

Supplemental online content for:

Derivation and Validation of a Risk Assessment Model for Immunomodulatory Drug–Associated Thrombosis Among Patients With Multiple Myeloma

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eTable 1. Administrative Claims Codes Search Matrix

	ICD-9-CM Diagnosis Codes ^b	ICD-9-CM Procedure Codes	CPT4/HCPCS	NDC	Comment
MedPAR	ADMDXCDE DGN_CD1–DGN_CD25	SRGCDE1–SRGCDE25			To remove SNF claims, drop if SNFIND=N
OUTPAT	DGN_CD1–DGN_CD25	PRCDR_CD1–PRCDR_CD13	HCPCS	IDENDC	Drop denied claims
NCH	PDGNS_CD DGN_CD1–DGN_CD12 LINEDIAG		HCPCS		Drop denied claims
DME	PDGNS_CD DGN_CD1–DGN_CD12 LINEDIAG		HCPCS	NDC_CD	Use for chemotherapy/drug but not for comorbidity or outcomes Drop denied claims
PDE				GNN	

Abbreviations: CPT4, Current Procedural Terminology, 4th edition; DME, durable medical equipment; HCPCS, Healthcare Common Procedure Coding System; MEDPAR, Medicare Provider Analysis and Review; NCH, National Claims History (carrier claims); NDC, National Drug Code; OUTPAT, outpatient claims; PDE, Medicare Part D Prescription Drug Event; SNF, skilled nursing facility; VTE, venous thromboembolism.

eTable 2. Administrative Claims Codes: Outcomes and Comorbidities

VTE outcome (day 7+ look-forward window) ^{1,2}	
Pulmonary embolism	ICD-9-CM diagnosis: 415.11, 415.12, 415.13, 415.19
Deep vein thrombosis	ICD-9-CM diagnosis: 453.2, 453.40, 453.41, 453.42, 453.8, 453.82, 453.83, 453.84, 453.85, 453.86, 453.87, 453.89, 453.9
Phlebitis	ICD-9-CM diagnosis: 451.11, 451.19, 451.2, 451.81, 451.83, 451.84, 451.89, 451.9
NCI Comorbidity Index (365-day lookback window) ³	
Myocardial infarction	ICD-9-CM diagnosis: 410.xx with inpatient length of stay >2 d; ICD-9-CM diagnosis: 412.bb
Congestive heart failure	ICD-9-CM diagnosis: 398.91, 425.4x–425.5x, 425.7x–425.9x, 428.xx
Paralysis/Immobilization	ICD-9-CM diagnosis: 342.xx, 344.0x–344.6x, 344.9x
Diabetes	ICD-9-CM diagnosis: 250.bb, 250.0x–250.3x, 250.4x–250.9x, 362.0x
Renal disease	ICD-9-CM diagnosis: 403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582.xx–583.xx, 585.xx–586.xx, 588.xx, V42.0x, V45.1x, V56.xx ICD-9-CM procedure: 39.27, 39.42, 39.95, 54.98, 55.69
Liver disease	ICD-9-CM diagnosis: 070.22–070.23, 070.32–070.33, 070.44, 070.54, 456.0x–456.2x, 571.2x, 571.4x–571.6x, 572.2x–572.8x, V42.7x ICD-9-CM procedure: 39.1b, 42.91, 50.5x
Elixhauser comorbidity index (365-day lookback window) ⁴	
Cardiac arrhythmias	ICD-9-CM diagnosis: 426.10, 426.11, 426.13, 426.2–426.53, 426.6–426.8, 427.0, 427.2, 427.31, 427.60, 427.9, 785.0, V45.0, V53.3
Hypertension	ICD-9-CM diagnosis: 401.1, 401.9, 402.10, 402.90, 404.10, 404.90, 405.1, 405.9
Coagulopathy	ICD-9-CM diagnosis: 286.x, 287.1, 287.3–287.5
Anemia	ICD-9-CM diagnosis: 280.0, 280.1–281.9, 285.9
Obesity	ICD-9-CM diagnosis: 278.0
VTE-specific risk factors (365-day lookback window unless stated)	
Central venous catheter ⁵	ICD-9-CM diagnosis: 38.97 CPT4: 36555–36558, 36560–36561, 36563, 36565–36566, 36568–36571, 36575–36576, 36578, 36580–36585, 36597–36598
Sepsis (90-day lookback window ⁶)	ICD-9-CM diagnosis: 003.1, 020.2, 022.3, 036.2, 038.x, 054.5, 449, 785.52, 785.5x, 790.7, 995.91, 995.92

(continued on next page)

Abbreviations: CPT4, Current Procedural Terminology, version 4; HCPCS, Healthcare Common Procedure Coding System; VTE, venous thromboembolism.

eTable 2. Administrative Claims Codes: Outcomes and Comorbidities (cont.)

VTE-specific risk factors (365-day lookback window unless stated) (cont.)

