### Supplementary Material 2: Summary of the included publications

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<th>Author</th>
<th>(publication year)</th>
<th>Country/perspective</th>
<th>Disease</th>
<th>Treatment</th>
<th>Active ingredient</th>
<th>Biomarker</th>
<th>Treatment strategy</th>
<th>Result/[price year]</th>
<th>Consideration of test costs/sensitivity and specificity</th>
<th>Funding</th>
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<td>van den Akker-van Marle, M. E. / Gurwitz, D./ Detmar, S. R. et al. (2006) [32]</td>
<td>Four European member states (Germany, Ireland, Netherlands, UK)/societal perspective</td>
<td>Acute lymphoblastic leukaemia (ALL)</td>
<td>n.s.</td>
<td>Mercaptopurine</td>
<td>TPMT</td>
<td>(a) TPMT-genotyping: dosing mercaptopurine according to TPMT activity (wildtype normal), intermediate, or deficient (b) no TPMT-testing: standard doses</td>
<td>ICER (a) vs. (b): €4800 ($5702) per LYG [price year 2004]</td>
<td>yes/yes</td>
<td>European Commissions; European Science and Technology Observatory network (ESTO)</td>
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<tr>
<td>Boldt A. S./ Goddard K. A./ Flottemesch T. J. et al. (2012) [33]</td>
<td>USA/perspec tive n. s.</td>
<td>Metastatic colorectal cancer (mCRC)</td>
<td>Second-line therapy (after neoadjuvant chemotherapy)</td>
<td>Cetuximab vs. BSC</td>
<td>KRAS + (BRAF)</td>
<td>(a) No KRAS-Testing and no anti-EGFR therapy (Cetuximab): all patients receive BSC (b) KRAS and BRAF-mutation screening: Patients without KRAS and BRAF mutation receive anti-EGFR therapy (Cetuximab) (c) KRAS mutation screening: Patients without KRAS mutation receive Cetuximab (d) no KRAS testing: anti-EGFR therapy (Cetuximab)</td>
<td>ICER (b) vs (a): €648,396 per LYS ICER (b) vs. (d): most cost effective strategy (significantly lower costs at marginally less benefit) ICER (c) vs. (d): is dominated by (b) vs. (d) [price year 2010]</td>
<td>yes/no</td>
<td>National Cancer Institute at the National Institutes of Health</td>
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<td>Blank, P. R./ Schwenkglenks, M./ Moch, H. et al. (2010) [34]</td>
<td>Switzerland/health care system</td>
<td>Breast cancer (early stage)</td>
<td>Second-line therapy (after adjuvant or neoadjuvant chemotherapy)</td>
<td>Trastuzumab</td>
<td>HER2</td>
<td>(a) IHC / FISH-Test: all patients: reference strategy (no Trastuzumab) (b) IHC-test and subsequent FISH-test for IHC2+ patients: trastuzumab treatment for FISH+ or IHC3+ patients; standard therapy for all other patients (c) FISH-Test: trastuzumab treatment for FISH+ patients; standard therapy for all other patients (d) IHC-Test: trastuzumab treatment for IHC 2+ and IHC3+ patients; standard therapy for all other patients (e) IHC-test and FISH-test (parallel): trastuzumab treatment for IHC2+ and IHC3+ and/or FISH+ patients; standard therapy for all other patients (f) No IHC-test/FISH-Test: all patients receive trastuzumab</td>
<td>ICER (c) vs. (a): €12,245 ($15,676) per QALY ICER (f) vs. (e): €13,456,577 ($US17,226,646) per QALY ICER (c) vs. (e): €400,154 ($US518,323) per QALY ICER (b) vs (a) dominated (higher costs and less effective) (e) vs. (f) is dominated by (c) vs. (f) (d) is dominated by (c): less effective and more expensive (b) is extendedly dominated by (c): less expensive but also less cost-effective [price year n. s.]</td>
<td>yes/yes</td>
<td>ETH Zurich Foundation; Competence Center for Systems Physiology and Metabolic Diseases (CC-SpMD)</td>
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<tr>
<td>Blank, P. R./ Moch, H./ Stuzo, T. D. et al. (2011) [35]</td>
<td>Switzerland/health system</td>
<td>Metastatic colorectal cancer (mCRC)</td>
<td>Second-line therapy (after failed chemotherapy)</td>
<td>Cetuximab + BSC vs. BSC</td>
<td>KRAS + (BRAF)</td>
