FEBRUARY
2022 UPDATE

DOSING & ADMINISTRATION **FOR DARZALEX®** (daratumumab)

Please see Indications and full Important Safety Information on pages 52–55 and click here for full DARZALEX® Prescribing Information.

DARZALEX®
(daratumumab)
injection for intravenous infusion
100 mg/5 mL, 400 mg/20 mL

Indications and mechanisms of action[1]

DARZALEX® (daratumumab) is indicated for the treatment of adult patients with multiple myeloma:

- In combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy
- In combination with bortezomib, melphalan, and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant
- In combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant
- In combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
- In combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy
- In combination with pomalidomide and dexamethasone in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor
- As monotherapy in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent

DARZALEX® is a first-in-class monoclonal antibody that targets CD38[1]

- CD38 is expressed on hematopoietic cells, other cell types and tissues, and is highly expressed on multiple myeloma cells[1]
- DARZALEX® inhibits tumor cell growth through immune-mediated, direct on-tumor, and immunomodulatory actions. DARZALEX® may also have an effect on normal cells[1]

Select Important Safety Information

CONTRAINDICATIONS

DARZALEX® is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions.

How DARZALEX® is supplied

Dosage form and strengths[1]

DARZALEX® is a colorless to pale yellow, preservative-free solution for intravenous (IV) infusion.

- DARZALEX® is supplied in single-dose vial

100 mg/5 mL (20 mg/mL)

400 mg/20 mL (20 mg/mL)

Storage[1]

- Store in a refrigerator at 2°C to 8°C (36°F to 46°F)
- Do not freeze or shake. Protect from light. This product contains no preservative

Select Important Safety Information

Neutropenia and Thrombocytopenia

DARZALEX® may increase neutropenia and thrombocytopenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Monitor patients with neutropenia for signs of infection. Consider withholding DARZALEX® until recovery of neutrophils or for recovery of platelets.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX®
(daratumumab)
injection for intravenous infusion
100 mg/5 mL, 400 mg/20 mL

Notes:

DARZALEX® (daratumumab) + lenalidomide + dexamethasone (DRd)

DOSING & SAFETY

for adult patients with newly diagnosed, transplant-ineligible multiple myeloma

Please see Indications and full Important Safety Information on pages 52–55 and click here for full DARZALEX® Prescribing Information.

DARZALEX® (daratumumab) + Rd dosing

In adult patients with newly diagnosed, transplant-ineligible multiple myeloma[1]

Dosing schedule based on a phase 3, randomized, active-controlled trial

DARZALEX® in combination with Revlimid® (lenalidomide) and dexamethasone (Rd) (n=368) vs Rd alone (n=369)

Recommended dosage and schedule for DARZALEX®[1]

4 Doses Per Cycle given as **1 weekly** infusion (Cycles 1* to 2; Weeks 1 to 8)

2 Doses Per Cycle given as 1 infusion **every 2 weeks** (twice per 4-week cycle; Cycles 3 to 6; Weeks 9 to 24)

1 Dose Per Cycle given as 1 infusion **every 4 weeks** (Cycle 7+; Week 25+ until disease progression)

23 estimated Year 1 infusion visits

See table on page 7 ►

- Revlimid® (lenalidomide) 25 mg is given orally on Days 1–21 of each cycle†
- Dexamethasone 40 mg is given orally or IV once a week‡
  - On DARZALEX® infusion days, the entire dexamethasone dose was given as a pre-infusion medication

Revlimid® is a registered trademark of Celgene Corporation.

*The first prescribed 16 mg/kg dose at Week 1 may be split over 2 consecutive days. See page 60 for details.

†For dosing instructions of combination agents administered with DARZALEX®, see Clinical Studies (14.1) section of the full Prescribing Information for DARZALEX® and the respective manufacturer's prescribing information.

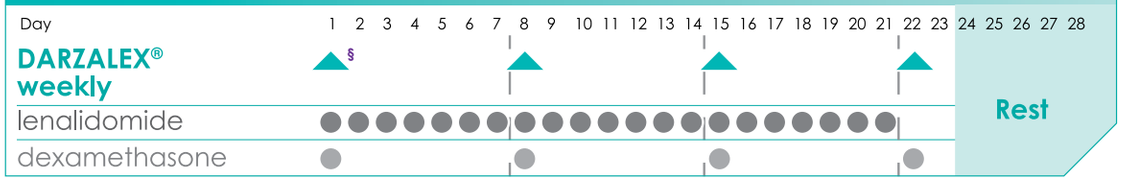
‡Please see the DARZALEX® full Prescribing Information for more information regarding dexamethasone dosage and administration.

Please see Indications and full Important Safety Information on pages 52–55 and click here for full DARZALEX® Prescribing Information.

DARZALEX® + Rd dosing schedule for adult patients with newly diagnosed, transplant-ineligible multiple myeloma

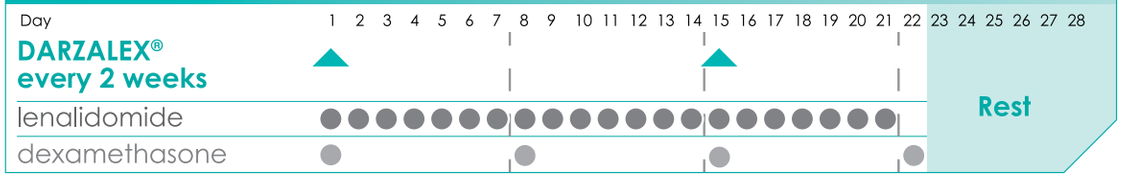
DARZALEX® dosing frequency decreases over time[1]

Cycles 1–2 (each lasting 28 days) — **Total of 8 DARZALEX® doses**

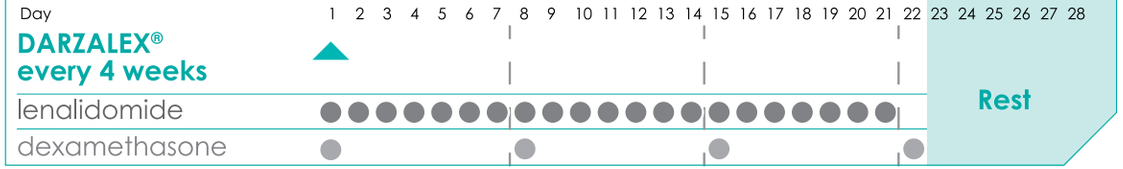


§The first prescribed 16 mg/kg dose at Week 1 may be split over 2 consecutive days. See page 60 for details.

Cycles 3–6 (each lasting 28 days) — **Total of 8 DARZALEX® doses**



Cycle 7 onward (each lasting 28 days)



Continue DARZALEX® + Rd until disease progression or unacceptable toxicity

Infusion-related reactions of any grade or severity may be managed by interruption, modification, and/or discontinuation of the infusion. DARZALEX® should be permanently discontinued upon the third occurrence of a Grade 3 infusion-related reaction and upon any occurrence of a Grade 4 infusion-related reaction.

No dose reductions of DARZALEX® are recommended. Dose delay may be required to allow recovery of blood cell counts in the event of hematological toxicity *[see Warnings and Precautions (5.3, 5.4)]*. For information concerning drugs given in combination with DARZALEX®, see manufacturer's prescribing information.

Select Important Safety Information

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Select Important Information[1]

- DARZALEX® should be administered by a healthcare provider, with immediate access to emergency equipment and appropriate medical support to manage infusion-related reactions if they occur
- If a dose of DARZALEX® is missed, administer the dose as soon as possible and adjust the dosing schedule to maintain the dosing interval

Select Important Safety Information

CONTRAINDICATIONS

DARZALEX® is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions. Less than 1% of patients had a Grade 3/4 infusion-related reaction at Week 2 or subsequent infusions. The median time to onset was 1.5 hours (range: 0 to 73 hours). Nearly all reactions occurred during infusion or within 4 hours of completing DARZALEX®. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, tachycardia, headache, laryngeal edema, pulmonary edema, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting, and nausea. Less common signs and symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, hypotension, and blurred vision.

When DARZALEX® dosing was interrupted in the setting of ASCT (CASSIOPEIA) for a median of 3.75 months (range: 2.4 to 6.9 months), upon re-initiation of DARZALEX®, the incidence of infusion-related reactions was 11% for the first infusion following ASCT. Infusion-related reactions occurring at re-initiation of DARZALEX® following ASCT were consistent in terms of symptoms and severity (Grade 3 or 4: <1%) with those reported in previous studies at Week 2 or subsequent infusions. In EQUULEUS, patients receiving combination treatment (n=97) were administered the first 16 mg/kg dose at Week 1 split over two days, ie, 8 mg/kg on Day 1 and Day 2, respectively. The incidence of any grade infusion-related reactions was 42%, with 36% of patients experiencing infusion-related reactions on Day 1 of Week 1, 4% on Day 2 of Week 1, and 8% with subsequent infusions.

Pre-medicate patients with antihistamines, antipyretics, and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt DARZALEX® infusion for reactions of any severity and institute medical management as needed. Permanently discontinue DARZALEX® therapy if an anaphylactic reaction or life-threatening (Grade 4) reaction occurs and institute appropriate emergency care. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion.

To reduce the risk of delayed infusion-related reactions, administer oral corticosteroids to all patients following DARZALEX® infusions. Patients with a history of chronic obstructive pulmonary disease may require additional post-infusion medications to manage respiratory complications. Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with chronic obstructive pulmonary disease.

Ocular adverse reactions, including acute myopia and narrowing of the anterior chamber angle due to ciliochoroidal effusions with potential for increased intraocular pressure or glaucoma, have occurred with DARZALEX® infusion. If ocular symptoms occur, interrupt DARZALEX® infusion and seek immediate ophthalmologic evaluation prior to restarting DARZALEX®.

Interference With Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive indirect antiglobulin test (indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab infusion. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type is not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX®. Type and screen patients prior to starting DARZALEX®.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Safety results demonstrated in combination with Rd

Most frequent adverse reactions and laboratory abnormalities reported in ≥20% of patients and with at least a 5% greater frequency in the DARZALEX® + Rd arm[1]*

Adverse reactions						
	DARZALEX® + Rd (n=364)			Rd (n=365)		
Treatment-emergent event	Any grade (%)	Grade 3 (%)	Grade 4 (%)	Any grade (%)	Grade 3 (%)	Grade 4 (%)
Diarrhea	57	7	0	46	4	0
Upper respiratory tract infection	52	2	<1	36	2	<1
Infusion-related reactions	41	2	<1	0	0	0
Constipation	41	1	<1	36	<1	0
Peripheral edema	41	2	0	33	1	0
Fatigue	40	8	0	28	4	0
Back pain	34	3	<1	26	3	<1
Asthenia	32	4	0	25	3	<1
Nausea	32	1	0	23	1	0
Dyspnea	32	3	<1	20	1	0
Cough	30	<1	0	18	0	0
Bronchitis	29	3	0	21	1	0
Muscle spasms	29	1	0	22	1	0
Pneumonia	26	14	1	14	7	1
Peripheral sensory neuropathy	24	1	0	15	0	0
Pyrexia	23	2	0	18	2	0
Decreased appetite	22	1	0	15	<1	<1

*Adverse reactions that occurred with a frequency of ≥10% and <20%, and with at least a 5% greater frequency in the DARZALEX® + Rd arm were: headache, urinary tract infection, hyperglycemia, hypercalcemia, vomiting, chills, paresthesia, and hypertension.

Serious adverse reactions (ARs) with at least a 2% greater incidence in the DRd arm compared to the Rd arm were pneumonia (DRd 15% vs Rd 8%), bronchitis (DRd 4% vs Rd 2%), and dehydration (DRd 2% vs Rd <1%).[1]

Laboratory abnormalities						
	DARZALEX® + Rd (n=364)			Rd (n=365)		
Treatment-emergent event	Any grade (%)	Grade 3 (%)	Grade 4 (%)	Any grade (%)	Grade 3 (%)	Grade 4 (%)
Neutropenia	91	39	17	77	28	11
Leukopenia	90	30	5	82	20	4
Lymphopenia	84	41	11	75	36	6
Thrombocytopenia	67	6	3	58	7	4
Anemia	47	13	0	57	24	0

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

Safety results demonstrated in combination with Rd in adult patients with newly diagnosed, transplant-ineligible multiple myeloma

- Discontinuation rates due to ARs: 7% with DRd vs 16% with Rd[2]
- Infusion-related reactions (IRRs) with DRd occurred in 41% of patients; 2% were Grade 3 and <1% were Grade 4[1]
- IRRs of any grade or severity may require management by interruption, modification, and/or discontinuation of the infusion[1]
- Most IRRs occurred during the first infusion[1]

See previous page for additional results.

Notes:

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

DARZALEX® (daratumumab) + lenalidomide + dexamethasone (DRd)

DOSING & SAFETY

for adult patients with relapsed/refractory multiple myeloma

Please see Indications and full Important Safety Information on pages 52–55 and click here for full DARZALEX® Prescribing Information.

