Vegzelma™
bevacizumab

Vegzelma™ demonstrated equivalence in pharmacokinetic and efficacy profiles and high similarity in safety and immunogenicity relative to reference bevacizumab.[1,2]

"We Walk Together.
Now and Always"

Data Sheets and Consumer Medicine Information can be obtained from the Medsafe website at https://www.medsafe.govt.nz/medicines/infosearch.asp

HEALTHCARE
CELLTRION

Celltrion Healthcare is the global biopharmaceutical company specialised in biosimilars.

- We distribute our products in more than 110 countries.[3]

(as of 2022)

Celltrion's products are manufactured in state-of-the-art facilities.

- Celltrion's facilities meet the global standard in both quality and capacity with global supply capacity.

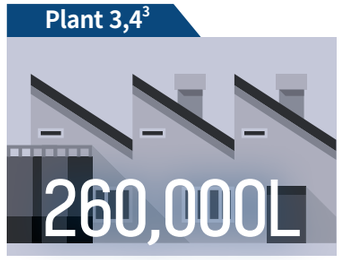
Plant 1[4]

12,500L x 8 Line

Plant 2[4]

15,000L x 6 Line

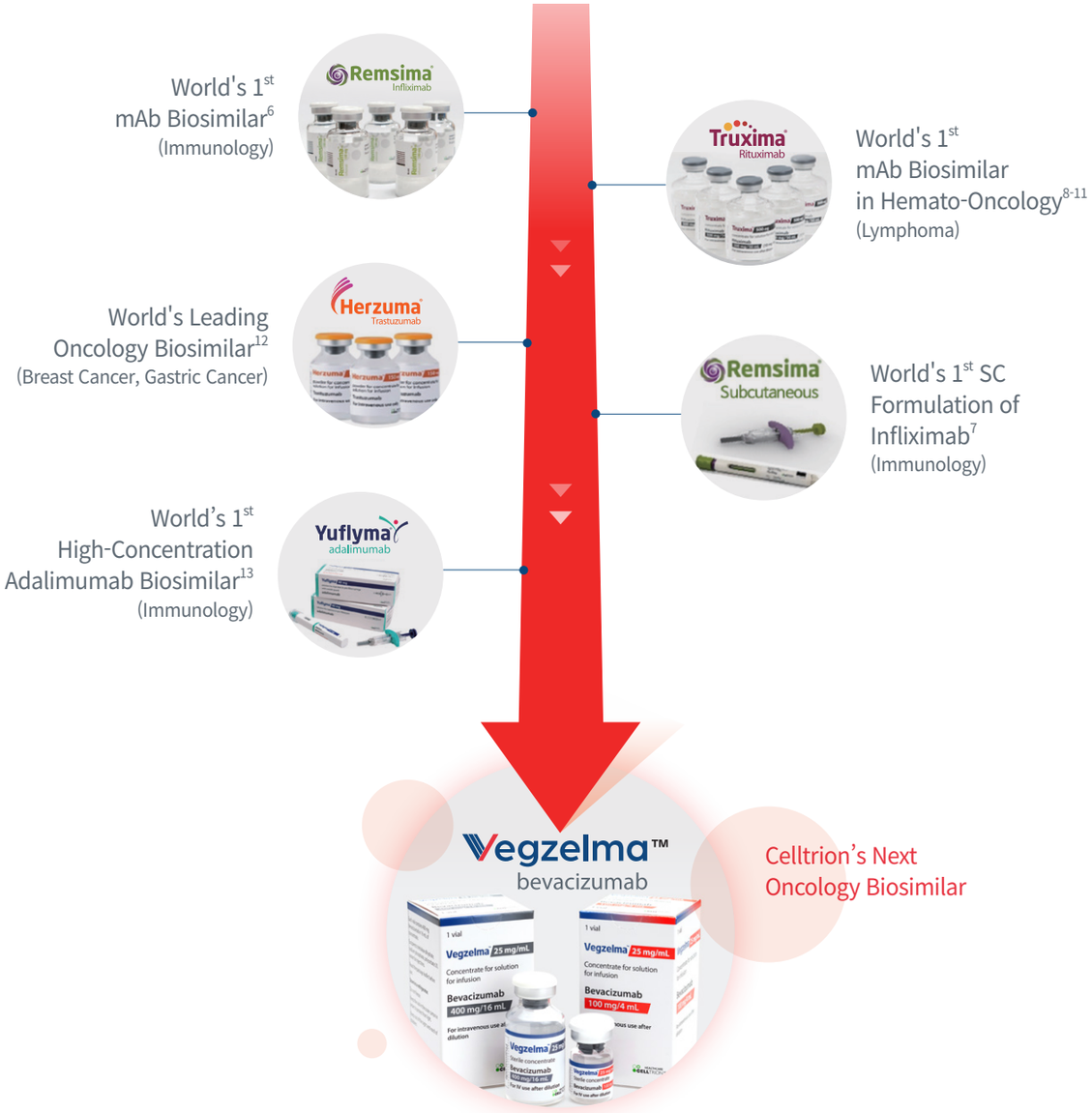
Plant 3,4[3]



