**Supplement**

**Table~S1. Case definitions (metastatic melanoma)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Valid case |  | Criteria |  |  |
| Incident metastatic melanoma of skin | | a) Age ≥18 years | | |
| b) Continuously insured between 2010 and 2020; deceased persons were included (2012-2020) | | |
|  |  |
|  |  | c) Washout Phase 2010-2011 – individuals with one inpatient or one confirmed outpatient cancer diagnosis (ICD-10-GM C00-C97, except C44) within the washout phase were excluded | | |
|  |  | d) One inpatient record of ICD-10-GM code C43 or at least three outpatient records with C43 within one year in different quarters issued by a medical specialist (not by a general practitioner); first two records with diagnostic modifier 'confirmed', last record without 'suspicion' or 'exclusion' | | |
|  |  |
|  |  |
|  |  |
|  |  | e) In addition the presence of a synchronous or metachronous distant metastasis (one record of ICD-10-GM C78-79 in inpatient or (confirmed) outpatient data at the same time or after first record of melanoma) – for sensitivity all persons with a locoregional metastasis were included (C77) | | |
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|  |  |
|  |  |
| ICD-10-GM, International Classification of Diseases, 10th Revision, German Modification | | | | |
|  | | | | |

**Table~S2. Types of therapy and identification codes used**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Type of therapy** | **Sector** | **Active substance** | **Used Codes** | **Coding System** |
| ***Classical chemotherapeutics*** | |  |  |  |
| Chemotherapy | inpatient | Diverse substances | 8-542, 8-543, 8-544 | OPS |
| Chemotherapy | outpatient | Dacarbazine | L01AX04 | ATC |
|  |  | Mitobronitol | L01AX01 | ATC |
|  |  | Temozolomide | L01AX03 | ATC |
|  |  | Hydroxycarbamide | L01XX05 | ATC |
|  |  | Estramustin | L01XX11 | ATC |
|  |  | Mitomycin | L01DC03 | ATC |
|  |  | Cyclophosphamide | L01AA01 | ATC |
|  |  | Chlorambucil | L01AA02 | ATC |
|  |  | Melphalan | L01AA03 | ATC |
|  |  | Lomustine | L01AD02 | ATC |
|  |  | Methotrexate | L01BA01 | ATC |
|  |  | Fluorouracil | L01BC02 | ATC |
|  |  | Capecitabine | L01BC06 | ATC |
|  | outpatient | Diverse substances | 96502 | GOP |
|  |  | Diverse substances | 96503 | GOP |
|  | outpatient | Diverse substances | 9999092 | PZN |
| Interferon | outpatient | Interferon | L03AB | ATC |
| ***Novel therapies*** |  |  |  |  |
| Targeted therapy | inpatient | Vemurafenib | 6-006.f | OPS |
|  |  | Dabrafenib | 6-007.5 | OPS |
|  |  | Encorafenib | 6-00b.9 | OPS |
|  |  | Binimetinib | 6-00b.2 | OPS |
|  |  | Cobimetinib | 6-008.c | OPS |
|  |  | Trametinib | 6-009.7 | OPS |
|  |  | Imatinib | 6-001.g | OPS |
|  |  | Dasatinib | 6-004.3 | OPS |
|  |  | Nilotinib | 6-004.6 | OPS |
|  |  |  |  |  |
| Immune Checkpoint Inhibitor | inpatient | Nivolumab | 6-008.m | OPS |
|  | Pembrolizumab | 6-009.3 | OPS |
|  | Ipilimumab | 6-006.j | OPS |
|  | Atezolizumab | 6-00a.1 | OPS |
|  | Diverse substances | 8-547.0 | OPS |
|  | Diverse substances | 8-547.1 | OPS |
|  | Diverse substances | 8-547.3 | OPS |
|  |  |  |  |
|  |  |  |  |
| Targeted therapy | outpatient | Imatinib | L01XE01 | ATC |
|  |  | Dasatinib | L01XE06 | ATC |
|  |  | Nilotinib | L01XE08 | ATC |
|  |  | Vemurafenib | L01XE15 | ATC |
|  |  | Dabrafenib | L01XE23 | ATC |
|  |  | Trametinib | L01XE25 | ATC |
|  |  | Cobimetinib | L01XE38 | ATC |
|  |  | Binimetinib | L01XE41 | ATC |
|  |  | Encorafenib | L01XE46 | ATC |
| Immune Checkpoint Inhibitor | outpatient | Ipilimumab | L01XC11 | ATC |
|  | Nivolumab | L01XC17 | ATC |
|  | Pembrolizumab | L01XC18 | ATC |
|  | Atezolizumab | L01XC32 | ATC |
| outpatient | Diverse substances | 2567478 | PZN |
|  | outpatient | Diverse substances | 96505 | GOP |
| OPS Operation and Procedure Classification System | | |  |  |
| ATC Anatomical Therapeutic Chemical Classification System (DIMDI Version 2020) | | | | |
| PZN Pharmazentralnummer - German identification code for pharmaceutical products | | | |  |
| GOP Uniform Value Scale - German assessment standard of the outpatient billing data | | | |  |