

**TRANSPLANTATION OF SOLID ORGANS**

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Status: Current

**Summary of Changes**

Addition: I.B.10.i – Added cross reference to the Cellular and Gene Therapy policy # 91638 for criteria for cellular therapy (e.g. Lantidra).

**I. POLICY/CRITERIA**

A. The following applies to all solid organ transplants (except cornea):

1. One evaluation per transplant. A second opinion consult only to determine transplant candidacy would be approved at a contracted or in network transplant facility if a second transplant evaluation is requested and the member has been previously turned down for transplant.
2. Solid organ transplants are covered as defined in coverage documents. Related services including evaluation, donor expenses, and donor searches are limited as defined in coverage documents.
3. All transplant evaluations and transplants must be pre-authorized by Priority Health and performed at a Priority Health approved facility. Requests for authorization should be submitted on the Solid Organ Transplant prior authorization form.
4. Transplant referrals are directed to facilities in Priority Health's network or contracted networks. For more information, please refer to the [Provider Manual](#).
5. Patients with a history of using alcohol, tobacco, and other substances of abuse must be abstinent for a minimum of three months prior to approval of the transplant by Priority Health. Drug testing may be required at the discretion of Priority Health. Use of marijuana for medical purposes requires documentation from the treating physician and transplant eligibility is subject to the transplanting institution's criteria. Evaluations for transplantation are covered even for patients who have active substance abuse at the time of the evaluation.
6. Patients must be willing and able to adhere to post-transplant lifestyle restrictions and medical regimen.
7. Donor expenses
  - a. Expenses incurred after the harvesting of the organ and discharge from the hospital are not covered for donors who are not Priority Health members and have other active health insurance.
  - b. For donors without other health insurance, medical expenses directly related to or as a result of the surgery to donate the organ

will be covered for 30 days post discharge from the hospital immediately following the transplant.

8. Transportation and lodging for the patient, donor, or family are not covered benefits, unless otherwise specified in coverage documents.
  9. Post-transplant care
    - a. Follow-up care and services are covered at the transplant facility for one year following the transplant, for both contracted and non-contracted transplant facilities.
    - b. Follow-up care beyond one-year post-transplant:
      - i. Covered at contracted transplant facilities
      - ii. Non-contracted facilities: Only physician services are covered. Testing, labs, and imaging are covered in network only.
  10. Priority Health does not cover re-transplantation when evidence exists, in the opinion of the Plan, that patient non-compliance with treatment recommendations was a significant contributor to transplant failure.
- B. Solid organ transplants are eligible for coverage as follows:
1. Cornea Transplants: corneal dystrophies and corneal opacities. Prior authorization is not required for corneal transplants.
  2. Kidney Transplants: When the transplanting institution's selection criteria are met.
  3. Heart Transplants: When the transplanting institution's selection criteria are met.
  4. Heart-Lung Transplants: When the transplanting institution's selection criteria are met.
  5. Liver Transplants:
    - a. Liver transplants (cadaver or living donor) are covered for adolescents and adults when the transplanting institution's selection criteria are met AND one of the following (i or ii):
      - i. A Model of End-stage Liver Disease (MELD) score greater than 15 [MELD score used for patients  $\geq 12$  years old not designated 1A or 1B per Organ Procurement and Transplantation Network (OPTN) Policies Criteria], **or**
      - ii. Approval for transplant received from the United Network for Organ Sharing (UNOS) Regional Review.
    - b. Liver transplants are covered for children  $< 12$  years of age when the transplanting institution's selection criteria are met
    - c. Liver transplantation is not a covered benefit for patients with malignancy outside the liver, except metastatic neuroendocrine tumors (carcinoid, apudoma, gastrinoma, glucagonoma) if metastasis is restricted to the liver, who are unresponsive to adjuvant therapy after aggressive surgical resection and reduction of hepatic metastasis or hepatic involvement in malignant epithelioid hemangioendothelioma.