Plant 3 under construction
Plant 4 planned

Vegzelma™ developed by the global leading biosimilar pharmaceutical company.

- The world's pioneer of mAb biosimilar and bio-innovatives.[5]



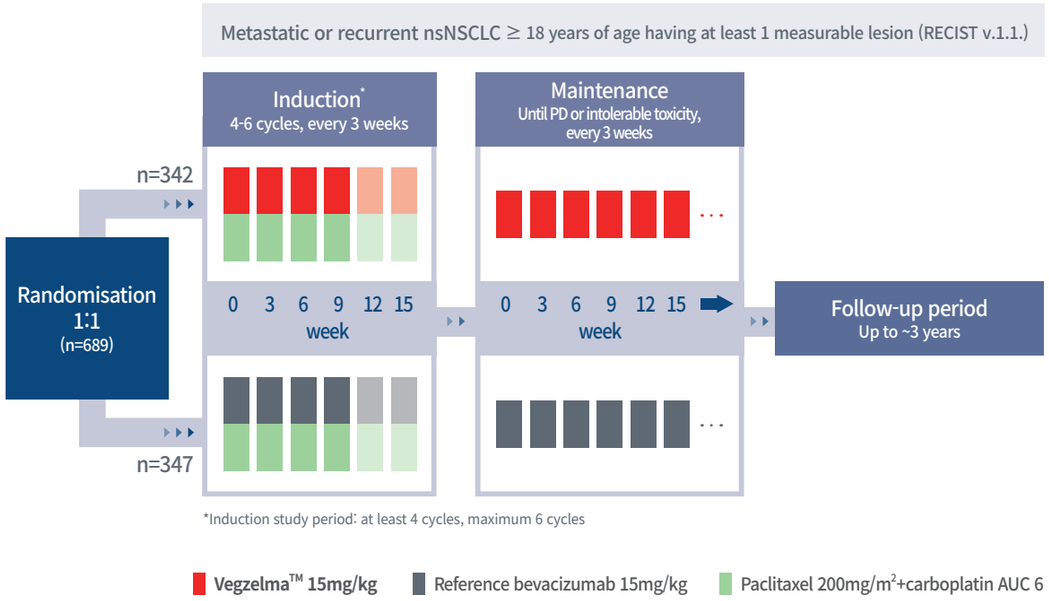
mAb, monoclonal antibody; **SC,** subcutaneous injection

Vegzelma™ demonstrated high similarity in PK, efficacy, safety and immunogenicity profiles relative to reference bevacizumab.[1]

Objectives[1]

This is an ongoing, double-blind, randomized, active-controlled, parallel group, phase 3 study comparing Vegzelma™ to reference bevacizumab in metastatic or recurrent nsNSCLC patients.

Study design[1]



