confirmation of distant metastasis |
| pM1a | Microscopic confirmation of metastasis confined to liver |
| pM1b | Microscopic confirmation of metastases in at least one extrahepatic site (e.g., |
| | lung, ovary, nonregional lymph node, peritoneum, bone) |
| pM1c | Microscopic confirmation of both hepatic and extrahepatic metastases |

AJCC Prognostic Stage Groups (紅字增修處)

| When T is | And N is | And M is | Then the stage group is |
|-----------|----------|----------|-------------------------|
| TI | NX, NO | M0 | I |
| T2, T3 | N0 | M0 | II |
| T4 | N0 | M0 | Ш |
| AnyT | N1 | M0 | III |
| AnyT | Any N | M1 | IV |

References:

Neuroendocrine Tumors of the Jejunum and Ileum

Summary of Changes:

- Included tumors overlapping the jejunum and ileum as well as small intestine, NOS.
- Histopathologic type updated according to the WHO Classification of Tumors, 5th Ed.
- New section on modalities used for diagnosis and staging
- Deleted chromogranin A, plasma pancreastatin and plasma serotonin level; added mesenteric fibrosis.
- Included age and patient comorbidities unrelated to the NET.
- Included somatostatin receptor type 2 positivity.

Definition of Primary Tumor (T) (紅字增修處)

| T Category | T Criteria |
|------------|--|
| TX | Primary tumor cannot be assessed |
| TO | No evidence of primary tumor |
| T1 | Tumor invades lamina propria the mucosa or submucosa, and less than or equal |
| | tol cm in size ≤ 1cm in greatest dimension |
| T2 | Tumor invades the muscularis propria or greater than 1 cm in size > 1 cm in greatest |
| | dimension with invasion of the mucosa or submucosa |
| Т3 | Tumor invades through the muscularis propria into subserosal tissue without |
| | penetration of overlying serosa |
| T4 | Tumor invades visceral peritoneum (serosal) or other organs or adjacent structures |

Note: Multiple tumors should be designated as such (the largest tumor should be used to assign T category):

- Use T(#); c.g., pT3(4) N0 M0, or
- Use the *m* suffix, T(m); e.g., pT3(m) N0 M0

Definition of Regional Lymph Node (N) (紅字增修處)

| N Category | N Criteria | |
|------------|---|--|
| NX | Regional lymph nodes cannot be assessed | |
| N0 | No tumor involvement of regional lymph node(s) | |
| N1 | Tumor involvement of less than 12 regional lymph nodes | |
| N2 | Tumor involvement of large mesenteric masses(> 2 cm) and/or extensive nodal deposits (12 or greater), especially those that encase the superior mesenteric vessels Note: Mesenteric masses ≤ 2 cm should be stated in the pathology report as being present and collected by registrars but do not affect stage. | |

Definition of Distant Metastasis (M) (紅字增修處)

| M Category | M Criteria |
|------------|--|
| cM0 | No distant metastasis |
| cM1 | Distant metastasis |
| cM1a | Metastasis confined to liver |
| cM1b | Metastases in at least one extrahepatic site (e.g., lung, ovary, nonregional lymph |
| | node, peritoneum, bone) |
| cM1c | Both hepatic and extrahepatic metastases |
| pM1 | Microscopic confirmation of distant metastasis |
| pM1a | Microscopic confirmation of metastasis confined to liver |
| pM1b | Microscopic confirmation of metastases in at least one extrahepatic site (e.g., |
| | lung, ovary, nonregional lymph node, peritoneum, bone) |
| pM1c | Microscopic confirmation of both hepatic and extrahepatic metastases |

References:

Neuroendocrine Tumors of the Appendix

Summary of Changes:

- Histopathologic Type updated according to WHO Classification of Tumors, 5th Ed.
- New section on modalities used for diagnosis and staging
- Included age and patient comorbidities unrelated to the NET.
- Included somatostatin receptor type 2 positivity.
- Discussed against routine use of chromogranin A and added data on emerging prognostic tools: PPQ and Clinical Score.
- T1NXM0 has been added to Stage I, and T2NXM0 has been added to Stage II.