- d. Patients with Hepatocellular Carcinoma (HCC) who do not meet UNOS or Milan criteria for liver transplant: The size or number of HCC lesions may exclude a patient from transplant eligibility. If the lesions are amenable to treatment with an ablative procedure (radiofrequency or chemo), the ablative procedure is a covered benefit. Following ablation, liver transplant coverage is determined as defined in a. above.
  - e. The following are considered investigational and are not covered because their safety and effectiveness has not been established:
    - i. Heterotopic (also known as ectopic or auxiliary) liver transplantation
    - ii. Xenotransplantation
    - iii. Hepatocellular transplantation
    - iv. Bioartificial liver transplantation
6. Lung Transplants: When the transplanting institution's selection criteria are met.
7. Pancreas Transplants-Simultaneous Pancreas-Kidney (SPK): When the transplanting institution's selection criteria are met.
8. Pancreas after Kidney (PAK) Transplantation: When the transplanting institution's selection criteria are met.
9. Pancreas Transplant Alone (PTA): When the transplanting institution's selection criteria are met.
10. Islet Cell Transplantation
- a. Autologous pancreas islet cell transplantation (i.e., transplantation of the member's own islet cells) is a covered benefit for patients undergoing near-total or total pancreatectomy for severe refractory chronic pancreatitis.
  - b. Autologous pancreas islet cell transplantation is not a covered benefit for any indication other than 10a.
  - c. Allogenic islet cell transplantation (i.e., transplantation of islet cells from a donor) is not a covered benefit.
    - i. For cellular therapy (e.g. Lantidra) see the Cellular and Gene Therapy policy # 91638
  - d. Islet cell xenografts are not a covered benefit.
  - e. Retransplantation is not a covered benefit
11. Intestinal Transplantation, Small Bowel/Liver or Multivisceral (small bowel/liver and or stomach, pancreas, colon) Transplant: **All** of the following (a, b & c) must be met:
- a. Irreversible intestinal failure when the patient can no longer be safely maintained on total parenteral nutrition (TPN). Examples of failed TPN include:
    - i. impending or overt liver failure due to TPN-induced liver injury.

- ii. thrombosis of the major central venous channels (jugular, femoral, subclavian).
    - iii. frequent line infection and sepsis.
    - iv. frequent episodes of severe dehydration despite IV fluids in addition to TPN.
  - b. All of the following must be present:
    - i. Adequate kidney function, defined as a creatinine clearance of greater than 50 ml/min; *and*
    - ii. Adequate cardiovascular function (ejection fraction *greater than or equal to 40%*); *and*
    - iii. Absence of acute or chronic active infections that are not effectively treated; *and*
    - iv. No uncontrolled and/or untreated psychiatric disorders that interfere with compliance to a strict treatment regimen; *and*
    - v. Absence of inadequately controlled HIV/AIDS. Controlled HIV is defined as:
      - 1. CD4 count greater than 200 cells/mm<sup>3</sup> for greater than 6 months; *and*
      - 2. HIV-1 RNA (viral load) undetectable; *and*
      - 3. On stable antiviral therapy greater than 3 months; *and*
      - 4. No other complications from AIDS, such as opportunistic infection or neoplasms.
  - c. None of the following:
    - i. Sepsis;
    - ii. Multi-organ failure;
    - iii. Advanced neurological disorders (e.g., neuroaxonal dystrophy, Tay-Sachs disease, Niemann-Pick disease and variants, neuronal ceroid lipofuscinosis, and Huntington disease);
    - iv. Presence of other gastrointestinal diseases (e.g., bleeding peptic ulcer, diverticulitis, chronic hepatitis);
    - v. Malignancy, other than non-melanomatous skin cancer,
    - vi. Congestive heart failure with refractory symptoms and ejection fraction less than 40%.
12. Xenotransplantation of any organ is considered experimental and is not a covered benefit.

C. TransMedics Organ Care System for preservation and transport of donor organs is not covered as it is considered experimental and investigational. Routine patient care costs may be covered in a clinical trial as defined for Investigational Devices in the Experimental /Investigational/ Unproven Care medical policy. The device is not a covered benefit. (Coverage for IDE trials is defined by product in Appendix C of the Experimental/Investigational/ Unproven Care medical policy.)

## **II. MEDICAL NECESSITY REVIEW**

Prior authorization for certain drug, services, and procedures may or may not be required. In cases where prior authorization is required, providers will submit a request demonstrating that a drug, service, or procedure is medically necessary. For more information, please refer to the [Priority Health Provider Manual](#).

