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Tumor Markers Indications

Adjudication Guideline

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Approved by:
Daman

Responsible:
Medical Standards & Research

Related Adjudication Guidelines:
None

Abstract

For Members

Tumour markers also known as biomarkers are proteins mostly produced by cancer or by other cells of the body in response to cancer or certain benign (non-cancerous) conditions. They are produced at higher levels in cancerous cases. These are found in blood, urine, stool, tumour tissue or other tissues or other bodily fluids. More than 20 tumour markers have been developed for clinical use.

Daman covers tumour markers if medically justified as per the best international medical practice and as per the policy terms and conditions of each Health Insurance Plan administered by Daman.

For Medical Professionals

The various tumour markers differ in their usefulness for screening, diagnosis, prognosis, assessing therapeutic response, and detecting recurrence.

As no tumour marker (except PSA) is proved to be ideal to be highly specific and sensitive, so they cannot be constructed as primary for the diagnosis of cancer. The main use of tumour marker in clinical medicine is as a supportive laboratory test for diagnosis or in follow up of a patient being treated for malignancy.

Daman covers the tumour markers for cancer management if medically necessary, for all plans administered by Daman as per the policy terms and conditions of each plan.

Tumor Markers Indications

Scope

This guideline emphasises on the indications and coverage of the given tumour markers for all the health insurance plans administered by Daman both as per the policy terms and conditions and as per the international best practice.

Adjudication Policy

Eligibility / Coverage Criteria

Tumour markers are covered as per best clinical practice and as per the plan wise coverage criteria for all health insurance plans administered by Daman.

1. **Clinical indications for acceptable tumor markers:**

Tumor Markers	Clinical Indications	Suggested Roles
Alpha-fetoprotein (AFP)	Hepatocellular carcinoma and testicular germ cell tumour.	To diagnose liver cancer and follow response to treatment; to assess stage, prognosis, and response to treatment of germ cell tumour.
Anaplastic Lymphoma Kinase (ALK gene)	Non-small cell lung cancer (NSCLC) and anaplastic large cell lymphoma	To determine treatment and prognosis.
Beta-2-microglobulin (B2M)	Multiple myeloma, chronic lymphocytic leukaemia, and some lymphomas.	To determine prognosis and follow response to treatment.
Beta-human chorionic gonadotropin (Beta-hCG)	Choriocarcinoma and testicular germ cell tumour	To assess stage, prognosis, response to treatment.
BCR-ABL fusion gene (Philadelphia chromosome)	Chronic Myeloid Leukaemia, Acute Lymphoblastic leukaemia, Acute Myelogenous leukaemia.	To confirm diagnosis, predict response to targeted therapy, monitor disease.
Bladder Tumour Ag (BTA)	Bladder cancer, cancer of kidneys and ureters.	Follow up treatment for bladder cancer or, monitoring for eradication of bladder cancer or, recurrences after eradication.
C-Kit / CD117	Gastrointestinal stromal tumour, Mucosal melanoma.	To diagnose and determine treatment.
CA-15-3 / CA27.29	Breast Cancer	For **screening***, treatment effectiveness or recurrence.
CA 19-9	Pancreatic cancer(Gold standard), gallbladder cancer, bile duct cancer, gastric cancer	To determine treatment effectiveness.
CA-125	Ovarian cancer	To help diagnose, response to treatment, recurrence.
Calcitonin	Medullary thyroid cancer	To diagnose, treatment effectiveness, recurrence.
Carcinoembryonic antigen (CEA)	Colorectal cancer	For treatment effectiveness or recurrence.
Chromogranin A (CgA)	Neuroendocrine tumour	To help in diagnosis, assessment of treatment response, and evaluation of recurrence.
Cytokeratin fragment 21-1	Lung cancer	To help in monitoring for recurrence.
Epidermal growth factor receptor (EGFR)	Non-small cell lung cancer (NSCLC)	To help determine treatment and prognosis.
Oestrogen receptor (ER)/progesterone receptor (PR)	Breast cancer	To determine whether treatment with hormone therapy and some targeted therapies is appropriate.
Fibrin/fibrinogen	Bladder cancer	To monitor progression and response to treatment.
Human Epididymis Protein 4 (HE4)	Ovarian cancer	To plan cancer treatment, assess disease progression, and monitor for recurrence **but not for screening.**

human epidermal growth factor receptor (HER2/neu)	Breast cancer, gastric cancer, and gastro esophageal junction adenocarcinoma.	To determine whether treatment with certain targeted therapies is appropriate.
Immunoglobulins	Multiple myeloma and Waldenström macroglobulinemia	To help diagnose disease, assess response to treatment, and look for recurrence.
Lactate dehydrogenase (LDH)	Testicular germ cell tumors, lymphoma, leukemia, melanoma, and neuroblastoma	To assess stage, prognosis, and response to treatment.
Myeloperoxidase (MPO)	Acute Myeloid Leukemia	Diagnosis of AML.
Prostate-specific antigen (PSA)	Prostate cancer	To help in **screening****, diagnosis, assess response to treatment, and look for recurrence
Placental Alkaline Phosphatase (PLAP)	Metastatic germ cell tumors	To diagnose germ cell seminoma and non-seminoma germ cell tumors.
Thyroglobulin	Thyroid cancer	To evaluate response to treatment and look for recurrence
Urokinase plasminogen activator (uPA) and plasminogen activator inhibitor (PAI-1)	Breast cancer	To determine aggressiveness of cancer and guide treatment
UroVysion	Bladder Cancer	Follow up treatment for bladder cancer or, monitoring for eradication of bladder cancer or, recurrences after eradication.
5-Protein signature (OVA1)	Ovarian cancer	To pre-operatively assess pelvic mass for suspected ovarian cancer
Nuclear matrix protein 22	Bladder cancer	To monitor response to treatment

