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Table 1. Duration of physician coverage per parenteral drugs

30 minutes	*60 minutes*	*3 hours*	*During entire infusion*	*During entire infusion PLUS additional time*
alemtuzumab avelumab bleomycin cabazitaxel CARBOplatin carfilzomib DOCEtaxel etoposide PACLitaxel riTUXimab†	cetuximab‡ siltuximab daratumumab subcut ‖	riTUXimab*	atezolizumab bendamustine brentuximab vedotin oBINutuzumab oxaliplatin	asparaginase¥ blinatumomab§ daratumumab IV# isatuximab‡‡‡ pegaspargase¥ PERTuzumab¶ polatuzumab vedotin** sacituzumab govitecan‡‡ tebentafusp§§ trastuzumab¶ trastuzumab deruxtecan *** trastuzumab emtansine*** enfortumab vedotin††

† Second and subsequent IV infusions

‡ 60 minutes following end of first and second infusion, may discontinue observation period if no infusion reactions occur for two consecutive doses.

* First IV infusion only; physician does not need to be on site for subcutaneous injection.

¥ 60 minutes following end of infusion

§ Hospitalization recommended for a minimum of the first 9 days of cycle 1 and the first 2 days of cycle 2. Subsequent cycles may be started as an outpatient.

30 minutes following end of IV infusion. Observation not required after 3 treatments with no reaction.

‖ For first dose: 60 minutes following injection if no prior daratumumab. If changing from daratumumab IV to subcutaneous, 30 minutes following the first injection. Observation not required after the first subcutaneous dose with no reaction.

¶ For first dose: additional 60 minutes after end of infusion. For second and third doses: additional 30 minutes after end of infusion. No additional observation period is needed if no reactions after 3 consecutive treatments.

** For first dose: additional 90 minutes after end of infusion. For subsequent doses: additional 30 minutes after end of infusion.

*** For first dose: additional 90 minutes after end of infusion. For subsequent doses if no reactions with first dose: additional 30 minutes after end of infusion. Observation period not required after 3 treatments with no reaction.

†† For first 3 consecutive doses: additional 60 minutes after end of infusion. Observation period not required after 3 treatments with no reaction.

‡‡ 30 minutes following end of infusion.

‡‡‡ 30 minutes following end of first infusion. Observation not required after first treatment with no reaction.

§§ Hospitalization required for minimum of the first 3 doses (Cycle 1 Days 1, 8, and 15). Observation required during infusion and for at least 16 hours following administration. Subsequent doses may be given in ambulatory setting if no Grade 2 or worse hypotension during or after Cycle 1 Day 15 dose. Hospitalization may be required for subsequent administrations after treatment interruption.

Table 2. Infusion-related toxicity, onset and incidence

The threshold for inclusion was largely based on the emphasis placed by the manufacturer, although in some cases (e.g. oxaliplatin) literature reports may also be pivotal. Any primary literature review would be based on MEDLINE search combining MeSHs of “drug hypersensitivity” or “immediate hypersensitivity” with “antineoplastic agents”, limited to humans and English language. Length of physician coverage takes into account of the likely documented onset of reactions and the usual infusion time.

Drug	*Toxicity*	*Onset*	*Incidence*
alemtuzumab[1]	infusion reactions (hypotension, rigors, fever, shortness of breath, bronchospasm, chills, rash)	not defined	26-96% (severe 9-16%)
asparaginase[2-4]	hypersensitivity reactions	30-60 min	severe 3-32%
atezolizumab	infusion reactions	not defined	1-2%
avelumab[48]	infusion reactions (flushing, chills, hypotension, dyspnea, wheezing, pyrexia, back pain, abdominal pain, urticaria)	not defined	up to 30% (severe 1%)