DARZALEX® (daratumumab) + Rd dosing for patients with relapsed/refractory multiple myeloma

In patients at first relapse[1]

Dosing schedule based on a phase 3, randomized, active-controlled trial

DARZALEX® in combination with Revlimid® (lenalidomide) and dexamethasone (Rd) (n=286) vs Rd alone (n=283)

Recommended dosage and schedule for DARZALEX®[1]

4 Doses Per Cycle given as **1 weekly** infusion (Cycles 1* to 2; Weeks 1 to 8)

2 Doses Per Cycle given as 1 infusion **every 2 weeks** (twice per 4-week cycle; Cycles 3 to 6; Weeks 9 to 24)

1 Dose Per Cycle given as 1 infusion **every 4 weeks** (Cycle 7+; Week 25+ until disease progression)

23 estimated Year 1 infusion visits

See table on page 13 ▸

- Revlimid® (lenalidomide) 25 mg is given orally on Days 1–21 of each cycle†
- Dexamethasone 40 mg is given orally or IV once a week‡
  - On DARZALEX® infusion days, 20 mg of the dexamethasone dose was given as a pre-infusion medication and the remainder given the day after the infusion
  - For patients on a reduced dexamethasone dose, the entire 20-mg dose was given as a DARZALEX® pre-infusion medication

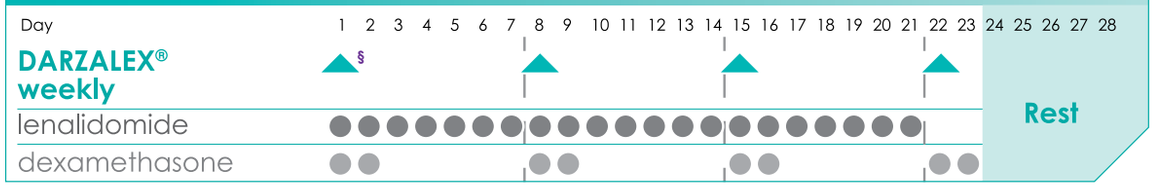
Revlimid® is a registered trademark of Celgene Corporation.
*The first prescribed 16 mg/kg dose at Week 1 may be split over 2 consecutive days. See page 60 for details.
†For dosing instructions of combination agents administered with DARZALEX®, see the Clinical Studies (14.2) section of the full Prescribing Information for DARZALEX® and the respective manufacturer's prescribing information.
‡Please see the DARZALEX® full Prescribing Information for more information regarding dexamethasone dosage and administration.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® + Rd dosing schedule for patients with relapsed/refractory multiple myeloma

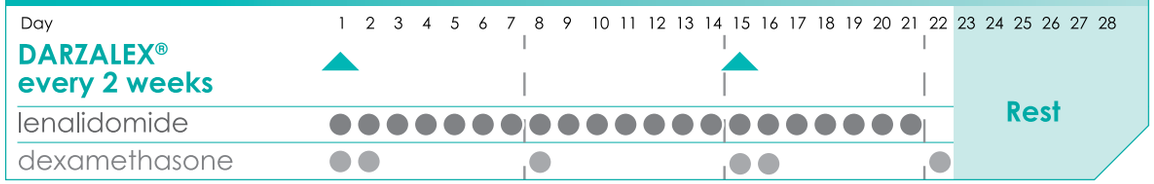
DARZALEX® dosing frequency decreases over time[1]

Cycles 1–2 (each lasting 28 days) — Total of 8 DARZALEX® doses

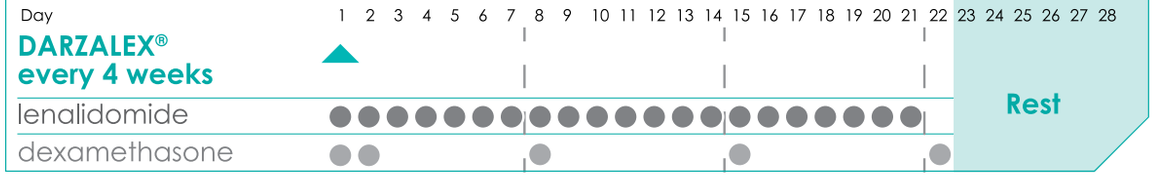


§The first prescribed 16 mg/kg dose at Week 1 may be split over 2 consecutive days. See page 60 for details.

Cycles 3–6 (each lasting 28 days) — Total of 8 DARZALEX® doses



Cycle 7 onward (each lasting 28 days)



Continue DARZALEX® + Rd until disease progression or unacceptable toxicity

Infusion-related reactions of any grade or severity may be managed by interruption, modification, and/or discontinuation of the infusion. DARZALEX® should be permanently discontinued upon the third occurrence of a Grade 3 infusion-related reaction and upon any occurrence of a Grade 4 infusion-related reaction.

No dose reductions of DARZALEX® are recommended. Dose delay may be required to allow recovery of blood cell counts in the event of hematological toxicity *[see Warnings and Precautions (5.3, 5.4)]*. For information concerning drugs given in combination with DARZALEX®, see manufacturer's prescribing information.

Select Important Safety Information

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL; 400 mg/20 mL

Select Important information[1]

- DARZALEX® should be administered by a healthcare provider, with immediate access to emergency equipment and appropriate medical support to manage infusion-related reactions if they occur
- If a dose of DARZALEX® is missed, administer the dose as soon as possible and adjust the dosing schedule to maintain the dosing interval

Select Important Safety Information

CONTRAINDICATIONS

DARZALEX® is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions. Less than 1% of patients had a Grade 3/4 infusion-related reaction at Week 2 or subsequent infusions. The median time to onset was 1.5 hours (range: 0 to 73 hours). Nearly all reactions occurred during infusion or within 4 hours of completing DARZALEX®. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, tachycardia, headache, laryngeal edema, pulmonary edema, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting, and nausea. Less common signs and symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, hypotension, and blurred vision.

When DARZALEX® dosing was interrupted in the setting of ASCT (CASSIOPEIA) for a median of 3.75 months (range: 2.4 to 6.9 months), upon re-initiation of DARZALEX®, the incidence of infusion-related reactions was 11% for the first infusion following ASCT. Infusion-related reactions occurring at re-initiation of DARZALEX® following ASCT were consistent in terms of symptoms and severity (Grade 3 or 4: <1%) with those reported in previous studies at Week 2 or subsequent infusions. In EQUULEUS, patients receiving combination treatment (n=97) were administered the first 16 mg/kg dose at Week 1 split over two days, ie, 8 mg/kg on Day 1 and Day 2, respectively. The incidence of any grade infusion-related reactions was 42%, with 36% of patients experiencing infusion-related reactions on Day 1 of Week 1, 4% on Day 2 of Week 1, and 8% with subsequent infusions.

Pre-medicate patients with antihistamines, antipyretics, and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt DARZALEX® infusion for reactions of any severity and institute medical management as needed. Permanently discontinue DARZALEX® therapy if an anaphylactic reaction or life-threatening (Grade 4) reaction occurs and institute appropriate emergency care. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion.

To reduce the risk of delayed infusion-related reactions, administer oral corticosteroids to all patients following DARZALEX® infusions. Patients with a history of chronic obstructive pulmonary disease may require additional post-infusion medications to manage respiratory complications. Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with chronic obstructive pulmonary disease.

Ocular adverse reactions, including acute myopia and narrowing of the anterior chamber angle due to ciliochoroidal effusions with potential for increased intraocular pressure or glaucoma, have occurred with DARZALEX® infusion. If ocular symptoms occur, interrupt DARZALEX® infusion and seek immediate ophthalmologic evaluation prior to restarting DARZALEX®.

Interference With Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive indirect antiglobulin test (indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab infusion. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type is not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX®. Type and screen patients prior to starting DARZALEX®.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

In patients with relapsed/refractory multiple myeloma

Safety results demonstrated in combination with Rd

Most frequent adverse reactions and laboratory abnormalities reported in ≥20% of patients and with at least a 5% greater frequency in the DARZALEX® + Rd arm[1]*

Adverse reactions						
Treatment-emergent event	**DARZALEX® + Rd** (n=283)			**Rd** (n=281)		
	Any grade (%)	Grade 3 (%)	Grade 4 (%)	Any grade (%)	Grade 3 (%)	Grade 4 (%)
Upper respiratory tract infection	65	6	<1	51	4	0
Infusion-related reactions	48	5	0	0	0	0
Diarrhea	43	5	0	25	3	0
Fatigue	35	6	<1	28	2	0
Cough	30	0	0	15	0	0
Muscle spasms	26	1	0	19	2	0
Nausea	24	1	0	14	0	0
Dyspnea	21	3	<1	12	1	0
Pyrexia	20	2	0	11	1	0

*Adverse reactions that occurred with a frequency of ≥10% and <20%, and with at least a 5% greater frequency in the DARZALEX® + Rd arm were: vomiting and headache.

Serious adverse reactions (ARs) with at least a 2% greater incidence in the DRd arm compared to the Rd arm were pneumonia (DRd 12% vs Rd 10%), upper respiratory tract infection (DRd 7% vs Rd 4%), influenza, and pyrexia (DRd 3% vs Rd 1% for each).[1]

Laboratory abnormalities						
Treatment-emergent event	**DARZALEX® + Rd** (n=283)			**Rd** (n=281)		
	Any grade (%)	Grade 3 (%)	Grade 4 (%)	Any grade (%)	Grade 3 (%)	Grade 4 (%)
Anemia	52	13	0	57	19	0
Thrombocytopenia	73	7	6	67	10	5
Neutropenia	92	36	17	87	32	8
Lymphopenia	95	42	10	87	32	6

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Safety results demonstrated in combination with Rd in patients with relapsed/refractory multiple myeloma

- Discontinuation rates due to ARs with DRd were similar to Rd alone (7% vs 8%, respectively)[1]
- Infusion-related reactions (IRRs) with DRd occurred in 48% of patients; 5% were Grade 3 and 0% were Grade 4[1]
- Grade 3/4 infections between study arms: 28% vs 23% with DRd and Rd, respectively[1]
- IRRs of any grade or severity may require management by interruption, modification, and/or discontinuation of the infusion[1]
- Most IRRs occurred during the first infusion[1]

See previous page for additional results.

Notes:

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX®
(daratumumab)
injection for intravenous infusion
100 mg/5 mL, 400 mg/20 mL

DARZALEX® (daratumumab) + bortezomib + thalidomide + dexamethasone (DVTd)

DOSING & SAFETY

Please see Indications and full Important Safety Information on pages 52-55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) + VTd dosing

In adult patients with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant[1]

Dosing schedule based on a phase 3, randomized, active-controlled trial

DARZALEX® in combination with Velcade® (bortezomib) + Thalomid® (thalidomide) + dexamethasone (VTd) (n=543) vs VTd alone (n=542)[1]

Recommended dosage and schedule for DARZALEX®[1]

Induction

4 Doses Per Cycle given as **1 weekly** infusion (Cycles 1* and 2; Weeks 1 to 8)

2 Doses Per Cycle given as 1 infusion **every 2 weeks** (twice per 4–week cycle; Cycles 3 and 4; Weeks 9 to 16)

STOP FOR HIGH-DOSE CHEMOTHERAPY AND ASCT

Consolidation

2 Doses Per Cycle given as 1 infusion **every 2 weeks** (twice per 4–week cycle; Cycles 5 and 6; Weeks 1 to 8 of consolidation phase)

16 estimated total infusion visits for induction and consolidation

See table on page 19 ►

- Velcade® (bortezomib) 1.3 mg/m^2 BSA is given SC or IV on Days 1, 4, 8, and 11 of each cycle[†]
- Thalomid® (thalidomide) 100 mg is given orally daily during each cycle[†]
- Dexamethasone 40 mg is given orally or IV on Days 1, 2, 8, 9, 15, 16, 22, and 23 of Cycles 1–2, and at 40 mg on Days 1–2 and 20 mg on subsequent dosing days (Days 8, 9, 15, 16) of Cycles 3–4; dexamethasone 20 mg is administered on Days 1, 2, 8, 9, 15, and 16 in Cycles 5–6[†‡]
  - On DARZALEX® infusion days, dexamethasone is administered IV as a pre-infusion medication

ASCT=autologous stem cell transplant; BSA=body surface area; IV=intravenous; SC=subcutaneous.

Thalomid® is a registered trademark of Celgene Corporation.

Velcade® is a registered trademark of Millennium Pharmaceuticals, Inc.

*The first prescribed 16 mg/kg dose at Week 1 may be split over 2 consecutive days.[1] See page 60 for details.

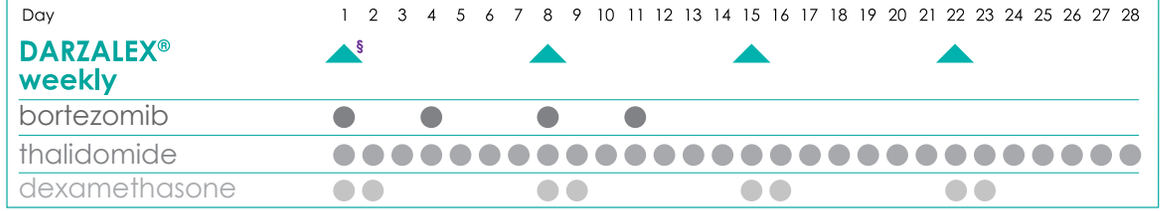
[†]For dosing instructions of combination agents administered with DARZALEX®, see the Clinical Studies (14.1) section of the full Prescribing Information for DARZALEX® and the respective manufacturer's prescribing information.

