Appendix to Provincial Systemic Therapy Policy III-60

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 asparaginase avelumab bleomycin cabazitaxel CARBOplatin carfilzomib DOCEtaxel etoposide PACLitaxel riTUXimab†	cetuximab‡ siltuximab	riTUXimab*	bendamustine brentuximab vedotin oBINutuzumab oxaliplatin	blinatumomab§ daratumumab# PERTuzumab¶ trastuzumab¶ trastuzumab emtansine¶

† 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.

§ 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 infusion

¶ 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.

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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%
avelumab[48]	infusion reactions (flushing, chills, hypotension, dyspnea, wheezing, pyrexia, back pain, abdominal pain, urticaria)	not defined	up to 30% (severe 1%)
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%)

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Drug	*Toxicity*	*Onset*	*Incidence*
CARBOplatin[14-17]	hypersensitivity reactions	usually immediately after start of the infusion; may delay for several hours	2-30%
daratumumab[46-47]	Infusion reactions (cough, wheeze, larynx and throat irritation, bronchospasm, laryngeal and pulmonary edema, hypertension, hypoxia and dyspnea)	not defined	Initial infusion 46-48% (severe 7%) Subsequent infusions 2-4% (severe <1%)
DOCEtaxel[18,19]	hypersensitivity reactions	a few minutes after start of the infusion	21% (severe 4%)
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%
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%)
PERTuzumab	infusion reactions (fever, chills, fatigue, headaches, asthenia, hypersensitivity, vomiting)	not defined	11%, (severe 2-5%)
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%)

Drug	*Toxicity*	*Onset*	*Incidence*
siltuximab[49]	infusion reactions (back pain, chest pain/discomfort, nausea, vomiting, flushing, erythema, palpitations)	not defined	severe 5-8%
trastuzumab (HERCEPTIN)[41-43]	infusion reactions (fever, chills)	usually during infusion	36-39%
trastuzumab emtansine (KADCYLA)[44]	infusion reactions (flushing, chills, pyrexia, dyspnea, hypotension, wheezing, bronchospasm, tachycardia)	not defined	1%

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