## **III. APPLICATION TO PRODUCTS**

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

- ❖ **HMO/EPO:** *This policy applies to insured HMO/EPO plans.*
- ❖ **POS:** *This policy applies to insured POS plans.*
- ❖ **PPO:** *This policy applies to insured PPO plans. Consult individual plan documents as state mandated benefits may apply. If there is a conflict between this policy and a plan document, the provisions of the plan document will govern.*
- ❖ **ASO:** *For self-funded plans, consult individual plan documents. If there is a conflict between this policy and a self-funded plan document, the provisions of the plan document will govern.*
- ❖ **INDIVIDUAL:** *For individual policies, consult the individual insurance policy. If there is a conflict between this medical policy and the individual insurance policy document, the provisions of the individual insurance policy will govern.*
- ❖ **MEDICARE:** *Coverage is determined by the Centers for Medicare and Medicaid Services (CMS) and/or the Evidence of Coverage (EOC); if a coverage determination has not been adopted by CMS, this policy applies.*
- ❖ **MEDICAID/HEALTHY MICHIGAN PLAN:** *For Medicaid/Healthy Michigan Plan members, this policy will apply. Coverage is based on medical necessity criteria being met and the appropriate code(s) from the coding section of this policy being included on the Michigan Medicaid Fee Schedule located at: [http://www.michigan.gov/mdch/0,1607,7-132-2945\\_42542\\_42543\\_42546\\_42551-159815--,00.html](http://www.michigan.gov/mdch/0,1607,7-132-2945_42542_42543_42546_42551-159815--,00.html). If there is a discrepancy between this policy and the Michigan Medicaid Provider Manual located at: [http://www.michigan.gov/mdch/0,1607,7-132-2945\\_5100-87572--,00.html](http://www.michigan.gov/mdch/0,1607,7-132-2945_5100-87572--,00.html), the Michigan Medicaid Provider Manual will govern. If there is a discrepancy or lack of guidance in the Michigan Medicaid Provider Manual, the Priority Health contract with Michigan Medicaid will govern. For Medical Supplies/DME/Prosthetics and Orthotics, please refer to the Michigan Medicaid Fee Schedule to verify coverage.*

## **IV. DESCRIPTION**

Solid organ transplants are covered as defined in coverage documents.

Tobacco use (e.g., cigarettes, pipe, cigar, chew etc.) is a contraindication to transplant surgery. Nicotine and its metabolites are biomarkers that can be tested to distinguish active tobacco use from passive exposure. Cotinine, a nicotine metabolite, is commonly used in tobacco cessation testing because it has a longer

half-life than nicotine and can be tested in urine, plasma, or serum. Tobacco products also contain alkaloids such as anabasine and nornicotine which can be tested to distinguish between use of tobacco products and nicotine replacement therapies. Anabasine is present in tobacco products, but not nicotine replacement therapies. The presence of nornicotine without anabasine is consistent with use of nicotine replacement products. Neither anabasine nor nornicotine accumulates from passive exposure. Urine testing is recommended over serum or plasma testing because it is less invasive and analytes are detectable for a longer period of time. There are no optimal cut-off values for cessation testing; urinary cotinine thresholds may vary between 10-50 ng/ml, and in general the presence of anabasine greater than 10 ng/mL or nornicotine greater than 30 ng/mL in urine indicates current tobacco use. In addition, reference ranges may vary by laboratory. The laboratory's threshold should be used to determine if there is a positive or negative indication of tobacco use.

## V. CODING INFORMATION

### ICD-10 Codes that may support medical necessity

Not specified – see criteria

### CPT/HCPCS Codes

#### Corneal Transplant – No preauthorization required

- 65710 Keratoplasty (corneal transplant); anterior lamellar
- 65730 Keratoplasty (corneal transplant); penetrating (except in aphakia or pseudophakia)
- 65750 Keratoplasty (corneal transplant); penetrating (in aphakia)
- 65755 Keratoplasty (corneal transplant); penetrating (in pseudophakia)
- 65756 Keratoplasty (corneal transplant); endothelial
- 65757 Backbench preparation of corneal endothelial allograft prior to transplantation (List separately in addition to code for primary procedure)
- V2785 Processing, preserving and transporting corneal tissue (*Corneal tissue reimbursement for ASC, OP Hosp*)
- 65780 Ocular surface reconstruction; amniotic membrane transplantation, multiple layers
- 65781 Ocular surface reconstruction; limbal stem cell allograft (eg, cadaveric or living donor)
- 65782 Ocular surface reconstruction; limbal conjunctival autograft (includes obtaining graft)