<td>(a) no KRAS-Test and no treatment with cetuximab: all patients receive BSC (b) KRAS Test and a subsequent BRAF Test: KRAS and BRAF wild-type tumour patients receive cetuximab + BSC; patients with a mutation of KRAS and/or BRAF gene receive BSC (c) KRAS Test: KRAS wild-type tumour patients receive cetuximab + BSC; patients with a mutation of KRAS gene receive BSC (d) no KRAS-Test: all patients receive cetuximab + BSC</td>
<td>ICER (b) vs (a): €62,653 ($US83,279) per QALY ICER (c) vs. (b): €313,537 ($US418,152) per QALY ICER (d) vs. (c): €314,588 ($US418,152) per QALY ICER (b) vs. (c): €13,456,577 ($US17,226,646) per QALY [price year n. s.]</td>
<td>yes/yes</td>
<td>ETH Zurich Foundation; Competence Center for Systems Physiology and Metabolic Diseases (CC-SpMD)</td>
<td></td>
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<tr>
<td>Cartlidge, J. J./ Garrison, L. P./ Ramsay, S. D. et al. (2009) [36]</td>
<td>USA/societal perspective</td>
<td>Advanced non-small cell lung cancer (NSCLC)</td>
<td>Erlotinib vs. docetaxel</td>
<td>EGFR</td>
<td>(a) EGFR protein expression test: high protein expression (positive) + erlotinib until progression; low protein expression (negative) + docetaxel until progression (IHC) (b) EGFR gene copy test: high gene copy number (positive) + erlotinib until progression; low gene copy number (negative) + docetaxel until progression (SC) (c) no EGFR-Test: erlotinib until progression</td>
<td>ICER (b) vs (c): $US162,018 per QALY ICER (a) vs. (c): $US179,612 per QALY ICER (b) vs (a): dominated (ICER of (b) vs. (a) is better than ICER of (a) vs. (c)) [price year 2006]</td>
<td>yes/no</td>
<td>The author was supported in part by a pre-doctoral Fellowship in Health outcomes from PhRMA Foundation</td>
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<tr>
<td>Reference</td>
<td>Setting/Study Design</td>
<td>Disease</td>
<td>First-line Therapy</td>
<td>Comparator</td>
<td>Comparator Description</td>
<td>ICER (b) vs. (a):</td>
<td>ICER (c) vs. (b):</td>
<td>ICER (d) vs. (c):</td>
<td>ICER (e) vs. (d):</td>
<td>ICER (f) vs. (e):</td>
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<tr>
<td>Dong, D. et al. (2012)</td>
<td>USA/societal perspective</td>
<td>Metastatic breast cancer</td>
<td>First-line therapy</td>
<td>Trastuzumab + chemotherapy vs. chemotherapy</td>
<td>HER2</td>
<td>(a) no IHC/FISH-Test: chemotherapy alone (b) IHC-Test: trastuzumab and chemotherapy for IHC +3 patients; for all others chemotherapy alone</td>
<td>ICER (b) vs. (a): less effective (ruled out by extended dominance)</td>
<td>ICER (d) vs. (c): dominated (more costly + equally effective)</td>
<td>ICER (g) vs. (f): dominated (higher costs + same effectiveness)</td>
<td>ICER (c) vs. (a): US$25,100 pro QALY</td>
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<tr>
<td>Dubinsky, M. C. et al. (2005)</td>
<td>Canada/health care system</td>
<td>Acute lymphoblastic leukaemia (ALL)</td>
<td>First-line therapy</td>
<td>Azathioprine (AZA)</td>
<td>TPMT</td>
<td>(a) Community care: therapy started on lowest AZA dose threshold of 50 mg; AZA dose could increase to 100 mg AZA, if a patient did not respond clinically at 3 months; After 6 months, patients responding to the 100 mg dose AZA continued current treatment.</td>
<td>(a) is dominated by (b), (c) and (d); higher costs and longer time to reach sustained response</td>
<td>(c) vs. (b): higher costs (US$49,487 vs. US$36,861 and faster time to reach sustained response (19.10 vs. 20.86 weeks) (no ICER is reported)</td>
<td>(d) vs. (c): higher costs (US$64,441 vs. US$58,877) and faster time to reach sustained response (18.66 vs. 19.86 weeks) (no ICER is reported)</td>
<td>yes/no</td>
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</table>

**Notes:**
- **ICER** stands for Incremental Cost-Effectiveness Ratio, which is a measure used to evaluate the cost-effectiveness of different treatment options. It represents the additional cost per additional unit of effectiveness.