[‡]Please see the DARZALEX® full Prescribing Information for more information regarding dexamethasone dosage and administration.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

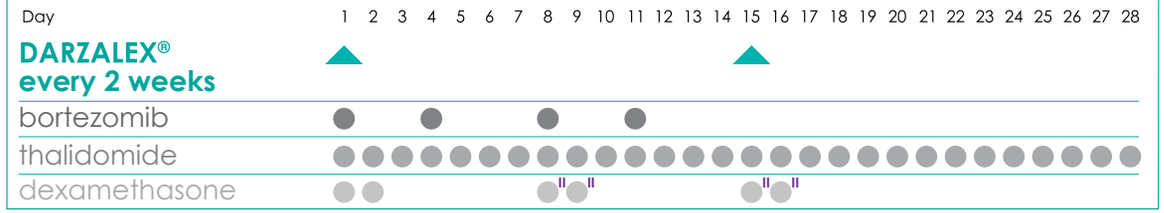
DARZALEX® (daratumumab) + VTd dosing schedule for adult patients with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant[1]

Induction Cycles 1–2 (each lasting 28 days) — **Total of 8 DARZALEX® doses**



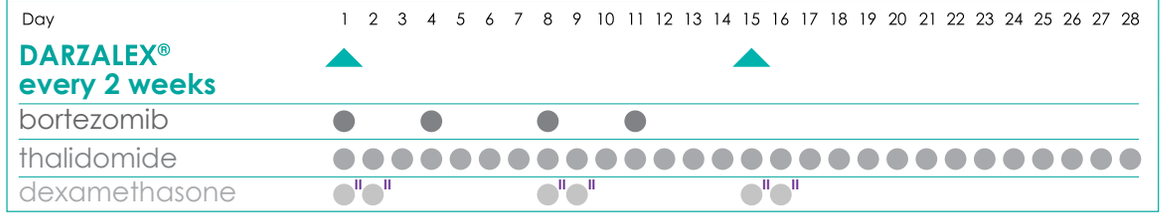
§The first prescribed 16 mg/kg dose at Week 1 may be split over 2 consecutive days.[1] See page 60 for details.

Induction Cycles 3–4 (each lasting 28 days) — **Total of 4 DARZALEX® doses**



STOP FOR HIGH DOSE CHEMOTHERAPY AND AUTOLOGOUS STEM CELL TRANSPLANT

Consolidation Cycles 5–6 (each lasting 28 days) — **Total of 4 DARZALEX® doses**



‖20-mg dose.

Infusion-related reactions of any grade or severity may be managed by interruption, modification, and/or discontinuation of the infusion. DARZALEX® should be permanently discontinued upon the third occurrence of a Grade 3 infusion-related reaction and upon any occurrence of a Grade 4 infusion-related reaction.[1]

No dose reductions of DARZALEX® are recommended. Dose delay may be required to allow recovery of blood cell counts in the event of hematological toxicity *[see Warnings and Precautions (5.3, 5.4)]*.[1] For information concerning drugs given in combination with DARZALEX®, see manufacturer's prescribing information.

Select Important Safety Information

CONTRAINDICATIONS

DARZALEX® is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Select Important Information[1]

- DARZALEX® should be administered by a healthcare provider, with immediate access to emergency equipment and appropriate medical support to manage infusion-related reactions if they occur
- If a dose of DARZALEX® is missed, administer the dose as soon as possible and adjust the dosing schedule to maintain the dosing interval

Select Important Safety Information

CONTRAINDICATIONS

DARZALEX® is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions. Less than 1% of patients had a Grade 3/4 infusion-related reaction at Week 2 or subsequent infusions. The median time to onset was 1.5 hours (range: 0 to 73 hours). Nearly all reactions occurred during infusion or within 4 hours of completing DARZALEX®. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, tachycardia, headache, laryngeal edema, pulmonary edema, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting, and nausea. Less common signs and symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, hypotension, and blurred vision.

When DARZALEX® dosing was interrupted in the setting of ASCT (CASSIOPEIA) for a median of 3.75 months (range: 2.4 to 6.9 months), upon re-initiation of DARZALEX®, the incidence of infusion-related reactions was 11% for the first infusion following ASCT. Infusion-related reactions occurring at re-initiation of DARZALEX® following ASCT were consistent in terms of symptoms and severity (Grade 3 or 4: <1%) with those reported in previous studies at Week 2 or subsequent infusions. In EQUULEUS, patients receiving combination treatment (n=97) were administered the first 16 mg/kg dose at Week 1 split over two days, ie, 8 mg/kg on Day 1 and Day 2, respectively. The incidence of any grade infusion-related reactions was 42%, with 36% of patients experiencing infusion-related reactions on Day 1 of Week 1, 4% on Day 2 of Week 1, and 8% with subsequent infusions.

Pre-medicate patients with antihistamines, antipyretics, and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt DARZALEX® infusion for reactions of any severity and institute medical management as needed. Permanently discontinue DARZALEX® therapy if an anaphylactic reaction or life-threatening (Grade 4) reaction occurs and institute appropriate emergency care. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion.

To reduce the risk of delayed infusion-related reactions, administer oral corticosteroids to all patients following DARZALEX® infusions. Patients with a history of chronic obstructive pulmonary disease may require additional post-infusion medications to manage respiratory complications. Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with chronic obstructive pulmonary disease.

Ocular adverse reactions, including acute myopia and narrowing of the anterior chamber angle due to ciliochoroidal effusions with potential for increased intraocular pressure or glaucoma, have occurred with DARZALEX® infusion. If ocular symptoms occur, interrupt DARZALEX® infusion and seek immediate ophthalmologic evaluation prior to restarting DARZALEX®.

Interference With Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive indirect antiglobulin test (indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab infusion. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type is not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX®. Type and screen patients prior to starting DARZALEX®.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Safety results demonstrated in combination with VTd

Most frequent adverse reactions and laboratory abnormalities reported in ≥20% of patients and with at least a 5% greater frequency in the DARZALEX® (daratumumab) + VTd arm[1]*

Adverse reactions						
	DARZALEX® + VTd (n=536)			**VTd** (n=538)		
Treatment-emergent event	**Any grade (%)**	**Grade 3 (%)**	**Grade 4 (%)**	**Any grade (%)**	**Grade 3 (%)**	**Grade 4 (%)**
Infusion-related reactions	35	3	<1	0	0	0
Nausea	30	4	0	24	2	<1
Upper respiratory tract infection	27	1	0	17	1	0
Pyrexia	26	2	<1	21	2	0
Bronchitis	20	1	0	13	1	0

*Adverse reactions that occurred with a frequency of ≥10% and <20%, and with at least a 5% greater frequency in the DARZALEX® + VTd arm were: cough, vomiting, and hypertension.

Serious adverse reactions with a 2% greater incidence in the DVTd arm compared with the VTd arm were bronchitis (DVTd 2% vs VTd <1%) and pneumonia (DVTd 6% vs VTd 4%).[1]

Laboratory abnormalities						
	DARZALEX® + VTd (n=536)			**VTd** (n=538)		
Treatment-emergent event	**Any grade (%)**	**Grade 3 (%)**	**Grade 4 (%)**	**Any grade (%)**	**Grade 3 (%)**	**Grade 4 (%)**
Lymphopenia	95	44	15	91	37	10
Leukopenia	82	14	10	57	6	9
Thrombocytopenia	81	9	5	58	8	3
Neutropenia	63	19	14	41	10	9
Anemia	36	4	0	35	5	0

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

Safety results demonstrated in combination with VTd

- Discontinuation rates due to any adverse event: 7% with DVTd vs 8% with VTd[3]
- Infusion-related reactions (IRRs) with DVTd occurred in 35% of patients; 3% were Grade 3 and <1% were Grade 4[1]
- IRRs of any grade or severity may require management by interruption, modification, and/or discontinuation of the infusion[1]
- Most IRRs occurred during the first infusion[1]
  - 27% of patients had IRRs with the **first infusion**[3]
  - 11% of patients had IRRs with the **first post-transplant infusion**[1]
- Grade 3/4 infections were similar between study arms: 22% vs 20% with DVTd vs VTd alone, respectively[1]

See previous page for additional results.

Important information before administering DARZALEX® (daratumumab)

Pre-infusion medications[1]

To reduce the risk of infusion-related reactions, administer to all patients approximately 1 hour to 3 hours prior to every infusion as follows:

- ✓ Dexamethasone 20 mg prior to every DARZALEX® infusion. When dexamethasone is the background regimen-specific corticosteroid, the dexamethasone treatment dose will also serve as premedication on DARZALEX® infusion days*
- ✓ During monotherapy, methylprednisolone 100 mg, or equivalent, administered intravenously. Following the second infusion, the dose of corticosteroid may be reduced (oral or intravenous methylprednisolone 60 mg)
- ✓ Oral antipyretics (acetaminophen 650 mg to 1000 mg), plus
- ✓ Oral or IV antihistamine (diphenhydramine 25 mg to 50 mg or equivalent)

*Dexamethasone is given intravenously prior to the first DARZALEX® infusion and oral administration may be considered prior to subsequent infusions. Additional background regimen-specific corticosteroids (eg, prednisone) should not be taken on DARZALEX® infusion days when patients receive dexamethasone (or equivalent) as pre-medication.

Post-infusion medications are recommended

Post-infusion medications[1]

To reduce the risk of delayed infusion-related reactions, administer the day after every infusion as follows:

- ✓ Oral corticosteroid (≤20 mg methylprednisolone or equivalent); however, if a background regimen-specific corticosteroid (eg, dexamethasone, prednisone) is administered the day after the DARZALEX® infusion, additional post-infusion medications may not be needed
- ✓ During monotherapy, administer oral corticosteroid (20 mg methylprednisolone or equivalent dose of an intermediate-acting or long-acting corticosteroid in accordance with local standards) on each of the 2 days following all DARZALEX® infusions (beginning the day after the infusion)

Note: *For patients with a history of chronic obstructive pulmonary disorder, consider including short- and long-acting bronchodilators and inhaled corticosteroids. Following the first 4 infusions, if the patient experiences no major infusion-related reactions, these additional inhaled post-infusion medications may be discontinued.*

More dosing and administration information for DARZALEX®

For information on preparation for administration, infusion rates, management of infusion-related reactions, and how DARZALEX® is supplied, please see the accompanying guide, *Dosing & Administration for DARZALEX® (daratumumab)*, and the full Prescribing Information.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

DARZALEX® (daratumumab) + bortezomib + melphalan + prednisone (DVMP)

DOSING & SAFETY

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) + VMP dosing

In adult patients with newly diagnosed, transplant-ineligible multiple myeloma

Dosing schedule based on a phase 3, randomized, active-controlled trial[3]

DARZALEX® in combination with Velcade® (bortezomib) and melphalan and prednisone (VMP) (n=350) vs VMP alone (n=356)

Recommended dosage and schedule for DARZALEX®[1]

6 Doses Per Cycle given as **1 weekly** infusion (Cycle 1*; Weeks 1 to 6)

2 Doses Per Cycle given as 1 infusion **every 3 weeks** (twice per 6-week cycle; Cycles 2 to 9; Weeks 7 to 54)

1 Dose Per Cycle given as 1 infusion **every 4 weeks** (Cycles 10+; Weeks 55+ until disease progression)

22 estimated Year 1 infusion visits

See table on page 25 ▸

- Velcade® (bortezomib) was administered by subcutaneous (SC) injection at a dose of 1.3 mg/m^2 twice weekly at Weeks 1, 2, 4, and 5 for the first 6-week cycle (Cycle 1; 8 doses), followed by once weekly administrations at Weeks 1, 2, 4, and 5 for eight more 6-week cycles (Cycles 2–9; 4 doses per cycle)
- Melphalan at 9 mg/m^2 and prednisone at 60 mg/m^2 were orally administered on Days 1 to 4 of the nine 6-week cycles (Cycles 1–9)
- DARZALEX® treatment was continued until disease progression or unacceptable toxicity

*The first prescribed 16 mg/kg dose at Week 1 may be split over 2 consecutive days. See page 60 for details.

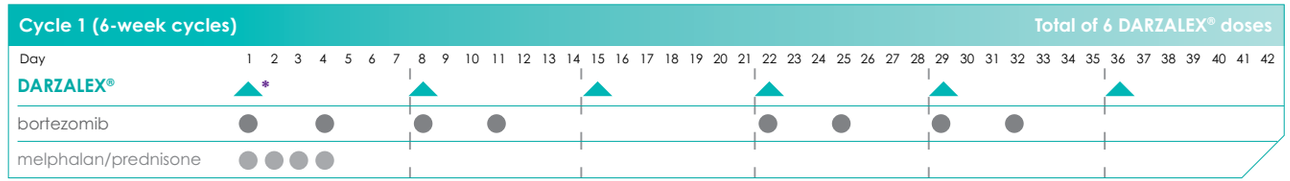
Velcade® is a registered trademark of Millennium Pharmaceuticals, Inc.

For dosing instructions of combination agents administered with DARZALEX®, see the Clinical Studies (14.1) section of the full Prescribing Information for DARZALEX® and the respective manufacturer's prescribing information.

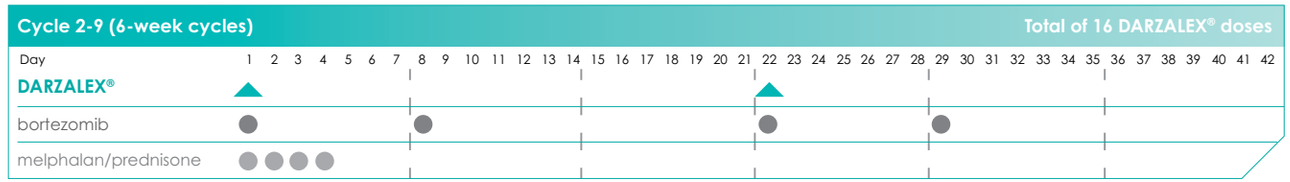
Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® + VMP dosing schedule

DARZALEX® dosing frequency decreases over time[1]



*The first prescribed 16 mg/kg dose at Week 1 may be split over 2 consecutive days. See page 60 for details.



Infusion-related reactions of any grade or severity may be managed by interruption, modification, and/or discontinuation of the infusion. DARZALEX® should be permanently discontinued upon the third occurrence of a Grade 3 infusion-related reaction and upon any occurrence of a Grade 4 infusion-related reaction.