#### Not separately payable:

- 66999 Unlisted procedure, anterior segment of eye. If billed for corneal incisions in the recipient cornea created using a laser, in preparation for penetrating or lamellar keratoplasty (*explanatory notes must accompany claim for unlisted procedures*)

#### Kidney Transplant

- 50300 Donor nephrectomy (including cold preservation); from cadaver donor, unilateral or bilateral
- 50320 Donor nephrectomy (including cold preservation); open, from living donor
- 50323 Backbench standard preparation of cadaver donor renal allograft prior to transplantation, including dissection and removal of perinephric fat, diaphragmatic and retroperitoneal attachments, excision of adrenal gland, and preparation of ureter(s), vein(s), and renal artery(s), ligating branches, as necessary
- 50325 Backbench standard preparation of living donor renal allograft (open or laparoscopic) prior to transplantation, including dissection and removal of perinephric fat and preparation of ureter(s), renal vein(s), and renal artery(s), ligating branches, as necessary
- 50327 Backbench reconstruction of cadaver or living donor renal allograft prior to transplantation; venous anastomosis, each
- 50328 Backbench reconstruction of cadaver or living donor renal allograft prior to transplantation; arterial anastomosis, each
- 50329 Backbench reconstruction of cadaver or living donor renal allograft prior to transplantation; ureteral anastomosis, each
- 50340 Recipient nephrectomy (separate procedure)
- 50360 Renal allotransplantation, implantation of graft; without recipient nephrectomy
- 50365 Renal allotransplantation, implantation of graft; with recipient nephrectomy
- 50370 Removal of transplanted renal allograft
- 50380 Renal autotransplantation, reimplantation of kidney

#### Heart Transplant

- 33940 Donor cardiectomy (including cold preservation) (*Not covered for Priority Health Medicaid*)
- 33944 Backbench standard preparation of cadaver donor heart allograft prior to transplantation, including dissection of allograft from surrounding soft tissues to prepare aorta, superior vena cava, inferior vena cava, pulmonary artery, and left atrium for implantation
- 33945 Heart transplant, with or without recipient cardiectomy

#### Heart-Lung Transplant

- 33930 Donor cardiectomy-pneumonectomy (including cold preservation) (*Not covered for Priority Health Medicaid*)
- 33933 Backbench standard preparation of cadaver donor heart/lung allograft prior to transplantation, including dissection of allograft from surrounding soft tissues to prepare aorta, superior vena cava, inferior vena cava, and trachea for implantation
- 33935 Heart-lung transplant with recipient cardiectomy-pneumonectomy

#### Liver Transplant

- 47133 Donor hepatectomy (including cold preservation), from cadaver donor
- 47135 Liver allotransplantation; orthotopic, partial or whole, from cadaver or living donor, any age
- 47140 Donor hepatectomy (including cold preservation), from living donor; left lateral segment only (segments II and III)

- 47141 Donor hepatectomy (including cold preservation), from living donor; total left lobectomy (segments II, III and IV)
- 47142 Donor hepatectomy (including cold preservation), from living donor; total right lobectomy (segments V, VI, VII and VIII)
- 47143 Backbench standard preparation of cadaver donor whole liver graft prior to allotransplantation, including cholecystectomy, if necessary, and dissection and removal of surrounding soft tissues to prepare the vena cava, portal vein, hepatic artery, and common bile duct for implantation; without trisegment or lobe split
- 47144 Backbench standard preparation of cadaver donor whole liver graft prior to allotransplantation, including cholecystectomy, if necessary, and dissection and removal of surrounding soft tissues to prepare the vena cava, portal vein, hepatic artery, and common bile duct for implantation; with trisegment split of whole liver graft into 2 partial liver grafts (ie, left lateral segment (segments II and III) and right trisegment (segments I and IV through VIII))
- 47145 Backbench standard preparation of cadaver donor whole liver graft prior to allotransplantation, including cholecystectomy, if necessary, and dissection and removal of surrounding soft tissues to prepare the vena cava, portal vein, hepatic artery, and common bile duct for implantation; with lobe split of whole liver graft into 2 partial liver grafts (i.e., left lobe (segments II, III, and IV) and right lobe (segments I and V through VIII))
- 47146 Backbench reconstruction of cadaver or living donor liver graft prior to allotransplantation; venous anastomosis, each
- 47147 Backbench reconstruction of cadaver or living donor liver graft prior to allotransplantation; arterial anastomosis, each