Surgery (90-day lookback window⁵):

ICD-9-CM diagnosis: V67.0x

ICD-9-CM procedure: 00.7x, 00.8x, 03.4, 03.5x, 03.9x, 79.85, 79.86, 80.45, 80.46, 80.6, 80.85, 80.86, 80.95, 80.96, 81.40, 81.42, 81.43, 81.51, 81.52, 81.53, 81.54, 81.55, 84.16, 84.18

CPT4: 01214–01215, 01402, 20930–20938, 22010–22015, 22100–22116, 22206–22226, 22318–22328, 22532–22534, 22548–22585, 22590–22632, 22800–22819, 22830, 22840–22865, 27075–27079, 27130–27138, 27218, 27226–27228, 27253, 27258–27259, 27299, 27447, 27486–27487, 29861–29863, 43644–43645, 43800–43881, 49570–49575, 50010–50045, 50070, 50100–50135, 50205–50290, 50320–50340, 50370, 50382–50384, 50400–50540, 50593, 50600–50630, 50650–50660, 50700–50940, 51020–51040, 51080, 53000–53085, 53210–53275, 53400–53520, 53855, 56620–56740, 56800–56810, 57000–57335, 57530–57556, 57720, 58140–58146, 58150–58294, 58400–58540, 58600–58615, 58700–58720, 58750–58770, 58820–58825, 58920–58960, 58999, 61320–61321, 61546, 61680–61692, 61697–61710, 62160–62165, 63001–63017, 63045–63051, 63055–63066, 63075–63091, 63101–63103, 63170–63200, 63250–63295, 63300–63308, 63650–63688

HCPCS: S2083, S2213

Traumatic injury (90-day lookback window⁶):

ICD-9-CM diagnosis: 800–959, except 905–909, 930–939

Personal history of VTE (183- to 365-day lookback window)

ICD-9-CM diagnosis: V12.51, V12.52, V12.55; 415.x, 451.x, 453.x

Personal history of bleeding⁷

ICD-9-CM diagnosis: 423.00, 430.00, 431.00, 432.00, 432.1, 432.9, 455.20, 455.50, 455.80, 459.00, 456.00, 456.20, 530.70, 530.80, 531.00, 531.01, 531.20, 531.21, 531.40, 531.41, 531.60, 531.61, 532.00, 532.01, 532.20, 532.21, 532.40, 532.41, 532.60, 532.61, 533.00, 533.01, 533.20, 533.21, 533.40, 533.41, 533.60, 533.61, 534.00, 534.01, 534.20, 534.21, 534.40, 534.41, 534.60, 534.61, 535.01, 535.11, 535.21, 535.31, 535.41, 535.51, 535.61, 537.80, 562.02, 562.03, 562.12, 568.81, 569.30, 569.85, 578.00, 578.10, 578.90, 593.81, 599.70, 623.80, 626.20, 626.60, 719.10, 719.11, 719.12, 719.13, 719.14, 719.15, 719.16, 719.17, 719.18, 784.70, 784.80, 786.30

Abbreviations: CPT4, Current Procedural Terminology, version 4; HCPCS, Healthcare Common Procedure Coding System; VTE, venous thromboembolism.

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eTable 3. Administrative Claims Codes for Medications and Chemotherapy

Concurrent chemotherapy \pm 30 d ¹
ICD-9 procedure: injection/infusion chemotherapy/immunotherapy (99.25, 99.28)
CPT4: injection/infusion chemotherapy (96401–96417), intra-arterial chemotherapy (96420–96425), other injection/infusion chemotherapy (96440–96549)
NDC: melphalan, cyclophosphamide, etoposide
HCPCS: chemotherapy infusion (Q0083–Q0085), melphalan (J8600, J9245), bendamustine (J9033, J9034, C9243), vincristine (J9370, J9371, J9375, J9380), cyclophosphamide (J8530, J9070, J9080, J9090, J9091–J9097, C9420, C9421), etoposide (J8560, J9181, J9182, C9414, C9425), carboplatin (J9045), cisplatin (J9060, J9062, C9418), mitoxantrone (J9293), daunorubicin (J9150, J9151, C9424), idarubicin (J9211, C9429), doxorubicin (J9000, J9001, J9002, Q2048, Q2049, Q2050, C9415), bortezomib (J9041, C9207)
Concurrent erythropoietin \pm 30 d ¹
GNN: darbepoetin alfa, epoetin alfa
NDC: darbepoetin, epoetin
HCPCS: Q4081, J0881, J0882, J0885, J0886
Concurrent dexamethasone \pm 30 d
GNN: dexamethasone
Concurrent anticoagulant <30 d to >7 d
GNN: enoxaparin, dalteparin, tinzaparin, fondaparinux, heparin, warfarin, dabigatran, rivaroxaban, apixaban, edoxaban

Abbreviations: CPT4, Current Procedural Terminology, version 4; GNN, generic drug name; HCPCS, Healthcare Common Procedure Coding System; NDC, National Drug Code.