- **N.S.** indicates that the test result was not significant or was not reported.
- **Price Year** indicates the year the price was reported.
USA/perspective n. s.
Idiopathic pulmonary fibrosis (IPF) n.s.
Anakinra (IL-1Ra) in combination with N-acetylcycteine and steroids vs. conservative therapy (no IL-1Ra)
TPTM
(a) TPTM: Test: Dosage of AZA according TPTM-activity: normal TPTM-activity: standard doses; TPTM-intermediate (reduced TPTM-activity): reduced doses; TPTM-deficient (absent TPTM-activity): conservative therapy without AZA
(b) no TPTM-Test: AZA
(c) conservative therapy
ICER (a) vs. (c): US$49,156 per QALY
ICER (a) vs. (b): US$29,663 per QALY
[price year 2007]
Hall, P. S., McCabe, C./Stein, R. C. et al. (2010) [33]
UK/NHS
Early-stage lymph node-positive breast cancer First-line therapy
Tamoxifen + chemotherapy vs. tamoxifen
HOXB13-IL17BR
(a) Test of recurrence (Oncotype DX): low recurrence score (RS ≤ 18): no chemotherapy, only tamoxifen; high recurrence score (RS > 18): chemotherapy + tamoxifen
(b) standard of care: chemotherapy + tamoxifen
ICER (a) vs. (b): £55.29 (US$85.52)* per QALY
Starting age of the patient cohort was 60 years
[price year 2011]
UK/NHS
HIV/AIDS First-line therapy
Abacavir-containing combination therapy vs. alternative highly active antiretroviral therapy (HAART) without abacavir
HIVR-B*5701
(a) HIVR-B*5701-Test: negative test result = Abacavir-containing regimens (by a HSR: further treatment with alternative HAART); positive test result = alternative HAART
(b) no HIVR-B*5701-Test: Abacavir-containing regimens (by a HSR: further treatment with alternative HAART)
(a) vs. (b): ranged from dominant strategy (less expensive + more effective) up to £22,811 (US$26,714) per avoid HSR (population of 1000 patients)
(b) depending on the costs of respective alternative HAART: low cost = ICER dominant; high cost = ICER up to £22,811 (US$26,714) per avoid HSR
[price year 2011]
Kapoor, R., Martinez-Vega, R., Dong, D. et al. (2015) [43]
Singapore/private healthcare system
HIV infection (early and late stage) First-line therapy
First-line ABC-based ART substituted with tenofovir-based ART as second-line in the event of side effects vs. first-line tenofovir-based ART substituted with ABC-based ART in the event of side effects
Tenofovir and abacavir can be prescribed as first-line treatment Early Stage
HIVR-B*5701
(a) No HIVR-B*5701-testing: ABC as first line (Chinese (a1); Malays (a2); Indians (a3)
(b) HIVR-B*5701-testing before ABC: Tenofovir as first line Chinese (c1); Malays (c2); Indians (c3)
(d) No HIVR-B*5701 done before ABC: Tenofovir as first-line (Chinese (d1); Malays (d2); Indians (d3))
Late stage
(c) No HIVR-B*5701-testing: ABC as first line Chinese (c1); Malays (c2); Indians (c3)
(f) HIVR-B*5701-testing before ABC: Tenofovir as first line Chinese (f1); Malays (f2); Indians (f3)
(g) No HIVR-B*5701 done before ABC: Tenofovir as first-line Chinese (g1); Malays (g2); Indians (g3)
Patients who are contraindicated to tenofovir Early stage
(l) No genetic testing Chinese (l1); Malays (l2); Indians (l3)
(j) HIVR-B*5701-testing Chinese (j1); Malays (j2); Indians (j3)
Late stage
(k) No genetic testing Chinese (k1); Malays (k2); Indians (k3)
(l) HIVR-B*5701-testing Chinese (l1); Malays (l2); Indians (l3)
ICER (b1) vs. (a1): US$415,945/QALY
ICER (b2) vs. (a2): US$310,029/QALY
ICER (b3) vs. (a3): US$208,231/QALY