Definition of Distant Metastasis (M) (紅字增修處)

| M Category | M Criteria | |
|------------|--|--|
| cM0 | No distant metastasis | |
| cM1 | Distant metastasis | |
| cM1a | Metastasis confined to liver | |
| cM1b | Metastases in at least one extrahepatic site (e.g., lung, ovary, nonregional lymph | |
| | node, peritoneum, bone) | |
| cM1c | Both hepatic and extrahepatic metastases | |
| pM1 | Microscopic confirmation of distant metastasis | |
| pM1a | Microscopic confirmation of metastasis confined to liver | |
| pM1b | Microscopic confirmation of metastasis in at least one extrahepatic site (e.g., | |
| | lung, ovary, nonregional lymph node, peritoneum, bone) | |
| pM1c | Microscopic confirmation of metastasis to sites other than peritoneum | |

AJCC Prognostic Stage Groups (紅字增修處)

| When T is | And N is | And M is | Then the stage group is |
|-----------|----------|----------|-------------------------|
| T1 | NX, NO | M0 | 1 |
| T2 | NX, NO | M0 | II |
| T3 | N0 | M0 | II |
| T4 | N0 | M0 | III |
| Any T | N1 | M0 | III |
| Any T | Any N | M1 | IV |

References:

Neuroendocrine Tumors of the Colon and Rectum

Summary of Changes:

- T1NXM0 has been added to Stage I.
- New section on modalities and imaging used for diagnosis and staging.
- New table describing diagnostic workup.
- New table describing pathological staging with information provided by the pathologist and staging by the managing physician.
- New section with staging rules for common staging scenarios.
- Updated prognostic tumor characteristics and added non-tumor factors.

Definition of Primary Tumor (T) (紅字增修處)

| T Category | T Criteria |
|------------|--|
| TX | Primary tumor cannot be assessed |
| TO | No evidence of primary tumor |
| T1 | Tumor invades the mucosa or submucosa, and ≤2 cm in greatest dimension |
| T1a | Tumor <1 cm in greatest dimension |
| T1b | Tumor > I cm but ≤2 cm in greatest dimension |
| T2 | Tumor invades the musct1laris propria, or is > 2 cm in greatest dimension with |
| | invasion of the mucosa or submucosa |
| T3 | Tumor invades through the muscularis propria into subserosal tissue without |
| | penetration of overlying serosa |
| T4 | Tumor invades the visceral peritoneum (serosa), or other organs or adjacent |
| | structt1res |

Note: Multiple tumors should be designated as such (the largest tumor should be used to assign T category):

- Use T(#); e.g., pT3(4) N0 M0, or
- Use the m suffix, T(m); e.g., pT3(m) N0 M0

Definition of Distant Metastasis (M) (紅字增修處)

| M Category | M Criteria |
|------------|--|
| cM0 | No distant metastasis |
| cM1 | Distant metastasis |
| cM1a | Metastasis confined to liver |
| cM1b | Metastases in at least one extrahepatic site (e.g., lung, ovary, nonregional lymph |
| | node, peritonet1m, bone) |
| cM1c | Both hepatic and extrahepatic metastases |
| pM1 | Microscopic confirmation of distant metastasis |
| pM1a | Microscopic confirmation of metastasis confined to liver |
| pM1b | Microscopic confirmation of metastases in at least one extrahepatic site |
| | (e.g.,lung, ovary, nonregional lymph node, peritonet1m, bone) |
| pM1c | Microscopic confirmation of both hepatic and extrahepatic metastases |

AJCC Prognostic Stage Groups (紅字增修處)

| When T is | And N is | And M is | Then the stage group is |
|-----------|----------|----------|-------------------------|
| T1 | NX, NO | M0 | 1 |
| T2 | N0 | M0 | IIA |
| T3 | N0 | M0 | IIB |
| T4 | N0 | M0 | IIIA |
| Any T | N1 | M0 | IIIB |
| Any T | Any N | M1 | IV |