No dose reductions of DARZALEX® are recommended. Dose delay may be required to allow recovery of blood cell counts in the event of hematological toxicity *[see Warnings and Precautions (5.3, 5.4)]*. For information concerning drugs given in combination with DARZALEX®, see manufacturer's prescribing information.

Select Important Safety Information

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Select Important Information[1]

- DARZALEX® should be administered by a healthcare provider, with immediate access to emergency equipment and appropriate medical support to manage infusion-related reactions if they occur
- If a dose of DARZALEX® is missed, administer the dose as soon as possible and adjust the dosing schedule to maintain the dosing interval

Select Important Safety Information

CONTRAINDICATIONS

DARZALEX® is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions. Less than 1% of patients had a Grade 3/4 infusion-related reaction at Week 2 or subsequent infusions. The median time to onset was 1.5 hours (range: 0 to 73 hours). Nearly all reactions occurred during infusion or within 4 hours of completing DARZALEX®. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, tachycardia, headache, laryngeal edema, pulmonary edema, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting, and nausea. Less common signs and symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, hypotension, and blurred vision.

When DARZALEX® dosing was interrupted in the setting of ASCT (CASSIOPEIA) for a median of 3.75 months (range: 2.4 to 6.9 months), upon re-initiation of DARZALEX®, the incidence of infusion-related reactions was 11% for the first infusion following ASCT. Infusion-related reactions occurring at re-initiation of DARZALEX® following ASCT were consistent in terms of symptoms and severity (Grade 3 or 4: <1%) with those reported in previous studies at Week 2 or subsequent infusions. In EQUULEUS, patients receiving combination treatment (n=97) were administered the first 16 mg/kg dose at Week 1 split over two days, ie, 8 mg/kg on Day 1 and Day 2, respectively. The incidence of any grade infusion-related reactions was 42%, with 36% of patients experiencing infusion-related reactions on Day 1 of Week 1, 4% on Day 2 of Week 1, and 8% with subsequent infusions.

Pre-medicate patients with antihistamines, antipyretics, and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt DARZALEX® infusion for reactions of any severity and institute medical management as needed. Permanently discontinue DARZALEX® therapy if an anaphylactic reaction or life-threatening (Grade 4) reaction occurs and institute appropriate emergency care. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion.

To reduce the risk of delayed infusion-related reactions, administer oral corticosteroids to all patients following DARZALEX® infusions. Patients with a history of chronic obstructive pulmonary disease may require additional post-infusion medications to manage respiratory complications. Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with chronic obstructive pulmonary disease.

Ocular adverse reactions, including acute myopia and narrowing of the anterior chamber angle due to ciliochoroidal effusions with potential for increased intraocular pressure or glaucoma, have occurred with DARZALEX® infusion. If ocular symptoms occur, interrupt DARZALEX® infusion and seek immediate ophthalmologic evaluation prior to restarting DARZALEX®.

Interference With Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive indirect antiglobulin test (indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab infusion. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type is not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX®. Type and screen patients prior to starting DARZALEX®.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Safety results demonstrated in combination with VMP

Most frequent adverse reactions and laboratory abnormalities reported in ≥10% of patients and with at least a 5% greater frequency in the DARZALEX® + VMP arm[1]

Adverse reactions						
	DARZALEX® + VMP (n=346)			**VMP** (n=354)		
Treatment-emergent event	**Any grade (%)**	**Grade 3 (%)**	**Grade 4 (%)**	**Any grade (%)**	**Grade 3 (%)**	**Grade 4 (%)**
Upper respiratory tract infection	48	5	0	28	3	0
Infusion-related reactions	28	4	1	0	0	0
Edema peripheral	21	1	<1	14	1	0
Pneumonia	16	12	<1	6	5	<1
Cough	16	<1	0	8	<1	0
Dyspnea	13	2	1	5	1	0
Hypertension	10	4	<1	3	2	0

Serious adverse reactions with at least a 2% greater incidence in the DVMP arm compared to the VMP arm were pneumonia (DVMP 11% vs VMP 4%), upper respiratory tract infection (DVMP 5% vs VMP 1%), and pulmonary edema (DVMP 2% vs VMP 0%).[1]

Laboratory abnormalities						
	DARZALEX® + VMP (n=346)			**VMP** (n=354)		
Treatment-emergent event	**Any grade (%)**	**Grade 3 (%)**	**Grade 4 (%)**	**Any grade (%)**	**Grade 3 (%)**	**Grade 4 (%)**
Anemia	47	18	0	50	21	0
Thrombocytopenia	88	27	11	88	26	16
Neutropenia	86	34	10	87	32	11
Lymphopenia	85	46	12	83	44	9

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Safety results demonstrated in combination with VMP

- Discontinuation rates due to any adverse event: 4.9% with DVMP vs 9.3% with VMP alone[4]
- Infusion-related reactions (IRRs) with DARZALEX® + VMP occurred in 28% of patients; 4% were Grade 3 and 1% were Grade 4[1]
- Grade 3/4 infections were 23% with DVMP vs 15% with VMP alone[1]
- IRRs of any grade or severity may require management by interruption, modification, and/or discontinuation of the infusion[1]
- Most IRRs occurred during the first infusion[1]

See previous page for additional results.

Notes:

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX®
(daratumumab)
injection for intravenous infusion
100 mg/5 mL, 400 mg/20 mL

DARZALEX® (daratumumab) + bortezomib + dexamethasone (DVd)

DOSING & SAFETY

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) + Vd dosing

In patients at first relapse[1]

Dosing schedule based on a phase 3, randomized, active-controlled trial

DARZALEX® in combination with Velcade® (bortezomib) and dexamethasone (Vd) (n=251) vs Vd alone (n=247)

Recommended dosage and schedule for DARZALEX®[1]

3 Doses Per Cycle given as **1 weekly** infusion (Cycles 1* to 3; Weeks 1 to 9)

1 Dose Per Cycle given as 1 infusion **every 3 weeks** (once per 3-week cycle; Cycles 4 to 8; Weeks 10 to 24)

1 Dose Per Cycle given as 1 infusion **every 4 weeks** (Cycles 9+; Weeks 25+ until disease progression)

21 estimated Year 1 infusion visits

See table on page 31 ►

- Velcade® (bortezomib) is administered by subcutaneous injection or IV infusion on Days 1, 4, 8, and 11 of each cycle for a total of 8 cycles†
- Dexamethasone 20 mg is given orally once daily on Days 1, 2, 4, 5, 8, 9, 11, and 12 for a total of 8 cycles‡
  - On the days of DARZALEX® infusion, 20 mg of the dexamethasone dose was administered as a pre-infusion medication and was continued as a pre-medication after Vd discontinuation
  - For patients on a reduced dexamethasone dose, the entire 20-mg dose was given as a DARZALEX® pre-infusion medication

Velcade® is a registered trademark of Millennium Pharmaceuticals, Inc.

*The first prescribed 16 mg/kg dose at Week 1 may be split over 2 consecutive days. See page 60 for details.

†Please refer to the bortezomib prescribing information for more detailed information about twice-weekly bortezomib dosing.

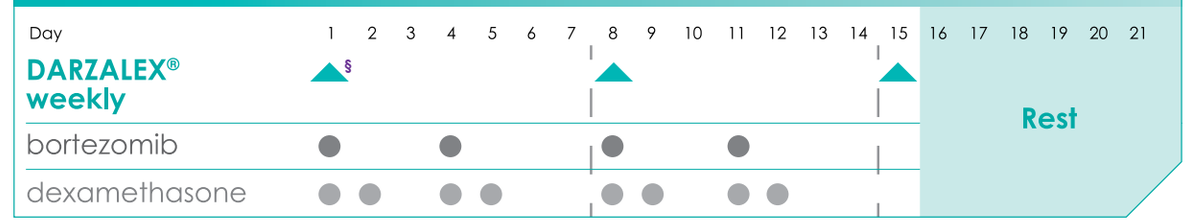
‡Please see the DARZALEX® full Prescribing Information for more information regarding dexamethasone dosage and administration.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® + Vd dosing schedule

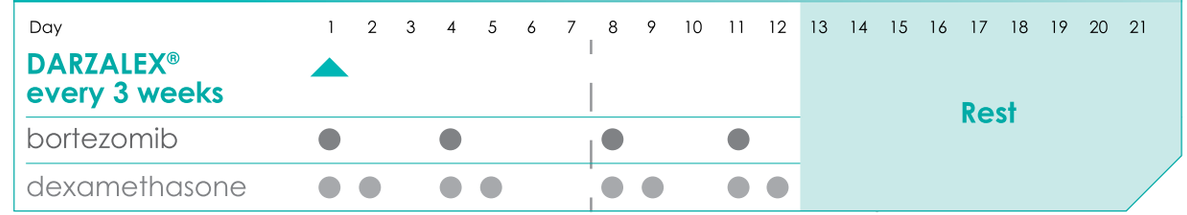
DARZALEX® dosing frequency decreases over time[1]

Cycles 1–3 (each lasting 21 days) — **Total of 9 DARZALEX® doses**



§The first prescribed 16 mg/kg dose at Week 1 may be split over 2 consecutive days. See page 60 for details.

Cycles 4–8 (each lasting 21 days) — **Total of 5 DARZALEX® doses**



Cycle 9 onward (each lasting 28 days)

Continue DARZALEX® once every 4 weeks until disease progression or unacceptable toxicity[1]

Note: Bortezomib and dexamethasone dosing should be stopped after 8 cycles.

Infusion-related reactions of any grade or severity may be managed by interruption, modification, and/or discontinuation of the infusion. DARZALEX® should be permanently discontinued upon the third occurrence of a Grade 3 infusion-related reaction and upon any occurrence of a Grade 4 infusion-related reaction.

No dose reductions of DARZALEX® are recommended. Dose delay may be required to allow recovery of blood cell counts in the event of hematological toxicity *[see Warnings and Precautions (5.3, 5.4)]*. For information concerning drugs given in combination with DARZALEX®, see manufacturer's prescribing information.

Select Important Safety Information

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Select Important Information[1]

- DARZALEX® should be administered by a healthcare provider, with immediate access to emergency equipment and appropriate medical support to manage infusion-related reactions if they occur
- If a dose of DARZALEX® is missed, administer the dose as soon as possible and adjust the dosing schedule to maintain the dosing interval

Select Important Safety Information

CONTRAINDICATIONS

DARZALEX® is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions. Less than 1% of patients had a Grade 3/4 infusion-related reaction at Week 2 or subsequent infusions. The median time to onset was 1.5 hours (range: 0 to 73 hours). Nearly all reactions occurred during infusion or within 4 hours of completing DARZALEX®. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, tachycardia, headache, laryngeal edema, pulmonary edema, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting, and nausea. Less common signs and symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, hypotension, and blurred vision.

When DARZALEX® dosing was interrupted in the setting of ASCT (CASSIOPEIA) for a median of 3.75 months (range: 2.4 to 6.9 months), upon re-initiation of DARZALEX®, the incidence of infusion-related reactions was 11% for the first infusion following ASCT. Infusion-related reactions occurring at re-initiation of DARZALEX® following ASCT were consistent in terms of symptoms and severity (Grade 3 or 4: <1%) with those reported in previous studies at Week 2 or subsequent infusions. In EQUULEUS, patients receiving combination treatment (n=97) were administered the first 16 mg/kg dose at Week 1 split over two days, ie, 8 mg/kg on Day 1 and Day 2, respectively. The incidence of any grade infusion-related reactions was 42%, with 36% of patients experiencing infusion-related reactions on Day 1 of Week 1, 4% on Day 2 of Week 1, and 8% with subsequent infusions.

Pre-medicate patients with antihistamines, antipyretics, and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt DARZALEX® infusion for reactions of any severity and institute medical management as needed. Permanently discontinue DARZALEX® therapy if an anaphylactic reaction or life-threatening (Grade 4) reaction occurs and institute appropriate emergency care. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion.

To reduce the risk of delayed infusion-related reactions, administer oral corticosteroids to all patients following DARZALEX® infusions. Patients with a history of chronic obstructive pulmonary disease may require additional post-infusion medications to manage respiratory complications. Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with chronic obstructive pulmonary disease.

Ocular adverse reactions, including acute myopia and narrowing of the anterior chamber angle due to ciliochoroidal effusions with potential for increased intraocular pressure or glaucoma, have occurred with DARZALEX® infusion. If ocular symptoms occur, interrupt DARZALEX® infusion and seek immediate ophthalmologic evaluation prior to restarting DARZALEX®.

Interference With Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive indirect antiglobulin test (indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab infusion. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type is not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX®. Type and screen patients prior to starting DARZALEX®.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Safety results demonstrated in combination with Vd

Most frequent adverse reactions and laboratory abnormalities reported in ≥20% of patients and with at least a 5% greater frequency in the DARZALEX® + Vd arm[1]*

Adverse reactions						
	DARZALEX® + Vd (n=243)			Vd (n=237)		
Treatment-emergent event	Any grade (%)	Grade 3 (%)	Grade 4 (%)	Any grade (%)	Grade 3 (%)	Grade 4 (%)
Peripheral sensory neuropathy	47	5	0	38	6	<1
Infusion-related reactions	45	9	0	0	0	0
Upper respiratory tract infection	44	6	0	30	3	<1
Diarrhea	32	3	<1	22	1	0
Cough	27	0	0	14	0	0
Edema peripheral	22	1	0	13	0	0
Dyspnea	21	4	0	11	1	0

*Adverse reactions that occurred with a frequency of ≥10% and <20%, and with at least a 5% greater frequency in the DARZALEX® + Vd arm were: pyrexia and vomiting.