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Drug	*Toxicity*	*Onset*	*Incidence*
bendamustine[5,6]	infusion reactions (fever, chills, pruritus, shortness of breath, hypotension, cyanosis, tachycardia, rash; rarely, severe anaphylactic and anaphylactoid reactions)	during or directly after drug administration	5% (severe 1%)
bleomycin[7,8]	hypersensitivity reactions	30 minutes to 6 hours after first or second dose	1%
blinatumomab[45]	cytokine release syndrome	2 days after start of infusion	11% (severe 1%)
brentuximab vedotin[9,10]	infusion reactions (chills, nausea, dyspnea, pruritus, pyrexia, cough, wheezing, difficulty breathing, hives, itching, swelling)	immediate or delayed up to 2 days	12%
cabazitaxel[11]	hypersensitivity reactions	not defined	severe <1%
carfilzomib[50]	infusion reactions (fever, chills, arthralgia, myalgia, facial flushing, facial edema, vomiting, weakness, shortness of breath, hypotension, syncope, chest tightness, angina)	immediate to within 24 hours of infusion	43% (severe 4%)
cetuximab[12,13]	infusion reactions (rapid onset of airway obstruction, urticaria, hypotension)	not defined	13-19% (severe 2-5%)
CARBOplatin[14-17]	hypersensitivity reactions	usually immediately after start of the infusion; may delay for several hours	2-30%
Daratumumab [46-47, 54]	IV: Infusion reactions (cough, wheeze, larynx and throat irritation, bronchospasm, laryngeal and pulmonary edema, hypertension, hypoxia and dyspnea)	generally occur during administration of the infusion or within four hours of its completion.	IV: initial infusion (35-48%, severe 5-7%), subsequent infusions (2-4%, severe <1%)
	Subcutaneous: administration-related systemic reactions. Signs and symptoms as with IV, above	majority occur on day of treatment with a median time to onset of 3.7 hours	subcut: initial injection (8-13%, severe <2%); subsequent injections (<1%, severe <1%)
DOCEtaxel[18,19]	hypersensitivity reactions	a few minutes after start of the infusion	21% (severe 4%)

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Drug	*Toxicity*	*Onset*	*Incidence*
enfortumab vedotin [55,56]	Infusion-related reactions	not defined	Infusion-related reactions: 9% (severe 1%)
etoposide[14,20,21]	hypersensitivity reactions	usually during infusion or within minutes after start of infusion; may occur after only a few milligrams have been infused or up to several hours after administration	1-3%
isatuximab[58]	infusion-related reactions (dyspnea, cough, chills, nasal congestion, nausea, hypertension, hypotension, bronchospasm, tachycardia)	Majority occur during first infusion. Median time to infusion interruption is 55 minutes.	38-46% (severe 3-5%)
oBINutuzumab	infusion reactions (nausea, vomiting, chills, hypotension, pyrexia, dyspnea, flushing, hypertension, headache, tachycardia, diarrhea)[22]	not well defined, but probably within 1-2 hours after start of infusion of first dose and more than 5 hours after start of infusion of second dose[23,24]	53% (severe 17%)[25]
oxaliplatin[26-36]	hypersensitivity reactions	usually within 30 min after start of infusion but may occur any time during infusion; rarely shortly after end of infusion	severe 3% (up to 18%)
	pharyngolaryngeal dysesthesia	shortly after end of infusion	1-2%
PACLitaxel[37]	hypersensitivity reactions	53% within 2-3 min after start of infusion and 78% within 10 min	41% (severe 2%)
pegaspargase[53]	Hypersensitivity reactions	not defined	10% (with no prior asparaginase hypersensitivity), 32% (with prior asparaginase hypersensitivity)
PERTuzumab	infusion reactions (fever, chills, fatigue, headaches, asthenia, hypersensitivity, vomiting)	not defined	11%, (severe 2-5%)

Drug	*Toxicity*	*Onset*	*Incidence*
polatuzumab vedotin[52]	Infusion reactions (fever, chills, flushing, dyspnea, hypotension, urticaria)	may be delayed (as late as 24 hours after administration)	7-33% (severe 2-7%)
sacituzumab govitecan[57]	Infusion-related reactions, including hypersensitivity reactions, dyspnea, dizziness, chills, rigors, fever, pruritus, flushing, chest discomfort, allergic rhinitis	Within 24 hours	37%, severe 2%
ritTUXimab[38-40]	infusion-related hypersensitivity (rash, urticaria, fever, chills, bronchospasm, angioedema, flushing, hypotension, rhinitis, nausea, asthenia, headache)[29,30]	< 1–2 h after start of first infusion[31]	up to 80% (severe 7%)
siltuximab[49]	infusion reactions (back pain, chest pain/discomfort, nausea, vomiting, flushing, erythema, palpitations)	not defined	severe 5-8%
tebentafusp[60]	cytokine release syndrome (fever, chills, hypotension, hypoxia, nausea, vomiting, rash, elevated transaminases, fatigue, dizziness, shortness of breath, myalgia, arthralgia, tachycardia, headache)	Mainly the first 3 infusions. Majority of episodes start the day of infusion.	89%, severe 1%
trastuzumab (HERCEPTIN)[41-43]	infusion reactions (fever, chills)	usually during infusion	36-39%
trastuzumab deruxtecan (ENHERTU)[59]	infusion-related reactions (chills, shaking, shortness of breath, wheezing, itching, rash, hives, flushing, dizziness, fever)	within 24 hours of infusion	1-3%
trastuzumab emtansine (KADCYLA)[44]	infusion reactions (flushing, chills, pyrexia, dyspnea, hypotension, wheezing, bronchospasm, tachycardia)	not defined	1%

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