ICER (f1) vs. (e1): US$926,938/QALY
ICER (f2) vs. (e2): US$624,297/QALY
ICER (g1) vs. (e1): US$284,590/QALY
ICER (g2) vs. (e2): US$154,490/QALY
ICER (g3) vs. (e3): US$44,649/QALY
ICER (k1) vs. (i1): US$757,270/QALY
ICER (k2) vs. (i2): US$454,223/QALY
ICER (k3) vs. (i3): US$114,069/QALY
USA/private healthcare system
HIV/AIDS First-line therapy
Abacavir and lamivudine + efavirenz (fixed dosed regimen) vs. alternative high active antiretroviral therapy (HAART) with tenofovir+emtricitabine+efavirenz (fixed dosed)
Gefitinib vs. chemotherapy Early Stage
HIVR-B*5701
(a) HIVR-B*5701-Test: negative test result = abacavir-containing regimens (by a HSR: further treatment with alternative HAART); positive test result = alternative HAART
(b) no HIVR-B*5701-Test: abacavir-containing regimens (by a HSR: further treatment with alternative HAART)
(a) vs. (b): US$328 per avoid HSR
[price year 2007]
de Lima Lopes, G., Segel, J. E., Tan, D. S. et al. (2012) [45]
Asia/perspective n. s.
Non-small cell lung cancer (NSCLC) First-or second-line therapy
EGFR
(a) no EGFR-testing: chemotherapy as first-line therapy, subsequent treatment with gefitinib as second-line treatment (standard therapy)
(b) EGFR-testing: patients with activating EGFR-mutation receive gefitinib as first-line therapy and chemotherapy as second-line therapy; patients without mutation receive chemotherapy as first-line therapy and BSC as second-line therapy
ICER (b) vs. (a): dominant (less expensive and more effective)
[price year 2010]
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<th>Disease</th>
<th>First-line therapy</th>
<th>Second-line therapy</th>
<th>Treatment options</th>
<th>Treatment outcomes</th>
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| Lyman et al. (2007) | USA/societal | Early-stage breast cancer | First-line therapy | Tamoxifen + chemotherapy vs. tamoxifen | (a) 21-gene RT-PCR assay: low risk patients (recurrence score <18): tamoxifen alone; intermediate (recurrence score 18-30) and high-risk patients (recurrence score ≥ 31) receive chemotherapy and tamoxifen. (b) no test: chemotherapy + tamoxifen. (c) no test: tamoxifen | ICER (a) vs. (c): US$1944 per LYS
ICER (a) vs. (b): US$3385 per LYS |
| Marra et al. (2011) | Canada/payer | Rheumatological conditions (rheumatoid arthritis and systemic lupus erythematosus) | n.s. | Azathioprine (AZA) | TPMT | (a) genotype TPMT-Test: AZA dosing according to genotype/TPMT-activity + TPMT homozygous wild type (normal TPMT-activity): target dose of 2.0 – 2.5 mg/kg/day; TPMT heterozygous (reduced TPMT-activity): target dose 1.0 mg/kg/day; TPMT homozygous mutant (deficient of TPMT-activity): target dose 0.25 mg/kg/day (b) no TPMT-Test: normal dosing |
| Nieves Galatriva, D. / De la Calle-Martin, O. / Tribarren-Layarte, J. (2009) | Spain/National Health System | HIV infection | First-line Therapy | Abacavir (ABC) | HLA-B*5701 | (a) HLA-B*5701-Test: positive test result: patients receive a HAART regimen without ABC; patients with a negative test result receive a HAART regimen with ABC (b) No HLA-B*5701-Test: all patients receive ABC |
| Oh et al. (2004) | Korea/societal | Rheumatoid arthritis and systemic lupus erythematosus | Second-line therapy | Azathioprine (AZA) | TPMT | (a) genotypeic TPMT-Test: AZA dosing according to genotype/TPMT-activity: • TPMT wild type (high activity): Initial dosage 1 mg/kg, dose increment began at 4 weeks; further increment: 0.5 mg/kg steps at 4-week-intervals (target daily dose: 2.5 mg/kg); • TPMT intermediate/heterozygous mutant type (reduced activity): Initial dosage: 0.5 mg/kg, dose increment began at 4 weeks, further increment: 0.5 mg/kg steps at 4-week-intervals (target daily dose: 1 mg/kg); • TPMT deficient/homozygous mutant type (low or no activity): Initial dosage: 0.25 mg/kg, no increment. (b) no TPMT-Test: conventional weight-based dosing of AZA started at 1 mg/kg daily, dose increase began at 8 weeks in 0.5 mg/kg steps (4-week-intervals) up to the target dose of 2.5 mg/kg. |
| Plumpton et al. (2015) | UK/National Health Service (NHS) | Epilepsy | First-line therapy | Carbamazepine (CBZ) | HLA-A*31:01 | (a) No HLA-A*31:01-testing: all patients receive CBZ (b) HLA-A*31:01-Testing: positive test result: patients receive CBZ; negative test result: patients receive lamotrigine |
| Priest et al. (2000) | New Zealand/payer | Inflammatory bowel disease (IBD) | First-line therapy | Azathioprine (AZA) | TPMT | (a) no TPMT-Test: standard dosage AZA (b) genotypic TPMT-Test: dosage of AZA according to TPMT-activity (c) phenotypic TPMT-Test: dosage of AZA according to TPMT-activity |
| Ratanasriponsong, W. / Koopitakkajorn, N. / Mahanirimongkol, S. et al. (2013) | Thailand/societal | Epilepsy and neuropathic pain | First-line therapy | Carbamazepine (CBZ) | HLA-B*15:02 | (a) No HLA-B*15:02-Screening: Patients receive CBZ (b) HLA-B*15:02-Screening: for all patients: patients with a positive test result receive the alternative drug; negative tested patients receive CBZ (c) No HLA-B*15:02-Screening: all patients receive an alternative drug treatment |

**Note:**
- **ICER:** Incremental Cost-Effectiveness Ratio
- **N.S.:** Not significant
- **US$:** United States Dollars
- **€:** Euros
- **THB:** Thai Baht
- **QALY:** Quality-adjusted Life Year
- **LYG:** Life Years Gain
- **CFR:** Cost-Forfeiture Ratio
- **ADR:** Adverse Drug Reaction
- **CBZ:** Carbamazepine
- **AZA:** Azathioprine
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<th>Author(s)</th>
<th>USA/perspec tive n. s.</th>
<th>HIV/AIDS</th>
<th>First-line therapy</th>
<th>Abacavir-based treatment vs. tenofovir-based treatment</th>
<th>HLA-B*5701</th>
<th>First-year costs (price year 2010)</th>
<th>ICER (a) vs. (b): is dominated (higher costs + less effective) yes/no</th>
<th>National Institute of Allergy and Infectious Diseases; National Institute on Drug Abuse</th>
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<tbody>
<tr>
<td>Schackman, R, R., Scott, C., A., Walensky, R. P., et al. (2008)</td>
<td>[53]</td>
<td>[price year 2006]</td>
<td>(a) HLA-B<em>5701-testing: negative test result: abacavir-based treatment (abacavir + lamivudine + efavirenz); positive test result: tenofovir-based treatment (b) No HLA-B</em>5701-testing: abacavir-based therapy (abacavir + lamivudine + efavirenz); occurrence of HSR: further treatment with tenofovir-based treatment (c) No HLA-B*5701-testing: tenofovir-based therapy (tenofovir + emtricitabine + efavirenz); occurrence of nephrotoxicity: substituting abacavir and lamivudine</td>
<td>ICER (a) vs. (b): US$36,700 pro QALY, US$230,000 pro QALY ICER (c) vs. (b): is dominated (higher costs + less effective)</td>
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<td>Shiroiwa, T., Motoo, Y., Tsutani, K. (2010)</td>