Serious adverse reactions (ARs) with at least a 2% greater incidence in the DVd arm compared to the Vd arm were upper respiratory tract infection (DVd 5% vs Vd 2%), diarrhea, and atrial fibrillation (DVd 2% vs Vd 0% for each).[1]

Laboratory abnormalities						
	DARZALEX® + Vd (n=243)			Vd (n=237)		
Treatment-emergent event	Any grade (%)	Grade 3 (%)	Grade 4 (%)	Any grade (%)	Grade 3 (%)	Grade 4 (%)
Anemia	48	13	0	56	14	0
Thrombocytopenia	90	28	19	85	22	13
Neutropenia	58	12	3	40	5	<1
Lymphopenia	89	41	7	81	24	3

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Safety results demonstrated in combination with Vd

- Discontinuation rates due to ARs with DVd were similar to Vd alone (7% vs 9%, respectively)[1]
- Infusion-related reactions (IRRs) with DVd occurred in 45% of patients; 9% were Grade 3 and 0% were Grade 4[1]
- Grade 3/4 infections were similar between study arms: 21% vs 19% with DVd vs Vd alone, respectively[1]
- IRRs of any grade or severity may require management by interruption, modification, and/or discontinuation of the infusion[1]
- Most IRRs occurred during the first infusion[1]

See previous page for additional results.

Notes:

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX®
(daratumumab)
injection for intravenous infusion
100 mg/5 mL, 400 mg/20 mL

DARZALEX® (daratumumab) + Kyprolis® (carfilzomib) + dexamethasone (DKd)

DOSING & SAFETY

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) + Kd dosing

In patients with 1 to 3 prior lines of therapy

Dosing schedule based on a phase 3, randomized, active-controlled trial

DARZALEX® in combination with Kyprolis® (carfilzomib) and dexamethasone (Kd) (n=312) vs Kd alone (n=154)

Recommended dosage and schedule for DARZALEX®[1]

5 Doses Per Cycle	Given as split dose infusion over **2 consecutive days** Week 2-4: given as **1 weekly** infusion
4 Doses Per Cycle	Given as **1 weekly** infusion (Cycle 2; Weeks 5-8)
2 Doses Per Cycle	Given as 1 infusion **every 2 weeks** (Cycles 3-6; Weeks 9-24)
1 Dose Per Cycle	Given as 1 infusion **every 4 weeks** (Cycles 7+; Weeks 25+ until disease progression)
24	estimated Year 1 infusion visits

See table on page 37 ►

- Carfilzomib is administered by IV infusion Days 1 and 2, 8, 9, 15, and 16 of each cycle for a total of 8 cycles.*
- Dexamethasone 20 mg is given orally or intravenously on Days 1, 2, 8, 9, 15 and 16 and then 40 mg orally or intravenously on Day 22 for a total of 8 cycles†
  - On the days of DARZALEX® infusion, 20 mg of the dexamethasone dose was administered as a pre-infusion medication and was continued as a pre-medication after Kd discontinuation
  - For patients on a reduced dexamethasone dose, the entire 20-mg dose was given as a DARZALEX® pre-infusion medication

Kyprolis® (carfilzomib) is a registered trademark of Amgen, Inc.

*Please refer to the carfilzomib prescribing information for more detailed information about twice-weekly and once-weekly carfilzomib dosing.

†Please see the DARZALEX® full Prescribing Information for more information regarding dexamethasone dosage and administration.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® + Kd dosing schedule

DARZALEX® dosing frequency decreases over time[1]

Cycles 1–2 (each lasting 28 days) with either ONCE-weekly or TWICE-weekly carfilzomib — **Total of 9 DARZALEX® doses**

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
DARZALEX® weekly	▲	▲	§					▲							▲							▲						
Once-weekly carfilzomib																												
carfilzomib‖	●							●							●													
dexamethasone	●	●						●	●						●	●						●	●					
Twice-weekly carfilzomib																												
carfilzomib¶	●	●						●	●						●	●												
dexamethasone	●	●						●	●						●	●						●						

§The first prescribed dose of 8 mg/kg in Cycle 1 on Days 1 and 2. See page 60 for details.

‖Carfilzomib was administered intravenously once weekly at a dose of 20 mg/m² on Cycle 1 Day 1 and escalated to dose of 70 mg/m² on Cycle 1 Days 8 and 15, and Days 1, 8, and 15 of each subsequent 28-day cycle.

¶Carfilzomib was administered intravenously at a dose of 20 mg/m² in Cycle 1 on Days 1 and 2; at a dose of 56 mg/m² in Cycle 1 on Days 8, 9, 15, and 16; and at a dose of 56 mg/m² on Days 1, 2, 8, 9, 15, and 16 of each 28-day cycle thereafter.

Cycles 3–6 (each lasting 28 days) with either ONCE-weekly or TWICE-weekly carfilzomib — **Total of 8 DARZALEX® doses**

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
DARZALEX® every 2 weeks	▲														▲													
Once-weekly carfilzomib																												
carfilzomib	●							●							●													
dexamethasone	●	●						●	●						●	●						●						
Twice-weekly carfilzomib																												
carfilzomib	●	●						●	●						●	●												
dexamethasone	●	●						●	●						●	●						●						

Cycle 7 onward (each cycle lasting 28 days) with either ONCE-weekly or TWICE-weekly carfilzomib — **Total of 8 DARZALEX® doses**

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Continue DARZALEX® once every 4 weeks until disease progression or unacceptable toxicity[1]	▲																											
Once-weekly carfilzomib																												
carfilzomib	●							●							●													
dexamethasone	●	●						●							●							●						
Twice-weekly carfilzomib																												
carfilzomib	●	●						●	●						●	●												
dexamethasone	●	●						●	●						●	●						●						

Infusion-related reactions of any grade or severity may be managed by interruption, modification, and/or discontinuation of the infusion. DARZALEX® should be permanently discontinued upon the third occurrence of a Grade 3 infusion-related reaction and upon any occurrence of a Grade 4 infusion-related reaction.

No dose reductions of DARZALEX® are recommended. Dose delay may be required to allow recovery of blood cell counts in the event of hematological toxicity *[see Warnings and Precautions (5.3, 5.4)]*. For information concerning drugs given in combination with DARZALEX®, see manufacturer's prescribing information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Select Important Information[1]

- DARZALEX® should be administered by a healthcare provider, with immediate access to emergency equipment and appropriate medical support to manage infusion-related reactions if they occur
- If a dose of DARZALEX® is missed, administer the dose as soon as possible and adjust the dosing schedule to maintain the dosing interval

Select Important Safety Information

CONTRAINDICATIONS

DARZALEX® is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions. Less than 1% of patients had a Grade 3/4 infusion-related reaction at Week 2 or subsequent infusions. The median time to onset was 1.5 hours (range: 0 to 73 hours). Nearly all reactions occurred during infusion or within 4 hours of completing DARZALEX®. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, tachycardia, headache, laryngeal edema, pulmonary edema, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting, and nausea. Less common signs and symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, hypotension, and blurred vision.

When DARZALEX® dosing was interrupted in the setting of ASCT (CASSIOPEIA) for a median of 3.75 months (range: 2.4 to 6.9 months), upon re-initiation of DARZALEX®, the incidence of infusion-related reactions was 11% for the first infusion following ASCT. Infusion-related reactions occurring at re-initiation of DARZALEX® following ASCT were consistent in terms of symptoms and severity (Grade 3 or 4: <1%) with those reported in previous studies at Week 2 or subsequent infusions. In EQUULEUS, patients receiving combination treatment (n=97) were administered the first 16 mg/kg dose at Week 1 split over two days, ie, 8 mg/kg on Day 1 and Day 2, respectively. The incidence of any grade infusion-related reactions was 42%, with 36% of patients experiencing infusion-related reactions on Day 1 of Week 1, 4% on Day 2 of Week 1, and 8% with subsequent infusions.

Pre-medicate patients with antihistamines, antipyretics, and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt DARZALEX® infusion for reactions of any severity and institute medical management as needed. Permanently discontinue DARZALEX® therapy if an anaphylactic reaction or life-threatening (Grade 4) reaction occurs and institute appropriate emergency care. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion.

To reduce the risk of delayed infusion-related reactions, administer oral corticosteroids to all patients following DARZALEX® infusions. Patients with a history of chronic obstructive pulmonary disease may require additional post-infusion medications to manage respiratory complications. Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with chronic obstructive pulmonary disease.

Ocular adverse reactions, including acute myopia and narrowing of the anterior chamber angle due to ciliochoroidal effusions with potential for increased intraocular pressure or glaucoma, have occurred with DARZALEX® infusion. If ocular symptoms occur, interrupt DARZALEX® infusion and seek immediate ophthalmologic evaluation prior to restarting DARZALEX®.

Interference With Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive indirect antiglobulin test (indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab infusion. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type is not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX®. Type and screen patients prior to starting DARZALEX®.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Safety results demonstrated in combination with Kd

Most frequent adverse reactions reported in ≥15% of patients who received DARZALEX® (daratumumab) + twice-weekly carfilzomib + dexamethasone*

Adverse reactions (CANDOR)				
	DKd (N=308)		Kd (N=153)	
Treatment-emergent event	All grades (%)	Grades 3 or 4 (%)	All grades (%)	Grades 3 or 4
Infusion-related reactions	41	12	28	5
Respiratory tract infection	40†	7	29	3.3
Thrombocytopenia	37	25	30	16
Anemia	33	17	31	14
Fatigue	32	11	28	8
Diarrhea	32	3.9	14	0.7
Hypertension	31	18	28	13
Cough	21	0	21	0
Pyrexia	20	1.9	15	0.7
Dyspnea	20	3.9	22	2.6
Pneumonia	18†	13	12	9
Nausea	18	0	13	0.7
Insomnia	18	3.9	11	2
Bronchitis	17	2.6	12	1.3
Back pain	16	1.9	10	1.3

†Includes fatal adverse reactions.

*The most frequent serious adverse reactions reported in the DKd arm as compared with the Kd arm were pneumonia (DKd 14% vs Kd 9%), pyrexia (DKd 4.2% vs Kd 2.0%), influenza (DKd 3.9% vs Kd 1.3%), sepsis (DKd 3.9% vs Kd 1.3%), anemia (DKd 2.3% vs Kd 0.7%), bronchitis (DKd 1.9% vs Kd 0%), and diarrhea (DKd 1.6% vs Kd 0%).

Fatal adverse reactions within 30 days of the last dose of any study treatment occurred in 10% of 308 patients who received DARZALEX in combination with Kd vs 5% of 153 patients who received Kd. The most frequent fatal adverse reaction was infection (4.5% vs 2.6%).

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

Safety results demonstrated in combination with Kd

- Discontinuation rates due to ARs with DKd were similar to Kd alone (22% vs 25%, respectively).
- Infusion-related reactions that occurred on the day of administration of any DARZALEX® dose or on the next day occurred in 18% of patients and that occurred on the day of administration of the first DARZALEX® dose or the next day occurred in 12%.[1]
- IRRs of any grade or severity may require management by interruption, modification, and/or discontinuation of the infusion[1]

See previous page for additional results.

Most frequent adverse reactions reported in ≥15% of patients who received DARZALEX® (daratumumab) + once-weekly carfilzomib + dexamethasone

Adverse reactions (EQUULEUS)		
Treatment-emergent event	DKd (N=85)	
	All grades (%)	Grades 3 or 4 (%)
Thrombocytopenia	68	32
Fatigue	54	18
Infusion-related reactions	53	12
Respiratory tract infection	53	3.5
Anemia	52	21
Nausea	42	1.2
Vomiting	40	1.2
Diarrhea	38	2.4
Pyrexia	37	1.2
Dyspnea	35	3.5
Cough	33	0
Hypertension	33	20
Insomnia	33	4.7
Neutropenia	31	21
Lymphopenia	29	25
Headache	27	1.2
Back pain	25	0
Bronchitis	19	0
Nasopharyngitis	18	0
Influenza	17	3.5
Constipation	17	0
Pain in extremity	15	0

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX®
(daratumumab)
injection for intravenous infusion
100 mg/5 mL, 400 mg/20 mL

DARZALEX® (daratumumab) + pomalidomide + dexamethasone (DPd)

DOSING & SAFETY

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) + Pd dosing

In patients with ≥2 prior lines of therapy including lenalidomide and a proteasome inhibitor (PI)[1]

Dosing schedule based on a phase 1b, open-label trial[1,6]

DARZALEX® in combination with Pomalyst® (pomalidomide) and dexamethasone (Pd) [N=103][1]

Recommended dosage and schedule for DARZALEX®[1]

4 Doses Per Cycle given as **1 weekly** infusion (Cycles 1* to 2; Weeks 1 to 8)

2 Doses Per Cycle given as 1 infusion **every 2 weeks** (twice per 4-week cycle; Cycles 3 to 6; Weeks 9 to 24)

1 Dose Per Cycle given as 1 infusion **every 4 weeks** (Cycle 7+; Week 25+ until disease progression)

23 estimated Year 1 infusion visits

See table on page 43 ►

- Pomalyst® (pomalidomide) 4 mg is given orally on Days 1–21 of each cycle†
- Dexamethasone 40 mg is given orally or IV once a week‡
  - On DARZALEX® infusion days, 20 mg of the dexamethasone dose was given as a pre-infusion medication and the remainder given the day after the infusion
  - For patients on a reduced dexamethasone dose, the entire 20-mg dose was given as a DARZALEX® pre-infusion medication

Pomalyst® is a registered trademark of Celgene Corporation.