Reference

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eTable 4. Univariate Analysis of Risk Factors Associated With VTE in Derivation Cohort

	HR	P Value
NCCN risk factors		
Prior VTE	3.20	<.01
Obesity	0.86	.63
Central venous catheter or pacemaker	0.75	.68
Cardiac disease (CHF, MI, CA)	1.00	.98
Chronic renal disease	1.14	.38
Diabetes	1.14	.38
Acute infection	1.42	.20
Immobilization	1.24	.71
General surgery or anesthesia	1.82	.12
Trauma	0.96	.83
Erythropoietin	0.89	.61
Blood-clotting disorders	0.96	.86
High-dose dexamethasone, ≥ 480 mg	1.09	.55
Doxorubicin ^a	NE	N/A
Multiagent (cytotoxic) chemotherapy	2.05	.48
Additional risk factors considered		
Age (every 10-y increase)	1.23	.04
Sex (female vs male)	1.21	.16
Race		
White	Ref	
Black	1.33	.13
Asian	0.25	<.01
Year of diagnosis (every 1-y increase)	0.98	.66
Geography (metropolitan vs rural)	0.92	.67
Liver disease	1.15	.81
Anemia	0.93	.58
Hypertension	1.28	.10
History of bleeding	1.22	.41
IMiD type (lenalidomide vs thalidomide)	1.13	.47
Concurrent chemotherapy		
Bortezomib	0.85	.37
Melphalan	1.72	.45
Cyclophosphamide	1.18	.77

(continued)

Abbreviations: CA, cardiac arrhythmia; CHF, congestive heart failure; HR, hazard ratio; IMiD, immunomodulatory drug; MI, myocardial infarction; N/A, not applicable; NE, no event; VTE, venous thromboembolism.

^aHR was not estimable for this variable because there was no VTE event in the comparison group.

^bDexamethasone was reorganized into modern conventional standard and high-dose categories.

eTable 4. Univariate Analysis of Risk Factors Associated With VTE in Derivation Cohort (cont.)

	HR	P Value
Additional risk factors considered (cont.)		
Concurrent dexamethasone^b		
None or low dose (<120 mg/cycle)	Ref	
Standard dose (120–160 mg/cycle)	1.27	.13
High dose (>160 mg/cycle)	1.42	.06
Concurrent anticoagulation		
None	Ref	
Warfarin	1.09	.69
Low-molecular-weight heparin	0.38	.34
Direct oral anticoagulant ^a	NE	N/A

Abbreviations: CA, cardiac arrhythmia; CHF, congestive heart failure; HR, hazard ratio; IMiD, immunomodulatory drug; MI, myocardial infarction; N/A, not applicable; NE, no event; VTE, venous thromboembolism.

^aHR was not estimable for this variable because there was no VTE event in the comparison group.

^bDexamethasone was reorganized into modern conventional standard and high-dose categories.

eTable 5. Comparison of Cohorts in SEER-Medicare Database

	IMiD Cohort (N=2,397) % (n)	MM Cohort (N=30,757) % (n)
Age, y		
<65	0	26% (7,873)
65–69	25% (592)	17% (5,274)
70–74	28% (671)	17% (5,247)
75–79	23% (542)	16% (4,917)
80–84	15% (360)	13% (4,078)
≥85	10% (232)	11% (3,368)
Sex		
Male	51% (1,216)	56% (17,161)
Female	49% (1,181)	44% (13,596)
Race		
White	80% (1,909)	75% (22,987)
Black	13% (303)	19% (5,878)
Asian/Pacific Islander	7% (146)	5% (1,486)
American Indian or Alaskan Native	0.5% (13)	0.4% (137)
Unknown/Missing	1% (26)	1% (269)
Year of diagnosis		
<2007	0	3% (1,072)
2007	8% (202)	13% (3,904)
2008	13% (311)	14% (4,142)
2009	12% (294)	14% (4,237)
2010	14% (341)	14% (4,346)
2011	15% (362)	14% (4,358)
2012	18% (419)	14% (4,401)
2013	20% (468)	14% (4,297)
SEER region		
California	32% (761)	36% (11,181)
Connecticut	5% (125)	5% (1,524)
Detroit	5% (119)	6% (1,931)
Georgia	13% (306)	13% (3,907)
Hawaii	1% (25)	1% (449)
Iowa	8% (180)	4% (1,360)
Kentucky	8% (180)	6% (1,768)
Louisiana	6% (152)	6% (1,875)
New Jersey	14% (324)	12% (3,656)
New Mexico	2% (50)	2% (643)
Seattle	6% (138)	6% (1,736)
Utah	2% (37)	1% (727)
Geographic region		
Metropolitan	87% (2,092)	92% (28,213)
Rural	13% (305)	8% (2,544)

Abbreviations: IMiD, immunomodulatory drug; MM, multiple myeloma.