#### Lung Transplant

- 32850 Donor pneumonectomy(s) (including cold preservation), from cadaver donor
- 32851 Lung transplant, single; without cardiopulmonary bypass
- 32852 Lung transplant, single; with cardiopulmonary bypass
- 32853 Lung transplant, double (bilateral sequential or en bloc); without cardiopulmonary bypass
- 32854 Lung transplant, double (bilateral sequential or en bloc); with cardiopulmonary bypass
- 32855 Backbench standard preparation of cadaver donor lung allograft prior to transplantation, including dissection of allograft from surrounding soft tissues to prepare pulmonary venous/atrial cuff, pulmonary artery, and bronchus; unilateral
- 32856 Backbench standard preparation of cadaver donor lung allograft prior to transplantation, including dissection of allograft from surrounding soft tissues to prepare pulmonary venous/atrial cuff, pulmonary artery, and bronchus; bilateral

- S2060 Lobar lung transplantation
- S2061 Donor lobectomy (lung) for transplantation, living donor  
*("S" codes not payable for Priority Health Medicare)*

#### Pancreas Transplant

- 48160 Pancreatectomy, total or subtotal, with autologous transplantation of pancreas or pancreatic islet cells (*Not covered for Priority Health Medicare*)
- 48550 Donor pancreatectomy (including cold preservation), with or without duodenal segment for transplantation
- 48551 Backbench standard preparation of cadaver donor pancreas allograft prior to transplantation, including dissection of allograft from surrounding soft tissues, splenectomy, duodenotomy, ligation of bile duct, ligation of mesenteric vessels, and Y-graft arterial anastomoses from iliac artery to superior mesenteric artery and to splenic artery
- 48552 Backbench reconstruction of cadaver donor pancreas allograft prior to transplantation, venous anastomosis, each
- 48554 Transplantation of pancreatic allograft
- 48556 Removal of transplanted pancreatic allograft
- S2065 Simultaneous pancreas kidney transplantation (*Not payable for Priority Health Medicare and Medicaid*)

**Pancreatic Islet Cell Transplant**

- G0341 Percutaneous islet cell transplant, includes portal vein catheterization and infusion
- G0342 Laparoscopy for islet cell transplant, includes portal vein catheterization and infusion
- G0343 Laparotomy for islet cell transplant, includes portal vein catheterization and infusion

*G-codes reportable for Priority Health Medicare when service is billed in the context of a clinical trial*

**Intestinal Transplantation**

- 44132 Donor enterectomy (including cold preservation), open; from cadaver donor
- 44133 Donor enterectomy (including cold preservation), open; partial, from living donor
- 44135 Intestinal allotransplantation; from cadaver donor
- 44136 Intestinal allotransplantation; from living donor
- 44137 Removal of transplanted intestinal allograft, complete
- 44715 Backbench standard preparation of cadaver or living donor intestine allograft prior to transplantation, including mobilization and fashioning of the superior mesenteric artery and vein
- 44720 Backbench reconstruction of cadaver or living donor intestine allograft prior to transplantation; venous anastomosis, each
- 44721 Backbench reconstruction of cadaver or living donor intestine allograft prior to transplantation; arterial anastomosis, each
- S2053 Transplantation of small intestine, and liver allografts
- S2054 Transplantation of multivisceral organs
- S2055 Harvesting of donor multivisceral organs, with preparation and maintenance of allografts; from cadaver donor

*("S" codes not payable for Priority Health Medicare or Medicaid)*

**Lab test for tobacco cessation verification**

(No prior authorization required; subject to drug testing limits; See *policy 91611 Drug Testing*)

- 80307\* Drug test(s), presumptive, any number of drug classes, any number of devices or procedures; by instrument chemistry analyzers (e.g., utilizing immunoassay [e.g., EIA, ELISA, EMIT, FPIA, IA, KIMS, RIA]), chromatography (e.g., GC, HPLC), and mass spectrometry either with or without chromatography, (e.g., DART, DESI, GC-MS, GC-MS/MS, LC-MS, LC-MS/MS, LDTD, MALDI, TOF) includes sample validation when performed, per date of service
- 80323\* Alkaloids, not otherwise specified
- G0480\* Drug test(s), definitive, utilizing (1) drug identification methods able to identify individual drugs and distinguish between structural isomers (but not necessarily stereoisomers), including, but not limited to, GC/MS (any type, single or tandem) and LC/MS (any type, single or tandem and excluding immunoassays (e.g., IA, EIA, ELISA, EMIT, FPIA) and enzymatic methods (e.g., alcohol dehydrogenase)), (2) stable isotope or other universally recognized internal standards in all samples (e.g., to control for matrix effects, interferences and variations in signal strength), and (3) method or drug-specific calibration and matrix-matched quality control material (e.g., to control for instrument variations and mass spectral drift); qualitative or quantitative, all sources, includes specimen validity testing, per day; 1-7 drug class(es), including metabolite(s) if performed

#### **Not Covered**

- 0494T Surgical preparation and cannulation of marginal (extended) cadaver donor lung(s) to ex vivo organ perfusion system, including decannulation, separation from the perfusion system, and cold preservation of the allograft prior to implantation, when performed
- 0495T Initiation and monitoring marginal (extended) cadaver donor lung(s) organ perfusion system by physician or qualified health care professional, including physiological and laboratory assessment (e.g., pulmonary artery flow, pulmonary artery pressure, left atrial pressure, pulmonary vascular resistance, mean/peak and plateau airway pressure, dynamic compliance and perfusate gas analysis), including bronchoscopy and X ray when performed; first two hours in sterile field
- 0496T Initiation and monitoring marginal (extended) cadaver donor lung(s) organ perfusion system by physician or qualified health care professional, including physiological and laboratory assessment (e.g., pulmonary artery flow, pulmonary artery pressure, left atrial pressure, pulmonary vascular resistance, mean/peak and plateau airway pressure, dynamic compliance and perfusate gas analysis), including bronchoscopy and X ray when performed; each additional hour (List separately in addition to code for primary procedure)
- 0894T Cannulation of the liver allograft in preparation for connection to the normothermic perfusion device and decannulation of the liver allograft following normothermic perfusion 0895T Connection of liver allograft to normothermic machine perfusion device, hemostasis control; initial 4 hours of monitoring time, including hourly physiological and laboratory assessments (eg, perfusate temperature, perfusate pH, hemodynamic parameters, bile production, bile pH, bile glucose, biliary bicarbonate, lactate levels, macroscopic assessment)

- 0896T Connection of liver allograft to normothermic machine perfusion device, hemostasis control; each additional hour, including physiological and laboratory assessments (eg, perfusate temperature, perfusate pH, hemodynamic parameters, bile production, bile pH, bile glucose, biliary bicarbonate, lactate levels, macroscopic assessment) (List separately in addition to code for primary procedure)
- S2102 Islet cell tissue transplant from pancreas; allogeneic
- S2103 Adrenal tissue transplant to brain
- S2152 Solid organ(s), complete or segmental, single organ or combination of organs; deceased or living donor (s), procurement, transplantation, and related complications; including: drugs; supplies; hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services, and the number of days of pre and posttransplant care in the global definition
- S9975 Transplant related lodging, meals and transportation, per diem
- 81560 Transplantation medicine (allograft rejection, pediatric liver and small bowel), measurement of donor and third-party-induced CD154+T-cytotoxic memory cells, utilizing whole peripheral blood, algorithm reported as a rejection risk score
- 0542U Nephrology (renal transplant), urine, nuclear magnetic resonance (NMR) spectroscopy measurement of 84 urinary metabolites, combined with patient data, quantification of BK virus (human polyomavirus 1) using real-time PCR and serum creatinine, algorithm reported as a probability score for allograft injury status
- 0581U Transplantation medicine, antibody to non-human leukocyte antigens (non-HLA), blood specimen, flow cytometry, single-antigen bead technology, 39 targets, individual positive antibodies reported

## VI. REFERENCES

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## APPENDIX A

### INDICATOR OF TOBACCO USE

	Tobacco Product User	Nicotine Replacement Product User	Non-tobacco user with passive exposure	Non-tobacco user with no passive exposure
Nicotine	+	+	+	-
Cotinine	+	+	+	-
Anabasine	+	-	-	-
Nornicotine	+	+	-	-

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