References:

Neuroendocrine Tumors of the Pancreas

Summary of Changes:

- Histopathologic type updated according to the WHO Classification of Tumors, 5th Ed.
- Included *DAXX/ATRX*, *ARX* and *PDX1* as potential biomarkers and several clinicopathologic factors for non-tumor factors.

| Prognostic Tumor Characteristics | Non-Tumor Factors |
|----------------------------------|--|
| 1. Mitotic count | 1. Age |
| 2. Ki-67 index | 2. Family history of cancer |
| 3. Associated genetic syndrome | 3. Smoking |
| 4. Chomogranin A (CgA) | 4. Alcohol consumption |
| 5. Functionality | 5. Increased body mass index |
| 6. DAXX/ATRXst | 6. Diabetes |
| 7. ARX, PDXI expression | 7. MEN1 and other rarer heritable gene conditions |
| | (neurofibromatosis type I, Cowden syndrome, tuberous |
| | sclerosis, von Rippel-Lindau syndrome) |

- Included DOTA PET scans in imaging used for diagnosis and the new clinical staging and workup table.
- Introduction discussed latest epidemiological data and treatment options including PRRT, capecitabine in combination with temozolomide (chemotherapy regimens).

Definition of Distant Metastasis (M) (紅字增修處)

| M Category | M Criteria | | |
|------------|--|--|--|
| cM0 | No distant metastasis | | |
| cM1 | Distant metastasis | | |
| cM1a | Metastasis confined to liver | | |
| cM1b | Metastases in at least one extrahepatic site (e.g., lung, ovary, nonregional lymph | | |
| | node, peritoneum, bone) | | |
| cM1c | Both hepatic and extrahepatic metastases | | |
| pM1 | Microscopic confirmation of distant metastasis | | |
| pM1a | Microscopic confirmation of metastasis confined to liver | | |
| pM1b | Microscopic confirmation of metastases in at least one extrahepatic site (e.g., | | |
| | lung, ovary, nonregional lymph node, peritoneum, bone) | | |
| pM1c | Microscopic confirmation of both hepatic and extrahepatic metastases | | |

References:

Vulva

Summary of Changes:

- New definition of depth of invasion measurement.
 Depth of invasion is measured from the basement membrane of the deepest adjacent tumor-free rete ridge to the deepest point of invasion.
- New T category, T4-Tumor fixed to pelvic bone.
- N category is reduced from 3 (NI-N3) categories to 2 categories (NI-N2).
- Imaging findings are allowed to be incorporated into T, N and M categories.

Definition of primary Tumor (T) (紅字增修處)

| T Category | FIGO | T Criteria | | | |
|------------|--|---|--|--|--|
| | Stage | | | | |
| TX | | Primary tumor cannot be assessed | | | |
| T0 | | No evidence of primary tumor | | | |
| T1 I | | Tumor confined to the vulva and/or perineum | | | |
| | | Multifocal lesions should be designated as such. The largest lesion or the | | | |
| | | lesion with the greatest depth of invasion will be the target lesion | | | |
| | | identified to address the highest pT stage. | | | |
| | | Depth of invasion is defined as the measurement of the tumor from the | | | |
| | | epithelial stromal junction of the adjacent most superficial dermal | | | |
| | | papilla to the deepest point of invasion | | | |
| T1a | IA | Tumor size Lesions 2 cm or less, confined to the vulva and/or perineum, | | | |
| | | and with stromal invasion of 1.0 mm or less | | | |
| | | Note: Depth of invasion is measured from the basement membrane of | | | |
| | | the deepest adjacent tumor-free rete ridge to the deepest point of invasion. | | | |
| | | Tumor size Lesions more than 2 cm, or any size with stromal invasion of | | | |
| 110 | | more than 1.0 mm, confined to the vulva and/or perineum | | | |
| | | Note: Depth of invasion is measured from the basement membrane of | | | |
| | | the deepest adjacent tumor-free rete ridge to the deepest point of | | | |
| | | invasion. | | | |
| T2 | II Tumor of any size with extension to adjacent perineal | | | | |
| | | (lower /distal third 1/3 of the urethra, lower /distal third 1/3 of the vagin | | | |
| | | or anus anal involvement) | | | |
| T3 | IIIA | Tumor of any size with disease extension to any of the following— | | | |
| | IVA | upper /proximal two thirds 2/3 of the urethra, upper /proximal two thirds | | | |
| | | 2/3 of the vagina, bladder mucosa, or rectal mucosa—or fixed to the | | | |
| | | pelvic bone | | | |
| T4 | IVA | Tumor fixed to pelvic bone | | | |

