



## Annex A – Tables and Figure

*Table 1. Indications of the different treatments in each country*

| Treatment group                          | Indication Spain                                                   | Indication France <sup>I</sup>                                                   | Indication Norway    | Indication Germany                                                                                   | Indication United Kingdom |
|------------------------------------------|--------------------------------------------------------------------|----------------------------------------------------------------------------------|----------------------|------------------------------------------------------------------------------------------------------|---------------------------|
| Plain codeine                            | Respiratory (89.5%), Pain (2.3%), Unknown (7.8%), Digestive (0.3%) | Cough only<br>Marketing cessation in 2013 for last medicine with pain indication | Pain only            | GPs: Cough (71%), Pain (7%), Unknown (21%)<br>Paediatricians: Cough (78%), Pain (2%), Unknown (19%)  | Cough                     |
| Codeine + NSAID                          | Respiratory (83%), Unknown (9.6%), Pain (6.4%), Digestive (1.0%)   | Pain only                                                                        | Pain only            | GPs: Pain (52%), Cough (31%), Unknown (17%)<br>Paediatricians: Pain (66%), Cough (8%), Unknown (27%) | Acute moderate pain       |
| Codeine + sympathomimetic or expectorant |                                                                    | Cough only                                                                       | (Not marketed in NO) | Cough                                                                                                | Cough                     |
| Tramadol                                 | Pain (100%)                                                        | Pain                                                                             | Pain                 | Pain                                                                                                 | Pain                      |
| Dihydrocodeine                           | Respiratory (100%)                                                 | Pain                                                                             | Pain                 | GPs: Cough (78%), Pain (5%), Unknown (18%), Paediatricians: Cough (60%), Pain (3%), Unknown (37%)    | Pain                      |
| Hydromorphone                            | Pain musculoskeletal (89%), Pain other (11%)                       | Pain                                                                             | Pain                 | Pain                                                                                                 | Pain                      |
| Ibuprofen                                | Respiratory (74%), Pain musculoskeletal (20%), Pain other (6%)     | Pain and or fever                                                                | Pain                 | GPs: Pain (40%), Fever (8%), Unknown (52%)<br>Paediatricians: Pain (24%), Fever (18%), Unknown (58%) | Pain, Fever, Other        |
| Morphine                                 | Pain other (85%), Pain musculoskeletal (15%)                       | Pain                                                                             | Pain                 | Pain                                                                                                 | Pain                      |
| Oxycodone                                | Pain musculoskeletal (95%), Pain other (5%),                       | Pain                                                                             | Pain                 | Pain                                                                                                 | Pain                      |
| Tilidine/naloxone                        | NA*                                                                | Not marketed or not reimbursed                                                   | NA <sup>II</sup>     | Pain                                                                                                 | Not marketed              |
| Metamizole                               | Pain musculoskeletal (70%), Pain other (30%)                       | Not marketed or not reimbursed                                                   |                      | GPs: Pain (61%), Fever (1%), Unknown (38%)<br>Paediatricians: Pain (58%), Fever (6%), Unknown (36%)  | Not marketed              |



| Treatment group                    | Indication Spain   | Indication France <sup>I</sup> | Indication Norway         | Indication Germany | Indication United Kingdom |
|------------------------------------|--------------------|--------------------------------|---------------------------|--------------------|---------------------------|
| Dextromethorphan and ethylmorphine | Respiratory (100%) | Not marketed or not reimbursed | Cough only <sup>III</sup> |                    |                           |

\* Tilidine/naloxone and ethylmorphine containing medicines are not available in Spain.

<sup>T</sup> based on indications of these drugs in their Marketing Authorisation during the period of interest.

<sup>II</sup> Tilidine is not marketed in Norway and metamizole only for veterinarian use.

<sup>III</sup> Dextromethorphan is not marketed in Norway.

*Table 2 - List of treatment groups/sub-groups included in the analysis including the breakdown of exposure data by sub-group in France, Norway, Germany, Spain and United Kingdom*

| France                                    |                                                                                                                 |                           |                                             |
|-------------------------------------------|-----------------------------------------------------------------------------------------------------------------|---------------------------|---------------------------------------------|
| Treatment group                           | Treatment sub-group                                                                                             | <i>n</i><br>Prescriptions | Within treatment<br>group proportion<br>(%) |
| 1. Codeine-containing products            | 1.1 Plain codeine                                                                                               | 1 011 404                 | 32,94                                       |
|                                           | 1.2 Codeine in combination with an analgesic or NSAID*                                                          | 1 341 331                 | 43,69                                       |
|                                           | 1.3 Codeine in combination with a sympathomimetic or expectorant                                                | 572 413                   | 18,64                                       |
|                                           | 1.4. Codeine in all other combinations (except opium)                                                           | 144 941                   | 4,72                                        |
| 2. Opioid antitussives, excluding codeine | 2.1. Dextromethorphan, incl. combinations with other agents                                                     | 4 475 212                 | 38,00                                       |
|                                           | 2.2 Ethylmorphine, incl. combinations with other agents                                                         | 7436                      | 0,06                                        |
|                                           | 2.3 Pholcodine, incl. combinations with other agents                                                            | 7 293 138                 | 61,93                                       |
|                                           | 2.4 Dihydrocodeine, incl. combinations where indicated for cough                                                | -                         | -                                           |
|                                           | 2.5. Opium derivatives and expectorants                                                                         | -                         | -                                           |
| 3. Opioid analgesics, excluding codeine   | 3.1 Hydromorphone, incl. combination with non-opioids                                                           | 124                       | 0,01                                        |
|                                           | 3.2 Morphine (incl. opium), incl. combination with non-opioids                                                  | 315674                    | 20,58                                       |
|                                           | 3.3 Oxycodone, incl. combination with non-opioids                                                               | 5366                      | 0,35                                        |
|                                           | 3.4 Tilidine/naloxone, incl. combination with non-opioids                                                       | -                         | -                                           |
|                                           | 3.5 Tramadol, incl. combination with non-opioids                                                                | 1 199 599                 | 78,21                                       |
|                                           | 3.6 Dihydrocodeine, incl. combination with non-opioids                                                          | 1347                      | 0,09                                        |
|                                           | 3.7 Buprenorphine, incl. combination preparations                                                               | 7642                      | 0,50                                        |
|                                           | 3.8 Diamorphine                                                                                                 | -                         | -                                           |
|                                           | 3.9 Fentanyl, transdermal, buccal or nasal administration only                                                  | 4139                      | 0,27                                        |
| 4. Non-opioid analgesics                  | 4.1 Metamizole, incl. combination with other non-opioid analgesics*                                             | -                         | -                                           |
|                                           | 4.2 Prescribed non-topical ibuprofen, incl. combination with other non-opioid analgesics except metamizole*     | 27 869 776                | 15,68                                       |
|                                           | 4.3 Prescribed paracetamol, incl. combination with other non-opioid analgesics except metamizole and ibuprofen* | 149 841 789               | 84,32                                       |
| 5. Non-opioid antitussives                | 5.1 Simple linctus, incl. simple linctus paediatric                                                             | -                         | -                                           |
|                                           | 5.2 Other non-opioid antitussives                                                                               | 17 267 047                | 100,00                                      |

| Norway                                    |                                                                                                                 |                           |                                             |
|-------------------------------------------|-----------------------------------------------------------------------------------------------------------------|---------------------------|---------------------------------------------|
| Treatment group                           | Treatment sub-group                                                                                             | <i>n</i><br>Prescriptions | Within treatment<br>group proportion<br>(%) |
| 1. Codeine-containing products            | 1.1 Plain codeine                                                                                               | 1726                      | 2.40                                        |
|                                           | 1.2 Codeine in combination with an analgesic or NSAID*                                                          | 71 084                    | 97.60                                       |
|                                           | 1.3 Codeine in combination with a sympathomimetic or expectorant                                                | -                         | -                                           |
|                                           | 1.4. Codeine in all other combinations (except opium)                                                           | -                         | -                                           |
| 2. Opioid antitussives, excluding codeine | 2.1. Dextromethorphan, incl. combinations with other agents                                                     | -                         | -                                           |
|                                           | 2.2 Ethylmorphine, incl. combinations with other agents                                                         | 222 639                   | 85.40                                       |
|                                           | 2.3 Pholcodine, incl. combinations with other agents                                                            | -                         | -                                           |
|                                           | 2.4 Dihydrocodeine, incl. combinations where indicated for cough                                                | -                         | -                                           |
|                                           | 2.5. Opium derivatives and expectorants                                                                         | 37 990                    | 14.60                                       |
| 3. Opioid analgesics, excluding codeine   | 3.1 Hydromorphone, incl. combination with non-opioids                                                           | -                         | -                                           |
|                                           | 3.2 Morphine (incl. opium), incl. combination with non-opioids                                                  | 901                       | 4.70                                        |
|                                           | 3.3 Oxycodone, incl. combination with non-opioids                                                               | 1861                      | 9.80                                        |
|                                           | 3.4 Tilidine/naloxone, incl. combination with non-opioids                                                       | -                         | -                                           |
|                                           | 3.5 Tramadol, incl. combination with non-opioids                                                                | 15 836                    | 84.50                                       |
|                                           | 3.6 Dihydrocodeine, incl. combination with non-opioids                                                          |                           |                                             |
|                                           | 3.7 Buprenorphine, incl. combination preparations                                                               | 245                       | 1.30                                        |
|                                           | 3.8 Diamorphine                                                                                                 |                           |                                             |
|                                           | 3.9 Fentanyl, transdermal, buccal or nasal administration only                                                  | 137                       | 0.70                                        |
| 4. Non-opioid analgesics                  | 4.1 Metamizole, incl. combination with other non-opioid analgesics*                                             | -                         | -                                           |
|                                           | 4.2 Prescribed non-topical ibuprofen, incl. combination with other non-opioid analgesics except metamizole*     | 84 587                    | 56.80                                       |
|                                           | 4.3 Prescribed paracetamol, incl. combination with other non-opioid analgesics except metamizole and ibuprofen* | 64 361                    | 43.20                                       |
| 5. Non-opioid antitussives                | 5.1 Simple linctus, incl. simple linctus paediatric                                                             | -                         | -                                           |
|                                           | 5.2 Other non-opioid antitussives                                                                               | -                         | -                                           |

## Germany

| Treatment group                           | Treatment sub-group                                                                                             | n Prescriptions | Within treatment group proportion (%) |
|-------------------------------------------|-----------------------------------------------------------------------------------------------------------------|-----------------|---------------------------------------|
| 1. Codeine-containing products            | 1.1 Plain codeine                                                                                               | 61 966          | 91.84                                 |
|                                           | 1.2 Codeine in combination with an analgesic or NSAID*                                                          | 5412            | 8.02                                  |
|                                           | 1.3 Codeine in combination with a sympathomimetic or expectorant                                                | 97              | 0.14                                  |
|                                           | 1.4. Codeine in all other combinations (except opium)                                                           | 0               |                                       |
| 2. Opioid antitussives, excluding codeine | 2.1. Dextromethorphan, incl. combinations with other agents                                                     | 25 863          | 43.42                                 |
|                                           | 2.2 Ethylmorphine, incl. combinations with other agents                                                         | 0               |                                       |
|                                           | 2.3 Pholcodine, incl. combinations with other agents                                                            | 0               |                                       |
|                                           | 2.4 Dihydrocodeine, incl. combinations where indicated for cough                                                | 33 702          | 56.58                                 |
|                                           | 2.5. Opium derivatives and expectorants                                                                         | 0               |                                       |
| 3. Opioid analgesics, excluding codeine   | 3.1 Hydromorphone, incl. combination with non-opioids                                                           | 50              | 1.28                                  |
|                                           | 3.2 Morphine (incl. opium), incl. combination with non-opioids                                                  | 952             | 24.38                                 |
|                                           | 3.3 Oxycodone, incl. combination with non-opioids                                                               | 160             | 4.10                                  |
|                                           | 3.4 Tilidine/naloxone, incl. combination with non-opioids                                                       | 327             | 8.37                                  |
|                                           | 3.5 Tramadol, incl. combination with non-opioids                                                                | 2166            | 55.47                                 |
|                                           | 3.6 Dihydrocodeine, incl. combination with non-opioids                                                          | 0               |                                       |
|                                           | 3.7 Buprenorphine, incl. combination preparations                                                               | 133             | 3.41                                  |
|                                           | 3.8 Diamorphine                                                                                                 | 0               |                                       |
|                                           | 3.9 Fentanyl, transdermal, buccal or nasal administration only                                                  | 117             | 3.00                                  |
| 4. Non-opioid analgesics                  | 4.1 Metamizole, incl. combination with other non-opioid analgesics*                                             | 54 555          | 1.41                                  |
|                                           | 4.2 Prescribed non-topical ibuprofen, incl. combination with other non-opioid analgesics except metamizole*     | 2 530 754       | 65.33                                 |
|                                           | 4.3 Prescribed paracetamol, incl. combination with other non-opioid analgesics except metamizole and ibuprofen* | 1 288 643       | 33.26                                 |
| 5. Non-opioid antitussives                | 5.1 Simple linctus, incl. simple linctus paediatric                                                             | 3 427 154       | 100.00                                |
|                                           | 5.2 Other non-opioid antitussives                                                                               |                 |                                       |

| Spain                                     |                                                                                                                 |                           |                                             |
|-------------------------------------------|-----------------------------------------------------------------------------------------------------------------|---------------------------|---------------------------------------------|
| Treatment group                           | Treatment sub-group                                                                                             | <i>n</i><br>Prescriptions | Within treatment<br>group proportion<br>(%) |
| 1. Codeine-containing products            | 1.1 Plain codeine                                                                                               | 109 157                   | 41.86                                       |
|                                           | 1.2 Codeine in combination with an analgesic or NSAID*                                                          | 151 533                   | 58.11                                       |
|                                           | 1.3 Codeine in combination with a sympathomimetic or expectorant                                                | 101                       | 0.04                                        |
|                                           | 1.4. Codeine in all other combinations (except opium)                                                           | 0                         | 0                                           |
| 2. Opioid antitussives, excluding codeine | 2.1. Dextromethorphan, incl. combinations with other agents                                                     | 146 389                   | 93.91                                       |
|                                           | 2.2 Ethylmorphine, incl. combinations with other agents                                                         | 0                         | 0                                           |
|                                           | 2.3 Pholcodine, incl. combinations with other agents                                                            | 0                         | 0                                           |
|                                           | 2.4 Dihydrocodeine, incl. combinations where indicated for cough                                                | 9495                      | 6.10                                        |
| 3. Opioid analgesics, excluding codeine   | 3.1 Hydromorphone, incl. combination with non-opioids                                                           | 10                        | 0.16                                        |
|                                           | 3.2 Morphine (incl. opium), incl. combination with non-opioids                                                  | 152                       | 2.45                                        |
|                                           | 3.3 Oxycodone, incl. combination with non-opioids                                                               | 69                        | 1.11                                        |
|                                           | 3.4 Tilidine/naloxone, incl. combination with non-opioids                                                       | 0                         | 0                                           |
|                                           | 3.5 Tramadol, incl. combination with non-opioids                                                                | 5722                      | 92.17                                       |
|                                           | 3.6 Dihydrocodeine, incl. combination with non-opioids                                                          | 0                         | 0                                           |
|                                           | 3.7 Buprenorphine, incl. combination preparations                                                               | 18                        | 0.29                                        |
|                                           | 3.8 Diamorphine                                                                                                 | 0                         | 0                                           |
|                                           | 3.9 Fentanyl, transdermal, buccal or nasal administration only                                                  | 237                       | 3.82                                        |
| 4. Non-opioid analgesics                  | 4.1 Metamizole, incl. combination with other non-opioid analgesics*                                             | 152 549                   | 1.82                                        |
|                                           | 4.2 Prescribed non-topical ibuprofen, incl. combination with other non-opioid analgesics except metamizole*     | 5 142 788                 | 61.45                                       |
|                                           | 4.3 Prescribed paracetamol, incl. combination with other non-opioid analgesics except metamizole and ibuprofen* | 3 073 384                 | 36.72                                       |
| 5. Non-opioid antitussives                | 5.1 Simple linctus, incl. simple linctus paediatric                                                             | 0                         | 0                                           |
|                                           | 5.2 Other non-opioid antitussives                                                                               | 50 6263                   | 100                                         |

## United Kingdom

| Treatment group                           | Treatment sub-group                                                                                             | <i>n</i><br>Prescriptions | Within treatment<br>group proportion<br>(%) |
|-------------------------------------------|-----------------------------------------------------------------------------------------------------------------|---------------------------|---------------------------------------------|
| 1. Codeine-containing products            | 1.1 Plain codeine                                                                                               | 29 073                    | 25.10                                       |
|                                           | 1.2 Codeine in combination with an analgesic or NSAID*                                                          | 86 768                    | 74.90                                       |
|                                           | 1.3 Codeine in combination with a sympathomimetic or expectorant                                                | 5                         | 0.0                                         |
|                                           | 1.4. Codeine in all other combinations (except opium)                                                           | -                         | -                                           |
| 2. Opioid antitussives, excluding codeine | 2.1. Dextromethorphan, incl. combinations with other agents                                                     | 184                       | 0.4                                         |
|                                           | 2.2 Ethylmorphine, incl. combinations with other agents                                                         | -                         | -                                           |
|                                           | 2.3 Pholcodine, incl. combinations with other agents                                                            | 42 223                    | 99.60                                       |
|                                           | 2.4 Dihydrocodeine, incl. combinations where indicated for cough                                                | -                         | -                                           |
| 3. Opioid analgesics, excluding codeine   | 3.1 Hydromorphone, incl. combination with non-opioids                                                           | -                         | -                                           |
|                                           | 3.2 Morphine (incl. opium), incl. combination with non-opioids                                                  | 5 073                     | 18.70                                       |
|                                           | 3.3 Oxycodone, incl. combination with non-opioids                                                               | 851                       | 3.10                                        |
|                                           | 3.4 Tilidine/naloxone, incl. combination with non-opioids                                                       | -                         | -                                           |
|                                           | 3.5 Tramadol, incl. combination with non-opioids                                                                | 7 587                     | 28.00                                       |
|                                           | 3.6 Dihydrocodeine, incl. combination with non-opioids                                                          | 11 356                    | 41.90                                       |
|                                           | 3.7 Buprenorphine, incl. combination preparations                                                               | 781                       | 2.90                                        |
|                                           | 3.8 Diamorphine                                                                                                 | 258                       | 1.00                                        |
|                                           | 3.9 Fentanyl, transdermal, buccal or nasal administration only                                                  | 1 204                     | 4.40                                        |
| 4. Non-opioid analgesics                  | 4.1 Metamizole, incl. combination with other non-opioid analgesics*                                             | -                         | -                                           |
|                                           | 4.2 Prescribed non-topical ibuprofen, incl. combination with other non-opioid analgesics except metamizole*     | 729 036                   | 31.00                                       |
|                                           | 4.3 Prescribed paracetamol, incl. combination with other non-opioid analgesics except metamizole and ibuprofen* | 1 620 364                 | 69.00                                       |
| 5. Non-opioid antitussives                | 5.1 Simple linctus, incl. simple linctus paediatric                                                             | 117 691                   | 100.00                                      |
|                                           | 5.2 Other non-opioid antitussives                                                                               | -                         | -                                           |

*Table 3. Number of children below 18 years of age per treatment group by quarter in France, Norway, Germany, Spain and United Kingdom, between 2010-2017*

| France         |                             |                                       |                                      |                       |                         |                                             |
|----------------|-----------------------------|---------------------------------------|--------------------------------------|-----------------------|-------------------------|---------------------------------------------|
| Year / Quarter | Treatment groups            |                                       |                                      |                       |                         | Total population N < 18 YOA in person years |
|                | Codeine-Containing products | Opioid antitussive, excluding codeine | Opioid analgesics, excluding codeine | Non-opioid analgesics | Non-opioid antitussives |                                             |
| 2010Q1         | 116140                      | 382151                                | 31594                                | 4075485               | 875570                  | 3216071                                     |
| 2010Q2         | 110534                      | 256716                                | 31239                                | 3632020               | 477317                  | 3251805                                     |
| 2010Q3         | 89157                       | 208296                                | 26475                                | 3183378               | 307940                  | 3287539                                     |
| 2010Q4         | 127324                      | 480520                                | 31206                                | 4357604               | 634176                  | 3287539                                     |
| 2011Q1         | 147803                      | 642917                                | 34817                                | 5080346               | 721702                  | 3233738                                     |
| 2011Q2         | 120834                      | 233582                                | 36464                                | 3655109               | 331552                  | 3269668                                     |
| 2011Q3         | 97203                       | 196604                                | 30027                                | 3219275               | 307773                  | 3305599                                     |
| 2011Q4         | 151025                      | 451415                                | 36317                                | 4452653               | 657350                  | 3305599                                     |
| 2012Q1         | 152785                      | 468495                                | 35161                                | 4617349               | 629712                  | 3247921                                     |
| 2012Q2         | 128835                      | 238414                                | 33726                                | 3646856               | 354147                  | 3247921                                     |
| 2012Q3         | 109995                      | 188994                                | 29220                                | 3223576               | 290738                  | 3283612                                     |
| 2012Q4         | 167655                      | 439646                                | 35693                                | 4549315               | 642349                  | 3283612                                     |
| 2013Q1         | 170982                      | 598476                                | 34785                                | 5158272               | 761379                  | 3232418                                     |
| 2013Q2         | 124475                      | 259758                                | 36330                                | 3670511               | 378277                  | 3268333                                     |
| 2013Q3         | 77681                       | 190561                                | 35408                                | 3365664               | 294624                  | 3304249                                     |
| 2013Q4         | 83024                       | 390597                                | 46160                                | 4313989               | 581673                  | 3304249                                     |
| 2014Q1         | 84389                       | 447928                                | 49193                                | 4500505               | 592974                  | 3245798                                     |
| 2014Q2         | 59823                       | 229082                                | 50627                                | 3599573               | 334760                  | 3281862                                     |
| 2014Q3         | 49792                       | 184881                                | 44481                                | 3211407               | 282220                  | 3317927                                     |
| 2014Q4         | 70736                       | 431670                                | 54150                                | 4362999               | 620862                  | 3317927                                     |
| 2015Q1         | 85468                       | 612673                                | 52703                                | 5010752               | 766621                  | 3261978                                     |
| 2015Q2         | 52329                       | 219073                                | 52740                                | 3484201               | 325078                  | 3298223                                     |
| 2015Q3         | 47094                       | 211265                                | 47302                                | 3361030               | 327446                  | 3334467                                     |
| 2015Q4         | 60980                       | 396091                                | 57272                                | 4281518               | 584485                  | 3334467                                     |
| 2016Q1         | 71327                       | 586145                                | 58110                                | 5128836               | 776400                  | 3310763                                     |
| 2016Q2         | 49787                       | 237423                                | 58529                                | 3672844               | 351106                  | 3310763                                     |
| 2016Q3         | 40519                       | 166794                                | 50232                                | 3147382               | 260949                  | 3347145                                     |
| 2016Q4         | 61511                       | 453286                                | 58988                                | 4448987               | 645235                  | 3347145                                     |
| 2017Q1         | 63875                       | 435728                                | 60170                                | 4419671               | 577363                  | 3294805                                     |
| 2017Q2         | 44782                       | 166096                                | 60304                                | 3327569               | 257673                  | 3331414                                     |
| 2017Q3         | 40803                       | 197668                                | 51071                                | 3217102               | 315314                  | 3368023                                     |
| 2017Q4         | 52263                       | 393337                                | 58328                                | 4272397               | 619632                  | 3368023                                     |



| Norway         |                             |                                       |                                      |                       |                         |                                             |
|----------------|-----------------------------|---------------------------------------|--------------------------------------|-----------------------|-------------------------|---------------------------------------------|
| Year / Quarter | Treatment groups            |                                       |                                      |                       |                         | Total population N < 18 YOA in person years |
|                | Codeine-Containing products | Opioid antitussive, excluding codeine | Opioid analgesics, excluding codeine | Non-opioid analgesics | Non-opioid antitussives |                                             |
| 2010Q1         | 2287                        | 10233                                 | 239                                  | 3399                  | NR                      | 4498243                                     |
| 2010Q2         | 2185                        | 6165                                  | 248                                  | 3251                  | NR                      | 4448812                                     |
| 2010Q3         | 1850                        | 4914                                  | 250                                  | 3066                  | NR                      | 4400455                                     |
| 2010Q4         | 2553                        | 12265                                 | 321                                  | 3851                  | NR                      | 4400455                                     |
| 2011Q1         | 2391                        | 13117                                 | 318                                  | 3930                  | NR                      | 4519405                                     |
| 2011Q2         | 2268                        | 5535                                  | 279                                  | 3250                  | NR                      | 4469741                                     |
| 2011Q3         | 2115                        | 5978                                  | 299                                  | 3095                  | NR                      | 4421157                                     |
| 2011Q4         | 2723                        | 17056                                 | 378                                  | 4212                  | NR                      | 4421157                                     |
| 2012Q1         | 2650                        | 15547                                 | 349                                  | 4184                  | NR                      | 4547448                                     |
| 2012Q2         | 2415                        | 5754                                  | 360                                  | 3435                  | NR                      | 4497476                                     |
| 2012Q3         | 2076                        | 4282                                  | 363                                  | 3205                  | NR                      | 4448590                                     |
| 2012Q4         | 2818                        | 9645                                  | 473                                  | 4181                  | NR                      | 4448590                                     |
| 2013Q1         | 2446                        | 12563                                 | 377                                  | 3913                  | NR                      | 4553971                                     |
| 2013Q2         | 2448                        | 4998                                  | 396                                  | 3551                  | NR                      | 4503927                                     |
| 2013Q3         | 1940                        | 3479                                  | 381                                  | 3317                  | NR                      | 4454971                                     |
| 2013Q4         | 2465                        | 6717                                  | 500                                  | 4485                  | NR                      | 4454971                                     |
| 2014Q1         | 1888                        | 8161                                  | 408                                  | 4257                  | NR                      | 4563152                                     |
| 2014Q2         | 1824                        | 4974                                  | 522                                  | 4218                  | NR                      | 4513008                                     |
| 2014Q3         | 1458                        | 4175                                  | 449                                  | 3726                  | NR                      | 4463953                                     |
| 2014Q4         | 1846                        | 9873                                  | 607                                  | 4957                  | NR                      | 4463953                                     |
| 2015Q1         | 1480                        | 11233                                 | 493                                  | 4627                  | NR                      | 4564949                                     |
| 2015Q2         | 1412                        | 4539                                  | 585                                  | 4061                  | NR                      | 4514785                                     |
| 2015Q3         | 1248                        | 3311                                  | 505                                  | 3655                  | NR                      | 4465711                                     |
| 2015Q4         | 1657                        | 8443                                  | 692                                  | 4830                  | NR                      | 4465711                                     |
| 2016Q1         | 1345                        | 9854                                  | 500                                  | 4784                  | NR                      | 4584768                                     |
| 2016Q2         | 1424                        | 4846                                  | 657                                  | 4666                  | NR                      | 4534386                                     |
| 2016Q3         | 1195                        | 4946                                  | 576                                  | 4101                  | NR                      | 4485099                                     |
| 2016Q4         | 1610                        | 11164                                 | 716                                  | 5533                  | NR                      | 4485099                                     |
| 2017Q1         | 1272                        | 10108                                 | 589                                  | 5442                  | NR                      | 4587040                                     |
| 2017Q2         | 1265                        | 5709                                  | 652                                  | 4821                  | NR                      | 4536633                                     |
| 2017Q3         | 1140                        | 4503                                  | 606                                  | 4665                  | NR                      | 4487321                                     |
| 2017Q4         | 1537                        | 9370                                  | 830                                  | 6231                  | NR                      | 4487321                                     |

| Germany        |                             |                                       |                                      |                       |                         |                                             |
|----------------|-----------------------------|---------------------------------------|--------------------------------------|-----------------------|-------------------------|---------------------------------------------|
| Year / Quarter | Treatment groups            |                                       |                                      |                       |                         | Total population N < 18 YOA in person years |
|                | Codeine-Containing products | Opioid antitussive, excluding codeine | Opioid analgesics, excluding codeine | Non-opioid analgesics | Non-opioid antitussives |                                             |
| 2010Q1         | 2604                        | 1792                                  | 997                                  | 62998                 | 71348                   | 108475                                      |
| 2010Q2         | 1554                        | 1371                                  | 616                                  | 49854                 | 44820                   | 113239                                      |
| 2010Q3         | 1288                        | 1024                                  | 485                                  | 51134                 | 39136                   | 117072                                      |
| 2010Q4         | 3312                        | 2070                                  | 1243                                 | 78619                 | 87728                   | 125051                                      |
| 2011Q1         | 4147                        | 2157                                  | 1650                                 | 102386                | 98590                   | 125835                                      |
| 2011Q2         | 1517                        | 879                                   | 575                                  | 59533                 | 45448                   | 132362                                      |
| 2011Q3         | 1448                        | 874                                   | 679                                  | 67122                 | 50608                   | 138604                                      |
| 2011Q4         | 4156                        | 2116                                  | 1469                                 | 90982                 | 99720                   | 145600                                      |
| 2012Q1         | 3852                        | 2022                                  | 1517                                 | 98271                 | 96839                   | 142795                                      |
| 2012Q2         | 1859                        | 952                                   | 770                                  | 69932                 | 54059                   | 146809                                      |
| 2012Q3         | 1453                        | 712                                   | 668                                  | 70498                 | 47192                   | 153725                                      |
| 2012Q4         | 3131                        | 1613                                  | 1201                                 | 97521                 | 95149                   | 161079                                      |
| 2013Q1         | 5864                        | 2543                                  | 2513                                 | 148427                | 136239                  | 157873                                      |
| 2013Q2         | 1903                        | 912                                   | 910                                  | 85932                 | 65440                   | 166524                                      |
| 2013Q3         | 1470                        | 269                                   | 707                                  | 88857                 | 55688                   | 173808                                      |
| 2013Q4         | 2966                        | 239                                   | 1125                                 | 102871                | 93955                   | 179129                                      |
| 2014Q1         | 3803                        | 147                                   | 1425                                 | 118218                | 109553                  | 172215                                      |
| 2014Q2         | 1748                        | 95                                    | 764                                  | 88971                 | 62226                   | 177567                                      |
| 2014Q3         | 1308                        | 73                                    | 677                                  | 89775                 | 53830                   | 183484                                      |
| 2014Q4         | 2673                        | 123                                   | 1584                                 | 117842                | 107914                  | 188161                                      |
| 2015Q1         | 3555                        | 206                                   | 2543                                 | 152759                | 133355                  | 179367                                      |
| 2015Q2         | 884                         | 55                                    | 728                                  | 88343                 | 59544                   | 183732                                      |
| 2015Q3         | 603                         | 69                                    | 552                                  | 94829                 | 54587                   | 188288                                      |
| 2015Q4         | 769                         | 131                                   | 1009                                 | 118878                | 99301                   | 191701                                      |
| 2016Q1         | 965                         | 202                                   | 1511                                 | 157899                | 127706                  | 184028                                      |
| 2016Q2         | 468                         | 95                                    | 700                                  | 100640                | 60872                   | 184895                                      |
| 2016Q3         | 382                         | 87                                    | 507                                  | 96764                 | 51562                   | 187677                                      |
| 2016Q4         | 881                         | 199                                   | 1130                                 | 127806                | 106893                  | 188387                                      |
| 2017Q1         | 1037                        | 239                                   | 1409                                 | 145368                | 120851                  | 176449                                      |
| 2017Q2         | 390                         | 83                                    | 531                                  | 91980                 | 54302                   | 177163                                      |
| 2017Q3         | 358                         | 78                                    | 534                                  | 95987                 | 55291                   | 177610                                      |
| 2017Q4         | 683                         | 163                                   | 850                                  | 115286                | 90437                   | 176126                                      |

| Spain          |                             |                                       |                                      |                       |                         |                                             |
|----------------|-----------------------------|---------------------------------------|--------------------------------------|-----------------------|-------------------------|---------------------------------------------|
| Year / Quarter | Treatment groups            |                                       |                                      |                       |                         | Total population N < 18 YOA in person years |
|                | Codeine-Containing products | Opioid antitussive, excluding codeine | Opioid analgesics, excluding codeine | Non-opioid analgesics | Non-opioid antitussives |                                             |
| 2010Q1         | 14197                       | 14012                                 | 125                                  | 177789                | 44064                   | 247655                                      |
| 2010Q2         | 9902                        | 9858                                  | 147                                  | 163865                | 32829                   | 254214                                      |
| 2010Q3         | 5262                        | 6106                                  | 103                                  | 124272                | 18802                   | 258970                                      |
| 2010Q4         | 14346                       | 15615                                 | 124                                  | 190345                | 48171                   | 261432                                      |
| 2011Q1         | 21604                       | 17454                                 | 129                                  | 246338                | 61519                   | 259216                                      |
| 2011Q2         | 9206                        | 8684                                  | 136                                  | 172080                | 30296                   | 262872                                      |
| 2011Q3         | 4883                        | 5692                                  | 109                                  | 132504                | 19100                   | 267199                                      |
| 2011Q4         | 12906                       | 15637                                 | 127                                  | 199139                | 48226                   | 267969                                      |
| 2012Q1         | 20535                       | 16778                                 | 172                                  | 275520                | 62676                   | 317270                                      |
| 2012Q2         | 8121                        | 8181                                  | 153                                  | 204067                | 29284                   | 326986                                      |
| 2012Q3         | 3239                        | 2679                                  | 123                                  | 144953                | 8012                    | 335766                                      |
| 2012Q4         | 6942                        | 2047                                  | 159                                  | 220527                | 3483                    | 339725                                      |
| 2013Q1         | 8712                        | 1641                                  | 145                                  | 275398                | 3839                    | 335169                                      |
| 2013Q2         | 4635                        | 980                                   | 171                                  | 202161                | 2776                    | 340271                                      |
| 2013Q3         | 2501                        | 472                                   | 132                                  | 156049                | 1589                    | 344869                                      |
| 2013Q4         | 6302                        | 1253                                  | 177                                  | 223851                | 3703                    | 345437                                      |
| 2014Q1         | 8803                        | 1427                                  | 189                                  | 255563                | 4183                    | 331333                                      |
| 2014Q2         | 3599                        | 1076                                  | 171                                  | 198336                | 2886                    | 335608                                      |
| 2014Q3         | 2585                        | 782                                   | 127                                  | 143443                | 1931                    | 340329                                      |
| 2014Q4         | 6851                        | 2007                                  | 168                                  | 218316                | 5053                    | 341100                                      |
| 2015Q1         | 12422                       | 2529                                  | 181                                  | 283517                | 6560                    | 332150                                      |
| 2015Q2         | 3382                        | 1017                                  | 147                                  | 180132                | 2664                    | 335806                                      |
| 2015Q3         | 2897                        | 674                                   | 135                                  | 143007                | 1656                    | 339136                                      |
| 2015Q4         | 6068                        | 1752                                  | 202                                  | 206736                | 3866                    | 339509                                      |
| 2016Q1         | 9418                        | 2168                                  | 178                                  | 260839                | 4791                    | 332647                                      |
| 2016Q2         | 4525                        | 1119                                  | 178                                  | 203727                | 2633                    | 330877                                      |
| 2016Q3         | 2747                        | 602                                   | 141                                  | 141387                | 1414                    | 333708                                      |
| 2016Q4         | 7772                        | 1632                                  | 161                                  | 217023                | 3680                    | 333971                                      |
| 2017Q1         | 8755                        | 1677                                  | 223                                  | 231195                | 4036                    | 320316                                      |
| 2017Q2         | 3186                        | 900                                   | 220                                  | 176220                | 2051                    | 323677                                      |
| 2017Q3         | 3320                        | 675                                   | 162                                  | 143690                | 1530                    | 327006                                      |
| 2017Q4         | 7295                        | 1383                                  | 179                                  | 211049                | 3364                    | 326748                                      |

| United Kingdom |                             |                                       |                                      |                       |                         |                                             |
|----------------|-----------------------------|---------------------------------------|--------------------------------------|-----------------------|-------------------------|---------------------------------------------|
| Year / Quarter | Treatment groups            |                                       |                                      |                       |                         | Total population N < 18 YOA in person years |
|                | Codeine-Containing products | Opioid antitussive, excluding codeine | Opioid analgesics, excluding codeine | Non-opioid analgesics | Non-opioid antitussives |                                             |
| 2010Q1         | 3041                        | 1457                                  | 477                                  | 55752                 | 3540                    | 274994                                      |
| 2010Q2         | 2689                        | 859                                   | 441                                  | 46907                 | 2309                    | 279825                                      |
| 2010Q3         | 1882                        | 554                                   | 307                                  | 37481                 | 1595                    | 270846                                      |
| 2010Q4         | 2590                        | 1759                                  | 377                                  | 63346                 | 5657                    | 275384                                      |
| 2011Q1         | 2958                        | 1370                                  | 448                                  | 58414                 | 4283                    | 273738                                      |
| 2011Q2         | 2585                        | 637                                   | 482                                  | 42694                 | 2267                    | 280788                                      |
| 2011Q3         | 1995                        | 515                                   | 320                                  | 36250                 | 1766                    | 272755                                      |
| 2011Q4         | 2325                        | 1300                                  | 368                                  | 52345                 | 4711                    | 276142                                      |
| 2012Q1         | 2951                        | 1294                                  | 462                                  | 57969                 | 4462                    | 278552                                      |
| 2012Q2         | 2534                        | 702                                   | 464                                  | 43100                 | 2478                    | 281975                                      |
| 2012Q3         | 1892                        | 494                                   | 303                                  | 33987                 | 1743                    | 273810                                      |
| 2012Q4         | 2404                        | 1049                                  | 375                                  | 52973                 | 4543                    | 275804                                      |
| 2013Q1         | 2585                        | 854                                   | 423                                  | 49577                 | 3398                    | 272334                                      |
| 2013Q2         | 2432                        | 439                                   | 444                                  | 37405                 | 2093                    | 276374                                      |
| 2013Q3         | 1661                        | 233                                   | 298                                  | 29306                 | 1356                    | 265903                                      |
| 2013Q4         | 1974                        | 501                                   | 352                                  | 41454                 | 3351                    | 261779                                      |
| 2014Q1         | 2309                        | 509                                   | 388                                  | 41513                 | 2880                    | 257708                                      |
| 2014Q2         | 2066                        | 310                                   | 414                                  | 32465                 | 1810                    | 261429                                      |
| 2014Q3         | 1505                        | 200                                   | 275                                  | 24304                 | 1088                    | 247194                                      |
| 2014Q4         | 1853                        | 560                                   | 323                                  | 39160                 | 3311                    | 242228                                      |
| 2015Q1         | 2113                        | 458                                   | 361                                  | 36503                 | 2472                    | 232309                                      |
| 2015Q2         | 1663                        | 216                                   | 315                                  | 25026                 | 1263                    | 228964                                      |
| 2015Q3         | 1174                        | 135                                   | 287                                  | 21357                 | 943                     | 217229                                      |
| 2015Q4         | 1383                        | 327                                   | 310                                  | 29038                 | 2344                    | 206177                                      |
| 2016Q1         | 1633                        | 369                                   | 321                                  | 27880                 | 1627                    | 199719                                      |
| 2016Q2         | 1417                        | 179                                   | 332                                  | 19841                 | 958                     | 197798                                      |
| 2016Q3         | 851                         | 130                                   | 216                                  | 14264                 | 626                     | 183491                                      |
| 2016Q4         | 1093                        | 278                                   | 229                                  | 19918                 | 1765                    | 182071                                      |
| 2017Q1         | 1248                        | 216                                   | 243                                  | 17691                 | 1144                    | 175269                                      |
| 2017Q2         | 1072                        | 97                                    | 232                                  | 12418                 | 541                     | 174500                                      |
| 2017Q3         | 741                         | 63                                    | 159                                  | 10100                 | 515                     | 165632                                      |
| 2017Q4         | 896                         | 133                                   | 192                                  | 14390                 | 1226                    | 162633                                      |

Figure section 6.3 - Prevalence of use of codeine and alternative medicines (patient level) for all children 0-17 years of age, in Spain, 2010-2017