*The first prescribed 16 mg/kg dose at Week 1 may be split over 2 consecutive days. See page 60 for details.

†Please refer to the pomalidomide prescribing information for more detailed information about pomalidomide dosing.

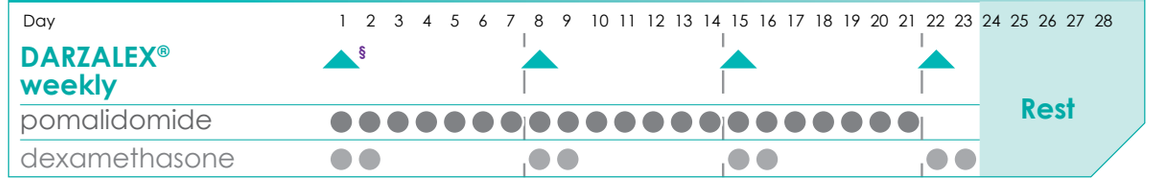
‡Please see the DARZALEX® full Prescribing Information for more information regarding dexamethasone dosage and administration.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® + Pd dosing schedule

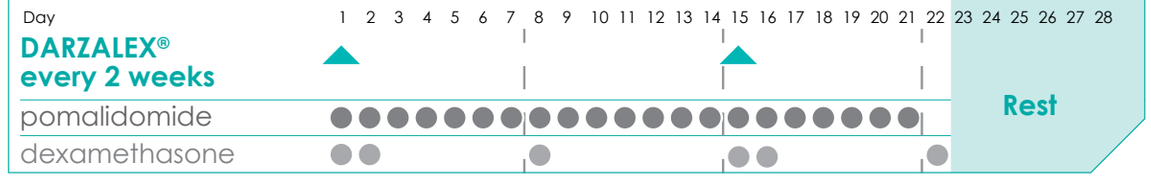
DARZALEX® dosing frequency decreases over time[1]

Cycles 1–2 (each lasting 28 days) — **Total of 8 DARZALEX® doses**

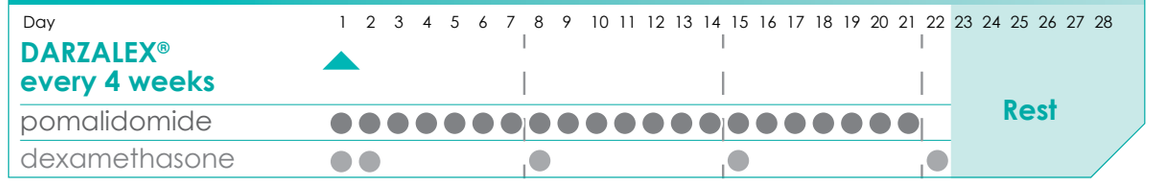


§The first prescribed 16 mg/kg dose at Week 1 may be split over 2 consecutive days. See page 60 for details.

Cycles 3–6 (each lasting 28 days) — **Total of 8 DARZALEX® doses**



Cycle 7 onward (each lasting 28 days)



Continue DARZALEX® + Pd until disease progression or unacceptable toxicity

Infusion-related reactions of any grade or severity may be managed by interruption, modification, and/or discontinuation of the infusion. DARZALEX® should be permanently discontinued upon the third occurrence of a Grade 3 infusion-related reaction and upon any occurrence of a Grade 4 infusion-related reaction.

No dose reductions of DARZALEX® are recommended. Dose delay may be required to allow recovery of blood cell counts in the event of hematological toxicity *[see Warnings and Precautions (5.3, 5.4)]*. For information concerning drugs given in combination with DARZALEX®, see manufacturer's prescribing information.

Select Important Safety Information

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Select Important Information[1]

- DARZALEX® should be administered by a healthcare provider, with immediate access to emergency equipment and appropriate medical support to manage infusion-related reactions if they occur
- If a dose of DARZALEX® is missed, administer the dose as soon as possible and adjust the dosing schedule to maintain the dosing interval

Select Important Safety Information

CONTRAINDICATIONS

DARZALEX® is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions. Less than 1% of patients had a Grade 3/4 infusion-related reaction at Week 2 or subsequent infusions. The median time to onset was 1.5 hours (range: 0 to 73 hours). Nearly all reactions occurred during infusion or within 4 hours of completing DARZALEX®. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, tachycardia, headache, laryngeal edema, pulmonary edema, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting, and nausea. Less common signs and symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, hypotension, and blurred vision.

When DARZALEX® dosing was interrupted in the setting of ASCT (CASSIOPEIA) for a median of 3.75 months (range: 2.4 to 6.9 months), upon re-initiation of DARZALEX®, the incidence of infusion-related reactions was 11% for the first infusion following ASCT. Infusion-related reactions occurring at re-initiation of DARZALEX® following ASCT were consistent in terms of symptoms and severity (Grade 3 or 4: <1%) with those reported in previous studies at Week 2 or subsequent infusions. In EQUULEUS, patients receiving combination treatment (n=97) were administered the first 16 mg/kg dose at Week 1 split over two days, ie, 8 mg/kg on Day 1 and Day 2, respectively. The incidence of any grade infusion-related reactions was 42%, with 36% of patients experiencing infusion-related reactions on Day 1 of Week 1, 4% on Day 2 of Week 1, and 8% with subsequent infusions.

Pre-medicate patients with antihistamines, antipyretics, and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt DARZALEX® infusion for reactions of any severity and institute medical management as needed. Permanently discontinue DARZALEX® therapy if an anaphylactic reaction or life-threatening (Grade 4) reaction occurs and institute appropriate emergency care. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion.

To reduce the risk of delayed infusion-related reactions, administer oral corticosteroids to all patients following DARZALEX® infusions. Patients with a history of chronic obstructive pulmonary disease may require additional post-infusion medications to manage respiratory complications. Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with chronic obstructive pulmonary disease.

Ocular adverse reactions, including acute myopia and narrowing of the anterior chamber angle due to ciliochoroidal effusions with potential for increased intraocular pressure or glaucoma, have occurred with DARZALEX® infusion. If ocular symptoms occur, interrupt DARZALEX® infusion and seek immediate ophthalmologic evaluation prior to restarting DARZALEX®.

Interference With Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive indirect antiglobulin test (indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab infusion. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type is not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX®. Type and screen patients prior to starting DARZALEX®.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Safety results demonstrated in combination with Pd

Most frequent adverse reactions and laboratory abnormalities reported in ≥20% of patients[1]*

Adverse reactions

Treatment-emergent event	DARZALEX® + Pd (N=103) Any grade (%)	Grade 3 (%)	Grade 4 (%)
Fatigue	50	10	0
Upper respiratory tract infection	50	4	1
Infusion-related reactions	50	4	0
Cough	43	1	0
Diarrhea	38	3	0
Dyspnea	33	6	1
Constipation	33	0	0
Nausea	30	0	0
Muscle spasms	26	1	0
Back pain	25	6	0
Pyrexia	25	1	0
Insomnia	23	2	0
Arthralgia	22	2	0
Vomiting	21	2	0
Dizziness	21	2	0
Chills	20	0	0

Laboratory abnormalities

Treatment-emergent event	DARZALEX® + Pd (N=103) Any grade (%)	Grade 3 (%)	Grade 4 (%)
Anemia	57	30	0
Thrombocytopenia	75	10	10
Neutropenia	95	36	46
Lymphopenia	94	45	26

*Adverse reactions that occurred with a frequency of ≥10% and <20% were: tremor, headache, edema peripheral, hypokalemia, nasal congestion, asthenia, noncardiac chest pain, pneumonia, pain in extremity, bone pain, hyperglycemia, musculoskeletal chest pain, anxiety, pain, and decreased appetite.

The overall incidence of serious adverse reactions (ARs) was 49%. Serious ARs reported in ≥5% of patients included pneumonia (7%).[1]

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Safety results demonstrated in combination with Pd

- Discontinuation rates due to ARs with DPd was 13%[1]
- Infusion-related reactions (IRRs) with DPd occurred in 50% of patients; 4% were Grade 3 and 0% were Grade 4[1]
- Grade 3/4 infections were reported in 28% of patients treated with DPd[1]
- IRRs of any grade or severity may require management by interruption, modification, and/or discontinuation of the infusion[1]
- Most IRRs occurred during the first infusion[1]

See previous page for additional results.

Notes:

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX®
(daratumumab)
injection for intravenous infusion
100 mg/5 mL, 400 mg/20 mL

DARZALEX® (daratumumab) MONOTHERAPY (single agent)

DOSING & SAFETY

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) dosing

In patients with ≥3 prior lines including a proteasome inhibitor (PI) and an immunomodulatory agent or who were double-refractory to a PI and an immunomodulatory agent[1,7]

Dosing schedule based on a phase 2, single agent trial (N=106)

Recommended dosage and schedule for DARZALEX®[1]

4 Doses Per Cycle given as **1 weekly** infusion (Cycles 1* to 2; Weeks 1 to 8)

2 Doses Per Cycle given as 1 infusion **every 2 weeks** (twice per 4-week cycle; Cycles 3 to 6; Weeks 9 to 24)

1 Dose Per Cycle given as 1 infusion **every 4 weeks** (Cycle 7+; Week 25+ until disease progression)

23 estimated Year 1 infusion visits

See table on page 49 ►

- Administer DARZALEX® only as an IV infusion after dilution

*The first prescribed 16 mg/kg dose at Week 1 may be split over 2 consecutive days. See page 60 for details.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® monotherapy dosing schedule

DARZALEX® dosing frequency decreases over time[1]

Cycles 1–2 (each lasting 28 days) — **Total of 8 DARZALEX® doses**

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
DARZALEX® weekly	▲†	Rest						▲	Rest						▲	Rest						▲	Rest					

†The first prescribed 16 mg/kg dose at Week 1 may be split over 2 consecutive days. See page 60 for details.

Cycles 3–6 (each lasting 28 days) — **Total of 8 DARZALEX® doses**

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
DARZALEX® every 2 weeks	▲	Rest													▲	Rest												

Cycle 7 onward (each lasting 28 days)

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
DARZALEX® every 4 weeks	▲							Rest																				

Continue until disease progression or unacceptable toxicity

Infusion-related reactions of any grade or severity may be managed by interruption, modification, and/or discontinuation of the infusion. DARZALEX® should be permanently discontinued upon the third occurrence of a Grade 3 infusion-related reaction and upon any occurrence of a Grade 4 infusion-related reaction.

No dose reductions of DARZALEX® are recommended. Dose delay may be required to allow recovery of blood cell counts in the event of hematological toxicity *[see Warnings and Precautions (5.3, 5.4)]*.

Select Important Safety Information

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Select Important Information[1]

- DARZALEX® should be administered by a healthcare provider, with immediate access to emergency equipment and appropriate medical support to manage infusion-related reactions if they occur
- If a dose of DARZALEX® is missed, administer the dose as soon as possible and adjust the dosing schedule to maintain the dosing interval

Select Important Safety Information

CONTRAINDICATIONS

DARZALEX® is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions. Less than 1% of patients had a Grade 3/4 infusion-related reaction at Week 2 or subsequent infusions. The median time to onset was 1.5 hours (range: 0 to 73 hours). Nearly all reactions occurred during infusion or within 4 hours of completing DARZALEX®. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, tachycardia, headache, laryngeal edema, pulmonary edema, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting, and nausea. Less common signs and symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, hypotension, and blurred vision.

Safety results with DARZALEX® monotherapy

Most frequent adverse reactions and laboratory abnormalities reported in ≥20% of patients[1]*

Adverse reactions			
Treatment-emergent event	DARZALEX® (N=156)		
	Any grade (%)	Grade 3 (%)	Grade 4 (%)
Infusion-related reactions	48	3	0
Fatigue	39	2	0
Nausea	27	0	0
Back pain	23	2	0
Cough	21	0	0
Pyrexia	21	1	0
Upper respiratory tract infection	20	1	0

*Adverse reactions that occurred with a frequency of ≥10% and <20% were: arthralgia, nasal congestion, diarrhea, decreased appetite, nasopharyngitis, constipation, pain in extremity, dyspnea, vomiting, headache, musculoskeletal chest pain, pneumonia, chills, and hypertension.

Serious adverse reactions were reported in 33% of patients. The most frequent serious adverse reactions were pneumonia (6%), general physical health deterioration (3%), and pyrexia (3%).[1]

Laboratory abnormalities			
Treatment-emergent event	DARZALEX® (N=156)		
	Any grade (%)	Grade 3 (%)	Grade 4 (%)
Anemia	45	19	0
Thrombocytopenia	48	10	8
Neutropenia	60	17	3
Lymphopenia	72	30	10

Safety results (cont'd)

- Discontinuation rates due to any adverse event: 4%[1]
- Infusion-related reactions (IRRs) with DARZALEX® occurred in 48% of patients; 3% were Grade 3 and 0% were Grade 4[1]
- IRRs of any grade or severity may require management by interruption, modification, and/or discontinuation of the infusion[1]
- Most IRRs occurred during the first infusion[1]

Select Important Safety Information

Neutropenia and Thrombocytopenia

DARZALEX® may increase neutropenia and thrombocytopenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Monitor patients with neutropenia for signs of infection. Consider withholding DARZALEX® until recovery of neutrophils or for recovery of platelets.

Please see additional Important Safety Information throughout and on pages 52–55, and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Indications and Important Safety Information

INDICATIONS

DARZALEX® (daratumumab) is indicated for the treatment of adult patients with multiple myeloma:

- In combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy
- In combination with bortezomib, melphalan, and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant
- In combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant
- In combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
- In combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy
- In combination with pomalidomide and dexamethasone in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor
- As monotherapy in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

DARZALEX® is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions. Less than 1% of patients had a Grade 3/4 infusion-related reaction at Week 2 or subsequent infusions. The median time to onset was 1.5 hours (range: 0 to 73 hours). Nearly all reactions occurred during infusion or within 4 hours of completing DARZALEX®. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, tachycardia, headache, laryngeal edema, pulmonary edema, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting, and nausea. Less common signs and symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, hypotension, and blurred vision.

When DARZALEX® dosing was interrupted in the setting of ASCT (CASSIOPEIA) for a median of 3.75 months (range: 2.4 to 6.9 months), upon re-initiation of DARZALEX®, the incidence of infusion-related reactions was 11% for the first infusion following ASCT. Infusion-related reactions occurring at re-initiation of DARZALEX® following ASCT were consistent in terms of symptoms and severity (Grade 3 or 4: <1%) with those reported in previous studies at Week 2 or subsequent infusions. In EQUULEUS, patients receiving combination treatment (n=97) were administered the first 16 mg/kg dose at Week 1 split over two days, ie, 8 mg/kg on Day 1 and Day 2, respectively. The incidence of any grade infusion-related reactions was 42%, with 36% of patients experiencing infusion-related reactions on Day 1 of Week 1, 4% on Day 2 of Week 1, and 8% with subsequent infusions.

Please click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Infusion-Related Reactions (cont'd)

Pre-medicate patients with antihistamines, antipyretics, and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt DARZALEX® infusion for reactions of any severity and institute medical management as needed. Permanently discontinue DARZALEX® therapy if an anaphylactic reaction or life-threatening (Grade 4) reaction occurs and institute appropriate emergency care. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion.

To reduce the risk of delayed infusion-related reactions, administer oral corticosteroids to all patients following DARZALEX® infusions. Patients with a history of chronic obstructive pulmonary disease may require additional post-infusion medications to manage respiratory complications. Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with chronic obstructive pulmonary disease.

Ocular adverse reactions, including acute myopia and narrowing of the anterior chamber angle due to ciliochoroidal effusions with potential for increased intraocular pressure or glaucoma, have occurred with DARZALEX® infusion. If ocular symptoms occur, interrupt DARZALEX® infusion and seek immediate ophthalmologic evaluation prior to restarting DARZALEX®.

Interference With Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive indirect antiglobulin test (indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab infusion. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type is not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX®. Type and screen patients prior to starting DARZALEX®.

Neutropenia and Thrombocytopenia

DARZALEX® may increase neutropenia and thrombocytopenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Monitor patients with neutropenia for signs of infection. Consider withholding DARZALEX® until recovery of neutrophils or for recovery of platelets.

Interference With Determination of Complete Response

Daratumumab is a human immunoglobulin G (IgG) kappa monoclonal antibody that can be detected on both the serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and of disease progression in some patients with IgG kappa myeloma protein.

Embryo-Fetal Toxicity

Based on the mechanism of action, DARZALEX® can cause fetal harm when administered to a pregnant woman. DARZALEX® may cause depletion of fetal immune cells and decreased bone density. Advise pregnant women of the potential risk to a fetus. Advise females with reproductive potential to use effective contraception during treatment with DARZALEX® and for 3 months after the last dose.

The combination of DARZALEX® with lenalidomide, pomalidomide, or thalidomide is contraindicated in pregnant women because lenalidomide, pomalidomide, and thalidomide may cause birth defects and death of the unborn child. Refer to the lenalidomide, pomalidomide, or thalidomide prescribing information on use during pregnancy.

ADVERSE REACTIONS

The most frequently reported adverse reactions (incidence ≥20%) were upper respiratory infection, neutropenia, infusion-related reactions, thrombocytopenia, diarrhea, constipation, anemia, peripheral sensory neuropathy, fatigue, peripheral edema, nausea, cough, pyrexia, dyspnea, and asthenia. The most common hematologic laboratory abnormalities (≥40%) with DARZALEX® are neutropenia, lymphopenia, thrombocytopenia, leukopenia, and anemia.

Please click here to see the full Prescribing Information.

cp-60862v8

DARZALEX®
(daratumumab)
injection for intravenous infusion
100 mg/5 mL, 400 mg/20 mL

DARZALEX® (daratumumab) administration

Preparation for administration[1]

Prepare the solution for infusion using aseptic technique as follows:

- Calculate the dose (mg), total volume (mL) of DARZALEX® solution required and the number of DARZALEX® vials needed based on patient actual body weight
- Check that the DARZALEX® solution is colorless to pale yellow. Do not use if opaque particles, discoloration or foreign particles are present
- Remove a volume of 0.9% Sodium Chloride Injection, USP from the infusion bag/container that is equal to the required volume of DARZALEX® solution
- Withdraw necessary amount of DARZALEX® solution and dilute to appropriate volume by adding to the infusion bag/container containing 0.9% Sodium Chloride Injection, USP. Infusion bags/containers must be made of either polyvinylchloride (PVC), polypropylene (PP), polyethylene (PE), or polyolefin blend (PP+PE). Dilute under appropriate aseptic conditions. Discard any unused portion left in the vial
- Gently invert the bag/container to mix the solution. Do not shake
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The diluted solution may develop very small, translucent to white proteinaceous particles, as daratumumab is a protein. Do not use if visibly opaque particles, discoloration or foreign particles are observed
- Since DARZALEX® does not contain a preservative, administer the diluted solution immediately at room temperature, 15°C to 25°C (59°F to 77°F) and in room light. Diluted solution may be kept at room temperature for a maximum of 15 hours (including infusion time)

Preparation for administration[1] (cont'd)

- If not used immediately, the diluted solution can be stored prior to administration for up to 24 hours at refrigerated conditions, 2°C to 8°C (36°F to 46°F) and protected from light. Do not freeze

Select Important Safety Information

ADVERSE REACTIONS

The most frequently reported adverse reactions (incidence ≥20%) were upper respiratory infection, neutropenia, infusion-related reactions, thrombocytopenia, diarrhea, constipation, anemia, peripheral sensory neuropathy, fatigue, peripheral edema, nausea, cough, pyrexia, dyspnea, and asthenia. The most common hematologic laboratory abnormalities (≥40%) with DARZALEX® are neutropenia, lymphopenia, thrombocytopenia, leukopenia, and anemia.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

DARZALEX® (daratumumab) administration (cont'd)

Administration[1]

- If stored in the refrigerator, allow the solution to come to room temperature. Administer diluted solution by intravenous infusion using an infusion set fitted with a flow regulator and with an in-line, sterile, non-pyrogenic, low protein-binding polyethersulfone (PES) filter (pore size 0.22 micrometer or 0.2 micrometer). Administration sets must be made of either polyurethane (PU), polybutadiene (PBD), PVC, PP, or PE
- Do not store any unused portion of the infusion solution for reuse. Any unused product or waste material should be disposed of in accordance with local requirements
- Do not infuse DARZALEX® concomitantly in the same intravenous line with other agents

Select Important Safety Information

Neutropenia and Thrombocytopenia

DARZALEX® may increase neutropenia and thrombocytopenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Monitor patients with neutropenia for signs of infection. Consider withholding DARZALEX® until recovery of neutrophils or for recovery of platelets.

Interference With Determination of Complete Response

Daratumumab is a human immunoglobulin G (IgG) kappa monoclonal antibody that can be detected on both the serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and of disease progression in some patients with IgG kappa myeloma protein.

Embryo-Fetal Toxicity

Based on the mechanism of action, DARZALEX® can cause fetal harm when administered to a pregnant woman. DARZALEX® may cause depletion of fetal immune cells and decreased bone density. Advise pregnant women of the potential risk to a fetus. Advise females with reproductive potential to use effective contraception during treatment with DARZALEX® and for 3 months after the last dose.

The combination of DARZALEX® with lenalidomide, pomalidomide, or thalidomide is contraindicated in pregnant women because lenalidomide, pomalidomide, and thalidomide may cause birth defects and death of the unborn child. Refer to the lenalidomide, pomalidomide, or thalidomide prescribing information on use during pregnancy.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Infusion rates for DARZALEX® (daratumumab)

Slower rate of infusion for the first DARZALEX® dose is recommended, as infusion-related reactions are more likely to occur with the first infusion[1]

	Dilution volume	Initial rate (first hour)	Rate increment*	Maximum rate
Week 1 infusion				
Option 1 (single-dose infusion)				
Week 1 Day 1 (16 mg/kg)	1000 mL	50 mL/hour	50 mL/hour every hour*	200 mL/hour
Option 2 (split-dose infusion)				
Week 1 Day 1 (8 mg/kg)	500 mL	50 mL/hour	50 mL/hour every hour*	200 mL/hour
Week 1 Day 2 (8 mg/kg)	500 mL	50 mL/hour	50 mL/hour every hour*	200 mL/hour
Week 2 (16 mg/kg) infusion†	500 mL	50 mL/hour	50 mL/hour every hour*	200 mL/hour
Subsequent (Week 3 onward, 16 mg/kg) infusions‡	500 mL	100 mL/ hour	50 mL/hour every hour*	200 mL/hour

*Consider incremental escalation of the infusion rate only in the absence of infusion-related reactions.
†Use a dilution volume of 500 mL for the 16 mg/kg dose only if there were no infusion-related reactions the previous week. Otherwise, use a dilution volume of 1000 mL.
‡Use a modified initial rate (100 mL/hour) for subsequent infusions (ie, Week 3 onward) only if there were no infusion-related reactions during the previous infusion. Otherwise, use instructions indicated in the table for the Week 2 infusion rate.

- To facilitate administration, the first prescribed 16 mg/kg dose at Week 1 may be split over 2 consecutive days, ie, 8 mg/kg on Day 1 and Day 2, respectively (see above table)

Median durations§ of 16 mg/kg infusions decreased after the first infusion across all trials (N=1530)[1,5]

- First week infusion was 7 hours
- Second week infusion was 4 hours
- Subsequent infusions were 3 hours

§When the first dose was administered as 2 infusions over 2 days (split dose) in the EQUULEUS study (n=97), the median durations of infusions were 4.2 hours for Week 1 Day 1, 4.2 hours for Week 1 Day 2, 4.1 hours for Week 2, and 3.4 hours for the subsequent infusions.[6‖]
‖Median infusion length for subsequent infusions (Week 2+ in aggregate). Administer the Week 2 (16 mg/kg) infusion according to the infusion rates outlined in Table 4 of the DARZALEX® full Prescribing Information.

Administration of pre- and post-infusion medications is recommended to reduce the risk of infusion-related reactions (see pages 67–68)[1]

Select Important Safety Information

CONTRAINDICATIONS

DARZALEX® is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions. Less than 1% of patients had a Grade 3/4 infusion-related reaction at Week 2 or subsequent infusions. The median time to onset was 1.5 hours (range: 0 to 73 hours). Nearly all reactions occurred during infusion or within 4 hours of completing DARZALEX®. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, tachycardia, headache, laryngeal edema, pulmonary edema, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting, and nausea. Less common signs and symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, hypotension, and blurred vision.

When DARZALEX® dosing was interrupted in the setting of ASCT (CASSIOPEIA) for a median of 3.75 months (range: 2.4 to 6.9 months), upon re-initiation of DARZALEX®, the incidence of infusion-related reactions was 11% for the first infusion following ASCT. Infusion-related reactions occurring at re-initiation of DARZALEX® following ASCT were consistent in terms of symptoms and severity (Grade 3 or 4: <1%) with those reported in previous studies at Week 2 or subsequent infusions. In EQUULEUS, patients receiving combination treatment (n=97) were administered the first 16 mg/kg dose at Week 1 split over two days, ie, 8 mg/kg on Day 1 and Day 2, respectively. The incidence of any grade infusion-related reactions was 42%, with 36% of patients experiencing infusion-related reactions on Day 1 of Week 1, 4% on Day 2 of Week 1, and 8% with subsequent infusions.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

In clinical trials (monotherapy and combination treatments; N=1530)

Most infusion-related reactions occurred during the first infusion[1]

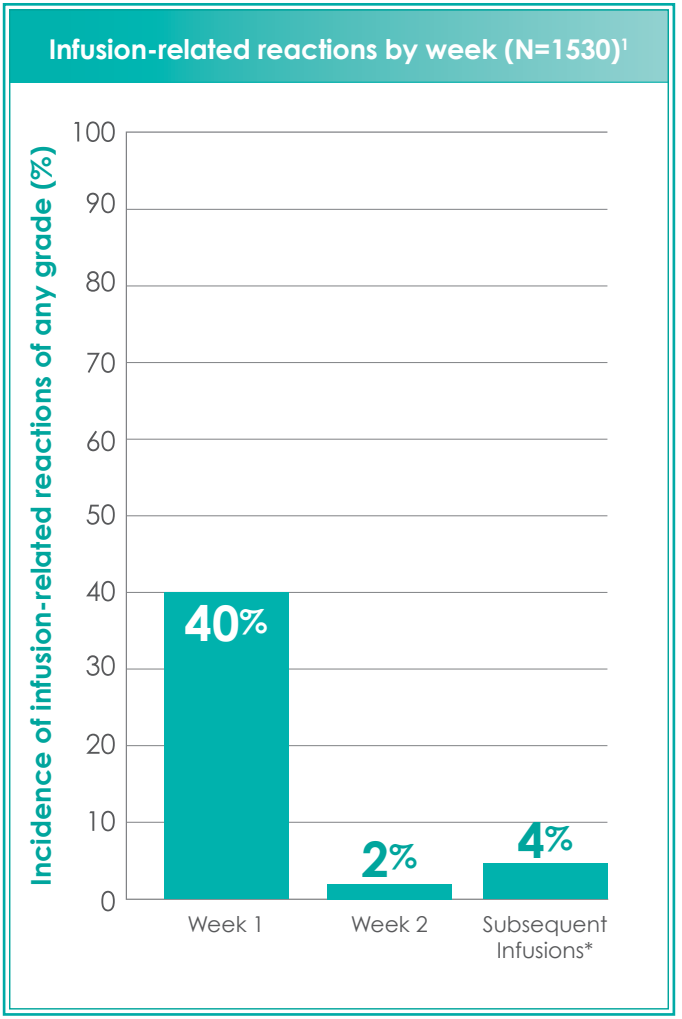
- For 40% of patients, infusion-related reactions (any grade) occurred with the first infusion, 2% of patients with the second infusion, and cumulatively, 4% of patients with subsequent infusions[1]
- The median time to onset of an infusion-related reaction was 1.5 hours (range: 0 to 72.8 hours)[1]
- Incidence of infusion modification due to reactions was 37%[1]
- DARZALEX® can cause severe infusion-related reactions. Severe infusion-related reactions included bronchospasm, hypoxia, dyspnea, hypertension, tachycardia, headache, laryngeal edema, and pulmonary edema. Other adverse infusion-related reactions included nasal congestion, cough, chills, throat irritation, vomiting, and nausea[1]
- For infusion-related reactions of any grade/severity, immediately interrupt the DARZALEX® infusion and manage symptoms. Management of infusion-related reactions may further require reduction in the rate of infusion, or permanent discontinuation of DARZALEX® for Grade 4 reactions[1]

Select Important Safety Information

Infusion-Related Reactions (cont'd)

Pre-medicate patients with antihistamines, antipyretics, and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt DARZALEX® infusion for reactions of any severity and institute medical management as needed. Permanently discontinue DARZALEX® therapy if an anaphylactic reaction or life-threatening (Grade 4) reaction occurs and institute appropriate emergency care. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion.

To reduce the risk of delayed infusion-related reactions, administer oral corticosteroids to all patients following DARZALEX® infusions. Patients with a history of chronic obstructive pulmonary disease may require additional post-infusion medications to manage respiratory complications. Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with chronic obstructive pulmonary disease.



*Cumulative incidence over subsequent infusions.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Management of infusion-related reactions

Infusion-related reactions of any grade or severity may be managed by interruption, modification, and/or discontinuation of the infusion[1]

- For infusion-related reactions of any grade/severity, immediately interrupt the DARZALEX® infusion and manage symptoms. Management of infusion-related reactions may further require reduction in the rate of infusion or treatment discontinuation of DARZALEX® as outlined below

Recommended management of infusion-related reactions[1]	
Infusion-related reaction grade	Dose interruptions/modifications
Grades 1 & 2 (mild to moderate)	Once symptoms resolve: • Resume the infusion at no more than half the rate at which the reaction occurred If the patient does not experience any further reaction symptoms: • Infusion rate escalation may resume at increments and intervals as clinically appropriate up to the maximum rate of 200 mL/hour
Grade 3 (severe)	Once symptoms resolve: • Consider restarting infusion at no more than half the rate at which the reaction occurred If the patient does not experience additional symptoms: • Resume infusion rate escalation at increments and intervals as appropriate In the event of recurrence of Grade 3 symptoms: • Repeat the procedure above If the patient experiences a third occurrence of a Grade 3 or higher infusion reaction: • Permanently discontinue DARZALEX®
Grade 4 (life-threatening)	Permanently discontinue DARZALEX®

Select Important Safety Information

CONTRAINDICATIONS

DARZALEX® is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions. Less than 1% of patients had a Grade 3/4 infusion-related reaction at Week 2 or subsequent infusions. The median time to onset was 1.5 hours (range: 0 to 73 hours). Nearly all reactions occurred during infusion or within 4 hours of completing DARZALEX®. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, tachycardia, headache, laryngeal edema, pulmonary edema, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting, and nausea. Less common signs and symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, hypotension, and blurred vision.

When DARZALEX® dosing was interrupted in the setting of ASCT (CASSIOPEIA) for a median of 3.75 months (range: 2.4 to 6.9 months), upon re-initiation of DARZALEX®, the incidence of infusion-related reactions was 11% for the first infusion following ASCT. Infusion-related reactions occurring at re-initiation of DARZALEX® following ASCT were consistent in terms of symptoms and severity (Grade 3 or 4: <1%) with those reported in previous studies at Week 2 or subsequent infusions. In EQUULEUS, patients receiving combination treatment (n=97) were administered the first 16 mg/kg dose at Week 1 split over two days, ie, 8 mg/kg on Day 1 and Day 2, respectively. The incidence of any grade infusion-related reactions was 42%, with 36% of patients experiencing infusion-related reactions on Day 1 of Week 1, 4% on Day 2 of Week 1, and 8% with subsequent infusions.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Important information before administering DARZALEX® (daratumumab)

Interference with serological testing[1]

- DARZALEX® binds to CD38 found on red blood cells (RBCs) and results in a positive indirect antiglobulin test (indirect Coombs test) that may persist for up to 6 months after the last DARZALEX® infusion

Reminders

- Type and screen patients before starting DARZALEX®
- Inform blood banks when a patient is taking DARZALEX®
- Identify any DARZALEX®-treated blood samples
- Ask patients to tell other healthcare professionals that they have taken DARZALEX®

Prophylaxis for herpes zoster reactivation[1]

- Initiate antiviral prophylaxis to prevent herpes zoster reactivation within 1 week of starting DARZALEX® and continue for 3 months following treatment

Select Important Safety Information

ADVERSE REACTIONS

The most frequently reported adverse reactions (incidence ≥20%) were upper respiratory infection, neutropenia, infusion-related reactions, thrombocytopenia, diarrhea, constipation, anemia, peripheral sensory neuropathy, fatigue, peripheral edema, nausea, cough, pyrexia, dyspnea, and asthenia. The most common hematologic laboratory abnormalities (≥40%) with DARZALEX® are neutropenia, lymphopenia, thrombocytopenia, leukopenia, and anemia.

Pre-infusion medications[1]

To reduce the risk of infusion-related reactions, administer to all patients approximately 1 hour to 3 hours prior to every infusion as follows:

- Dexamethasone 20 mg prior to every DARZALEX® infusion. When dexamethasone is the background regimen specific corticosteroid, the dexamethasone treatment dose will also serve as premedication on DARZALEX® infusion days*
- During monotherapy, methylprednisolone 100 mg, or equivalent, administered intravenously. Following the second infusion, the dose of corticosteroid may be reduced (oral or intravenous methylprednisolone 60 mg)
- Oral antipyretics (acetaminophen 650 mg to 1000 mg), plus
- Oral or IV antihistamine (diphenhydramine 25 mg to 50 mg or equivalent)

*Dexamethasone is given intravenously prior to the first DARZALEX® infusion and oral administration may be considered prior to subsequent infusions. Additional background regimen-specific corticosteroids (eg, prednisone) should not be taken on DARZALEX® infusion days when patients receive dexamethasone (or equivalent) as pre-medication.

Select Important Safety Information

Interference With Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive indirect antiglobulin test (indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab infusion. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type is not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX®. Type and screen patients prior to starting DARZALEX®.

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Post-infusion medications are recommended

Post-infusion medications[1]

To reduce the risk of delayed infusion-related reactions, administer the day after every infusion as follows:

- Oral corticosteroid (≤20 mg methylprednisolone or equivalent); however, if a background regimen-specific corticosteroid (eg, dexamethasone, prednisone) is administered the day after the DARZALEX® infusion, additional post-infusion medications may not be needed
- During monotherapy, administer oral corticosteroid (20 mg methylprednisolone or equivalent dose of an intermediate-acting or long-acting corticosteroid in accordance with local standards) on each of the 2 days following all DARZALEX® infusions (beginning the day after the infusion)

Note: *For patients with a history of chronic obstructive pulmonary disorder, consider including short- and long-acting bronchodilators and inhaled corticosteroids. Following the first 4 infusions, if the patient experiences no major infusion-related reactions, these additional inhaled post-infusion medications may be discontinued.*

Select Important Safety Information

Interference With Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive indirect antiglobulin test (indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab infusion. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type is not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX®. Type and screen patients prior to starting DARZALEX®.

Interference With Determination of Complete Response

Daratumumab is a human immunoglobulin G (IgG) kappa monoclonal antibody that can be detected on both the serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and of disease progression in some patients with IgG kappa myeloma protein.

Notes:

Please see Indications and full Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Patient checklist

Pre-infusion education

- Schedule patients to allow for adequate chair time
- Confirm appropriate infusion set is stocked
  - See pages 56–58 for additional details
- Explain length of infusion and suggest that patients bring activities to occupy themselves during their infusion
- Provide a patient brochure and walk the patient through all important details
- Provide the patient with a comfort kit
- Discuss Important Safety Information
- Inform patients about Janssen CarePath and what services it provides
  - Call: 1-844-55DARZA (1-844-553-2792) or visit JanssenCarePath.com/DARZALEX
  - Identifying cost support options that may help manage out-of-pocket costs for DARZALEX® (daratumumab)
  - Visit JanssenPrescriptionAssistance.com/DARZALEX

Discuss interference with serological testing

- Explain that DARZALEX® can affect blood test results used to match their blood for transfusions[1]
- Give the patient an Assay Interference Bracelet and Card
- Type and screen patients before starting DARZALEX®[1]
- Inform blood banks when a patient is on DARZALEX®[1]
- Identify any DARZALEX®-treated blood samples
- Ask patients to tell other healthcare professionals that they have taken DARZALEX®

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DARZALEX® (daratumumab) injection for intravenous infusion 100 mg/5 mL, 400 mg/20 mL

Administer pre- and post-infusion medications

- Initiate antiviral prophylaxis to prevent herpes zoster reactivation within 1 week of starting DARZALEX® and continue for 3 months following treatment[1]
- Administer pre-infusion medications approximately 1 hour to 3 hours prior to every infusion to reduce the risk of infusion-related reactions[1]
  - Refer to page 67 for guidelines
- Administer post-infusion medications to reduce the risk of delayed infusion-related reactions[1]
  - Refer to page 68 for guidelines

Review safety information

- If a newly diagnosed, transplant-ineligible patient is receiving DARZALEX® + Revlimid® (lenalidomide) + dexamethasone (DRd), refer to pages 5–10
- If a patient is receiving DARZALEX® + Revlimid® (lenalidomide) + dexamethasone (DRd) after a prior regimen, refer to pages 11–16
- If a patient is receiving DARZALEX® + bortezomib + thalidomide + dexamethasone (DVTd), refer to pages 17-22
- If a patient is receiving DARZALEX® + Velcade® (bortezomib) + melphalan + prednisone (DVMP), refer to pages 23–28
- If a patient is receiving DARZALEX® + bortezomib + dexamethasone (DVd), refer to pages 29–34
- If a patient is receiving DARZALEX® + Kyprolis® (carfilzomib) + dexamethasone (DKd), refer to pages 35-40
- If a patient is receiving DARZALEX® + Pomalyst® (pomalidomide) and dexamethasone (DPd), after prior treatment, refer to pages 41–46
- If a patient is receiving DARZALEX® as a monotherapy, refer to pages 47–51
- Monitor patient during the infusion process and assess for adverse reactions[1]
  - Refer to pages 62–64 for more information

We can help make it simple for you to help your patients

Janssen CarePath is your one source for access, affordability, and treatment support for your patients

Janssen CarePath helps verify insurance coverage for your patients, provides reimbursement information, helps find financial assistance options for eligible patients, and provides ongoing support to help patients start and stay on DARZALEX®.

Call a Janssen CarePath Care Coordinator at 877-CarePath (877-227-3728), Monday–Friday, 8:00 AM to 8:00 PM ET

Sign Up or Log In to the Provider Portal at JanssenCarePathPortal.com

Visit JanssenCarePath.com

Janssen CarePath

To contact Janssen Medical Information
Phone: **1-800-Janssen (1-800-526-7736)**
Email: Submit questions via **www.askjanssenmedinfo.com**
Search: **www.JanssenMD.com**

Please see Indications and Important Safety Information on pages 52–55 and click here for DARZALEX® full Prescribing Information.

References: 1. DARZALEX® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **2.** Facon T, Kumar S, Plesner T, et al; the MAIA Trial Investigators. Daratumumab plus lenalidomide and dexamethasone for untreated myeloma. *N Engl J Med*. 2019;380(22):2104-2115. **3.** Moreau P, Attal M, Hulin C, et al. Bortezomib, thalidomide, and dexamethasone with or without daratumumab before and after autologous stem-cell transplantation for newly diagnosed multiple myeloma (CASSIOPEIA): a randomised, open-label, phase 3 study. *Lancet*. 2019;394(10192):29-38. **4.** Mateos MV, Dimopoulos MA, Cavo M, et al; the ALCYONE Trial Investigators. Daratumumab plus bortezomib, melphalan, and prednisone for untreated myeloma. *N Engl J Med*. 2018;378(6):518-528. **5.** Palumbo A, Chanan-Khan A, Weisel K, et al; the CASTOR Investigators. Daratumumab, bortezomib, and dexamethasone for multiple myeloma. *N Engl J Med*. 2016;375(8):754-766. **6.** Data on file. Janssen Biotech, Inc. **7.** Lonial S, Weiss BM, Usmani SZ, et al. Daratumumab monotherapy in patients with treatment-refractory multiple myeloma (SIRIUS): an open-label, randomised, phase 2 trial. *Lancet*. 2016;387(10027):1551-1560.

Janssen Oncology

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(daratumumab)
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