

**Appendix Table 3. Adverse Events in Case Reports of Hydroxyurea for Sickle Cell Disease\***

<b>Outcome</b>	<b>Patients, <i>n</i></b>	<b>Men/Women, <i>n/n</i></b>	<b>Mean Age at Adverse Event, <i>y</i></b>	<b>Median Duration of HU Therapy until Adverse Event, <i>wk</i></b>	<b>Reports with Certain Causality, <i>n</i></b>	<b>Reports with Probable Causality, <i>n</i></b>	<b>Reports with Possible Causality, <i>n</i></b>	<b>Level of Evidence for This Outcome†</b>
Leg ulcer	1	1/0	45	104	0	0	1	3
Leukemia	3	3/0	32	288	0	0	3	3
Cytopenia	1	1/0	26	153	0	1	0	2
Avascular necrosis	2	2/0	17	NR	0	0	2	3
Splenomegaly	1	1/0	32	NR	0	0	1	3
Cryptosporidial infection	1	1/0	36	80	0	0	1	3
Intracerebral hemorrhage	1	0/1	22	52	0	0	1	3
Hodgkin lymphoma	1	0/1	8	24	0	0	1	3
Low sperm count/low motility	4	0/4	31	128	0	0	4	3
Acute myocardial infarction	1	0/1	28	NR	0	0	1	3
Skin hyperpigmentation	2	1/1	16	75	0	0	2	3

\*HU = hydroxyurea; NR = not reported.

†In the World Health Organization causality assessment, level 1 is the highest level of evidence, based on  $\geq 1$  case report with certain causality (**Appendix Table 2**).