Definition of Regional Lymph Node (N) (紅字增修處)

| N Category | FIGO | N Criteria | | | |
|------------------|-------|---|--|--|--|
| | Stage | | | | |
| NX | | Regional lymph nodes cannot be assessed | | | |
| N0 | | No regional lymph node metastasis | | | |
| N0(i+) | | Isolated tumor cells in regional lymph node(s) no greater than 0.2 mm, or single cells or clusters of cells <= 200 cells in a single lymph node cross-section | | | |
| N1 | III | Tumor involvement of non-fixed, non-ulcerated regional lymph nodes Regional lymph node metastasis with one or two lymph node metastases each less than 5 mm, or one lymph node metastasis greater than or equal to 5 mm | | | |
| N1mi | IIIA | Tumor involvement > 0.2 mm but <= 2.0 mm in diameter of regional lymph nodes | | | |
| N1a* | IIIA | Tumor involvement > 2.0 mm but <= 5mm of regional lymph nodes One or two lymph node metastases each less than 5mm | | | |
| N1b | IIIB | Tumor involvement > 5 mm of regional lymph nodes | | | |
| | HIA | One lymph node metastasis greater than or equal to 5 mm | | | |
| N1c | IIIC | Tumor involvement of regional lymph nodes with extranodal extension (ENE) | | | |
| N2 | IVA | Tumor involvement of fixed or ulcerated regional lymph nodes Regional lymph node metastasis with three or more lymph node metastases each less than 5 mm, or two or more lymph node metastases greater than or equal to 5 mm, or lymph node(s) with extranodal extension | | | |
| N2a * | HIB | Three or more lymph node metastases each less than 5 mm | | | |
| N2b | HIB | Two or more lymph node metastases greater than or equal to 5 mm | | | |
| N2c | HIC | Lymph node(s) with extranodal extension | | | |
| N3 | IVA | Fixed or ulcerated regional lymph node metastasis | | | |

^{*}Includes micrometastasis, N1mi and N2mi.

Definition of Distant Metastasis (M) (紅字增修處)

| | • | | | | | |
|------------|---|--|--|--|--|--|
| M Category | FIGO | M Criteria | | | | |
| | Stage | | | | | |
| cM0 | | No distant metastasis (no pathological M0; use clinical M to complet | | | | |
| | | stage group) | | | | |
| cM1 | IVB | Distant metastasis (including pelvic lymph node metastasis) | | | | |
| pM1 | IVB | Microscopic confirmation of distant metastasis | | | | |

AJCC Prognostic Stage Groups (紅字增修處)

| When T is | And N is | And M is | Then the stage group is |
|------------------------|------------------------|----------|-------------------------|
| T1 | N0 | M0 | 1 |
| T1a | N0 | M0 | IA |
| T1b | N0 | M0 | IB |
| T2 | N0 | M0 | II |
| TX-T3 T1-T2 | N1 -N2c | M0 | III |
| T3 | NO | M0 | IIIA |
| TX-T3 T1 T2 | N1mi, N1a | M0 | IIIA |
| TX-T3 T1-T2 | N1b N2a,N2b | M0 | IIIB |
| TX-T3 T1-T2 | N1c N2c | M0 | IIIC |
| T1 T3 | N3 | M0 M1 | ₩ |
| T4 T1-T2 | Any N N3 | M0 | IVA |
| Any T T3 | N2 Any N | M0 | IVA |
| Any T | Any N | M1 | IVB |

References: