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# Appendix

**Use of valproate in pregnancy and in women of childbearing age between 2014 and 2018 in Switzerland: a retrospective analysis of Swiss health care claims data**

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## Appendix 1: Inpatient and outpatient codes for identification of deliveries in the health care claims database of the Helsana group

- **TARMED codes**: 22.2110, 22.2120, 22.2130, 22.2140, 22.2150, 22.2160, 22.2170, 22.2180, 22.2190, 22.2200, 22.2210, 22.2410, 22.2420
- **DRG Codes**: O01A, O01B, O01C, O01D, O01E, O01F, O01G, O01H, O02A, O02B, O60A, O60B, O60C, O60D
- **Midwife codes**: B1, B2, B3, B4

## Appendix 2: Estimation of the number of women with an absolute indication for valproate during pregnancy in Switzerland

*The prevalence of epilepsy is between 0.5-0.7% in the general population of industrial countries (Hauser.1991, Forsgren.2005, Banerjee.2009, Ngugi.2010, Beghi.2014, Bell.2014, Helmers.2015). However, this prevalence is lower in women of childbearing age as the prevalence of epilepsy is about 20-40% higher in men than women (Forsgren, 2005) while there is no significant difference of prevalence in the group of 20 to 45 year-old women.*

Range of prevalence of epilepsy in women of childbearing age:

0.5%/140*10,000 – 0.7%/120*10,000 = **30/10,000 – 56/10,000**

*Fertility/fecundity (number of live births/woman, not considering terminations and abortions) of women with epilepsy is reduced between 25% (Wallace, 1998) and 12% (Artama, 2004) compared to women without epilepsy.*

Range of prevalence of epilepsy in pregnancy:

30/10,000 (-25%) – 56/10,000 (-12%) = **23/10,000 – 49/10,000**

*Generalized epilepsy syndromes (IGE) accounts for about 20% of epilepsies in women aged 20-45 years (Jallon & Latour, 2005). Assumption: IGE is distributed proportionally in women with epilepsy who become pregnant and women who do not become pregnant.*

Range of prevalence of IGE in pregnant women:

23/10,000 (-80%) – 49/10,000 (-80%) = **5/10,000** – **10/10,000**

*It is estimated that seizure control can only be achieved with valproate in about 5-15% of patients with IGE. Assumption: exclusive seizure control with VPA is distributed proportionally in women with epilepsy who become pregnant and women who do not become pregnant.*

Range of prevalence of pregnant women responding only to VPA:

5/10,000 (-95%) – 10/10,000 (-85%) **= 0.25/10,000 – 1.5/10,000**

Absolute number of pregnancies during which valproate is needed for seizure control in the weighted Helsana cohort:

| | **Number of pregnancies in the weighted pregnancy cohort** | **Estimated minimum absolute number of pregnancies with live birth responding to VPA only using 0.25/10,000** | **Estimated maximum absolute number of pregnancies with live birth responding to VPA only using 1.5/10,000** |
|---|---|---|---|
| 2014 | 75,462 | 1.9 | 11.3 |
| 2015 | 76,321 | 1.9 | 11.5 |
| 2016 | 78,609 | 2.0 | 11.8 |
| 2017 | 81,888 | 2.1 | 12.3 |
| 2018 | 75,137 | 1.9 | 11.3 |
| Total | 387,417 | **9.8** | **58.2** |

## Appendix 3: Estimation of the number of women of childbearing age with an absolute indication for valproate in Switzerland

*The prevalence of epilepsy is between 0.5-0.7% in the general population of industrial countries (Hauser, 1991; Forsgren, 200;, Banerjee, 2009; Ngugi, 2010; Beghi, 2014; Bell, 2014; Helmers, 2015). However, this prevalence is lower in women of childbearing age as the prevalence of epilepsy is about 20-40% higher in men than women (Forsgre, .2005) while there is no significant difference of prevalence in the group of 20 to 45 year-old women.*

Range of prevalence of epilepsy in women of childbearing age:

0.5%/140*10,000 – 0.7%/120*10,000 = **30/10,000 – 56/10,000**

*Generalized epilepsy syndromes (IGE) accounts for about 20% of epilepsies in women aged 20-45 years (Jallon & Latour, 2005).*

Range of prevalence of women in childbearing age with generalized epilepsy syndromes (IGE):

30/10,000 (-80%) – 56/10,000 (-80%) = **6/10,000** – **11/10,000**

*It is estimated that seizure control can only be achieved with valproate in about 5-15% of patients with IGE.*

Range of prevalence of women in childbearing age responding only to valproate:

6/10,000 (-95%) – 11/10,000 (-85%) = **0.3/10,000 – 1.7/10,000**

Absolute numbers of women of childbearing age during which valproate is needed for seizure control in the weighted Helsana cohort

| | **Number of women of childbearing age in the weighted cohort** | **Estimated minimum number of women responding to VPA only using 0.3/10,000** | **Estimated maximum number of women of responding to VPA only using 1.7/10,000** |
|---|---|---|---|
| 2014 | 207,742 | 6.2 | 35.3 |
| 2015 | 208,776 | 6.3 | 35.5 |
| 2016 | 203,509 | 6.1 | 34.6 |
| 2017 | 187,005 | 5.6 | 31.8 |
| 2018 | 194,974 | 5.8 | 33.2 |
| Total | 1,002,006 | **30** | **170** |

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