*** CA-15-3 done only if clinically indicated.**
**** PSA Cancer screening as per Daman's policy**

2. Non- malignant conditions associated with rise in tumor markers:

Marker	Associated Non-malignant Conditions
AFP	Viral Hepatitis, liver injury, Irritable Bowel Disease, pregnancy.
B-hCG	Testicular cancer, marijuana smokers, pregnancy, gestational trophoblastic disease.
CEA	Smokers, IBD, hepatitis, cirrhosis, pancreatitis, gastritis
CA-125	Peritoneal irritation, endometriosis, pelvic inflammatory disease, hepatitis, cirrhosis, First trimester of pregnancy, pancreatitis, ovarian cysts
PSA	Prostatitis, benign prostatic hyperplasia.

Requirements for Coverage

ICD and CPT codes must be coded to the highest level of specificity.

Non-Coverage

1. Daman does not cover tumour markers for the Visitor's Plan.
2. Daman does not cover any of the diagnosis and services considered to be experimental or unproven for doing tumour markers.
3. Daman does not cover any of the tumour markers which are considered to be experimental or unproven.

Payment and Coding Rules

Please apply DOH payment rules and regulations and relevant coding manuals for ICD, CPT, etc.

Denial codes

Code description
Service is not clinically indicated based on good clinical practice.
Service is not clinically indicated based on good clinical practice, without additional supporting diagnosis/activities.
Service/ supply may be appropriate, but too frequent.
Activity/ diagnosis inconsistent with clinician speciality.
Payment is included in the allowance for another service.
Use bundled code
Service(s) is (are) not covered.

Appendices

A. References

- http://www.cancer.ca/en/cancer-information/diagnosis-and-treatment/tests-and-procedures/tumour-markers/?region=on#ixzz5QmzrJHqb
- https://www.cancer.gov/about-cancer/diagnosis-staging/diagnosis/tumor-markers-fact-sheet
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2902207/
- http://www.aetna.com/cpb/medical/data/300_399/0352.html
- https://www.oncolink.org/cancer-treatment/procedures-diagnostic-tests/blood-tests-tumor-diagnostic-tests/patient-guide-to-tumor-markers
- https://emedicine.medscape.com/article/269839-overview
- https://www.nice.org.uk/guidance/QS12/chapter/Quality-statement-3-Gene-expression-profiling
- https://www.nice.org.uk/Guidance/DG10
- https://www.uptodate.com/contents/breast-cancer-guide-to-diagnosis-and-treatment-beyond-the-basics
- https://emedicine.medscape.com/article/1954174-overview
- https://www.uptodate.com/contents/overview-of-the-classification-and-management-of-cancers-of-unknown-primary-site?search=tumor%20markers&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1
- https://www.uptodate.com/contents/screening-for-ovarian-cancer?search=tumor%20markers&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2
- https://www.uptodate.com/contents/serum-tumor-markers-in-testicular-germ-cell-tumors?search=tumor%20markers&source=search_result&selectedTitle=3~150&usage_type=default&display_rank=3
- https://emedicine.medscape.com/article/255771-overview
- https://emedicine.medscape.com/article/280605-workup#c7
- https://emedicine.medscape.com/article/2086864-overview
- https://www.uptodate.com/contents/serum-tumor-markers-in-testicular-germ-cell-tumors?search=alpha%20fetoprotein&source=search_result&selectedTitle=3~150&usage_type=default&display_rank=3#H2
- https://www.uptodate.com/contents/personalized-genotype-directed-therapy-for-advanced-non-small-cell-lung-

cancer?search=ALK%20TUMOR%20MARKERS&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2#H3902141
- https://emedicine.medscape.com/article/2087557-overview#a2
- https://www.uptodate.com/contents/screening-for-ovarian-cancer?search=tumor%20markers&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2#H10
- https://www.uptodate.com/contents/serum-tumor-markers-in-testicular-germ-cell-tumors?search=alpha%20fetoprotein&source=search_result&selectedTitle=3~150&usage_type=default&display_rank=3#H13
- https://www.uptodate.com/contents/approach-to-the-patient-with-unexplained-eosinophilia?topicRef=2211&source=see_link#H7341756
- https://bestpractice.bmj.com/topics/en-gb/260/investigations -ovarian cancer
- https://bestpractice.bmj.com/topics/en-gb/260/monitoring -ovarian cysts
- https://bestpractice.bmj.com/topics/en-gb/791/investigations
- https://bestpractice.bmj.com/topics/en-gb/716/investigations
- https://bestpractice.bmj.com/topics/en-gb/980/investigations
- https://www.nice.org.uk/advice/mib27/chapter/Evidence-review - Oncotype Dx, Mamma print
- https://www.cancer.gov/about-cancer/diagnosis-staging/diagnosis/tumor-markers-fact-sheet
- http://www.immunohistochemistry.us/what-is-immunohistochemistry/IHC-application/immunohistochemistry-cancer.html

B. Revision History

Date	Change(s)
01-07-2012	Release of V1.0
01-07-2013	Release of V1.1 - New template
15-07-2014	Release of V2.0 - Disclaimer updated as per system requirements
09-01-2019	Release of V3.0 - Content update