<td>[54]</td>
<td>[price year 2010]</td>
<td>(a) KRAS wild-type receive cetuximab; patients with KRAS mutation receive BSC (b) no KRAS-testing: all patients receive cetuximab (c) no KRAS-testing: all patients receive BSC</td>
<td>ICER (a) vs. (c): US$160,000 pro LYG, US$210,000 pro QALY ICER (a) vs. (b): US$120,000 pro LYG, US$180,000 pro QALY ICER (a) vs. (b): dominant (lower cost with the same or better outcome) yes/no</td>
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<td>Thompson, A.J., Newman, A.G., Elliott, R.A., et al. (2014)</td>
<td>[12]</td>
<td>[price year 2009-2010]</td>
<td>(a) No TMPT-genotyping: combination therapy (US: cetuximab + irinotecan; Germany: cetuximab + FOLFIRI) Combination therapy (US: cetuximab + irinotecan; Germany: cetuximab + FOLFIRI); presence of TPMT levels (b) TMPT-genotyping: combination therapy (US: cetuximab + irinotecan; Germany: cetuximab + FOLFIRI); absence of TPMT levels Incremental costs (adjusted) for TPMT-genotyping: (b) vs. (a): £42.06 (US$65) Incremental QALY for TPMT-genotyping: (b) vs. (a): £0.008 Incremental net benefit (b) vs. (a): £56.89 ($81) yes/no</td>
<td>TARGET-Study: The Department of Health UK; A.J. Thompson: NIHR School for Primary Research; Prof. Payne-Research Councils UK (partly)</td>
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<tr>
<td>Vijayaraghavan, A., Elrasy, M., R., Goik, B., et al. (2012)</td>
<td>[55]</td>
<td>[price year 2009-2010]</td>
<td>(a) no KRAS-testing: panitumumab (b) KRAS-testing: panitumumab (c) no KRAS-testing: cetuximab (d) KRAS-testing: cetuximab (e) no KRAS-testing: combination therapy: USA: cetuximab + irinotecan, Germany: cetuximab + FOLFIRI (f) KRAS-testing: combination therapy: USA: cetuximab + irinotecan, Germany: cetuximab + FOLFIRI; (Assumption: patients with KRAS mutation will not receive chemotherapy) (g) KRAS-testing: combination therapy: USA: cetuximab + irinotecan, Germany: cetuximab + FOLFIRI; patients with KRAS mutation (wild type) receive irinotecan (US) and FOLFIRI (Germany)</td>
<td>ICER (b) vs. (a): dominant (lower costs + same effectiveness) ICER (d) vs. (c): dominant (lower costs + same effectiveness) ICER (f) vs. (e): less expensive + less effective = no ICER stated (g) vs. (e): lower costs + same effectiveness, no ICER stated ICER (g) vs. (f): US$35,539 pro LYS yes/yes</td>
<td>Roche Molecular Systems, Inc., United States (Roche)</td>
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<td>Winten, J., Walker, A., Shapiro, D., et al. (2004)</td>
<td>[56]</td>
<td>[price year n. s.]</td>
<td>(a) TMPT: Test: AZA dosing according to genotype/TPMT-activity: homozygote does not receive AZA, heterozygote receive a reduced dose AZA (b) no TMPT-Test: all patients receive AZA</td>
<td>ICER (a) vs. (b): £487 (US$776) per LYS for a 30 year old patient or £951 (US$1515) per LYS (for a 60 year old patient) yes/yes</td>
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Abbreviations: ICER: incremental cost-effectiveness ratio; LYS: life-year saved; LYG: life-year gained; QALY: quality adjusted life years; n.s.: not stated; HSR: hypersensitivity reaction; ADR: adverse drug reaction; THB: Thai Baht; CAD: Canadian Dollars

*As price year, the second year prior to the publication year, was assumed.
**Not calculated by the authors
***An average exchange rate of these two price years was calculated.