**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)  |
|   |   |
|   |   |
|  |   |
| 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  |   |