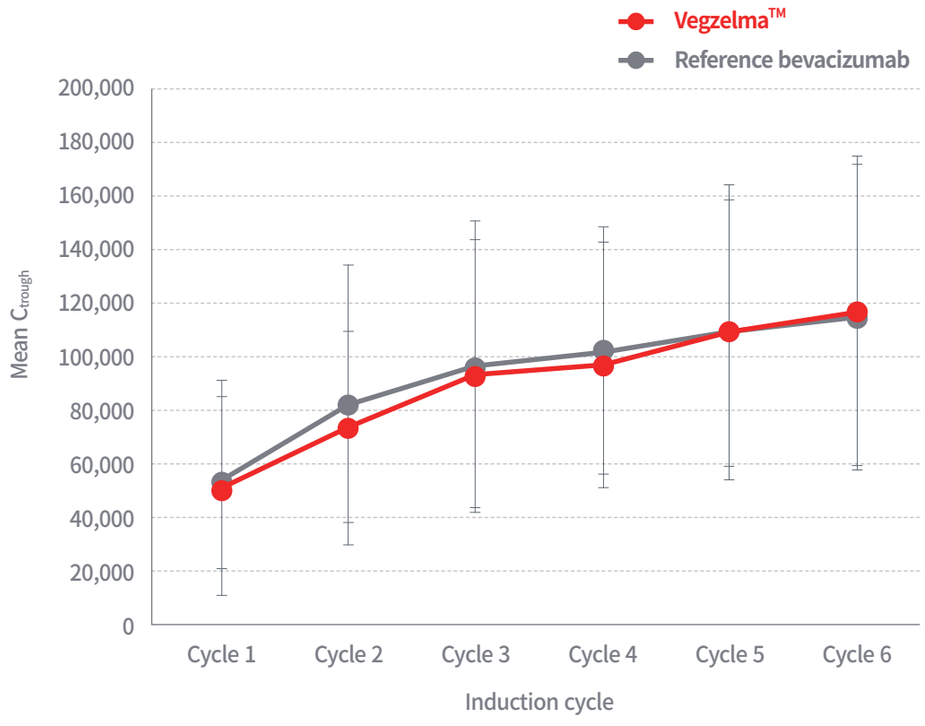
- Primary endpoint: ORR during the induction study period
- Secondary endpoints: ORR during the whole study period, Response duration, TTP, PFS, OS, PK of C_{trough}, Safety profile, QoL

nsNSCLC, non-squamous non-small cell lung cancer; **ORR,** objective response rate; **TTP,** time to progression; **PFS,** progression-free survival; **OS,** overall survival; **PK,** pharmacokinetics; **QoL,** quality of life; **RECIST,** Response Evaluation Criteria In Solid Tumors

Vegzelma™ showed PK similarities to reference bevacizumab in terms of mean C_{trough}.[1]

Mean C_{trough} of Bevacizumab (μg/L) : PK population

- The mean C_{trough} for Vegzelma™ at each cycle in the induction study period was similar to reference bevacizumab.



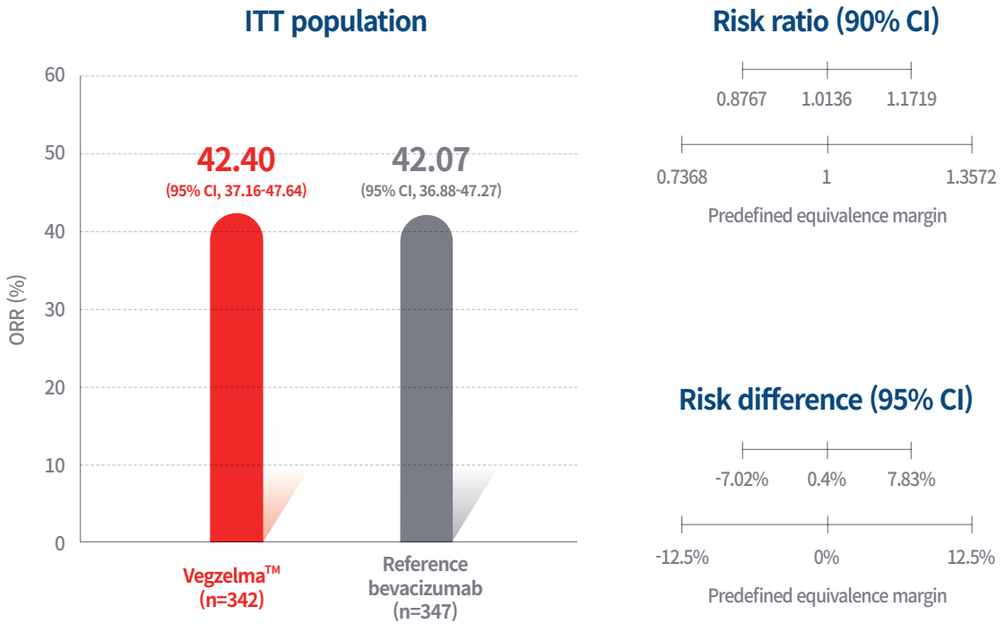
Patients (n)	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6
Vegzelma™	318	302	283	268	252	246
Ref. bevacizumab	316	287	269	254	238	228

PK, pharmacokinetics; **C_{trough},** trough serum concentration

Vegzelma™ demonstrated its therapeutic equivalence in terms of ORR to reference product.[1]

ORR during the induction study period

- In the primary analysis, the 95% CI for the risk difference (Vegzelma™ / reference bevacizumab) estimate in ORR was entirely within the predefined equivalence margin of -12.5 to 12.5 (-7.02 to 7.83).
- This result demonstrated **therapeutic similarity** between Vegzelma™ and reference bevacizumab.

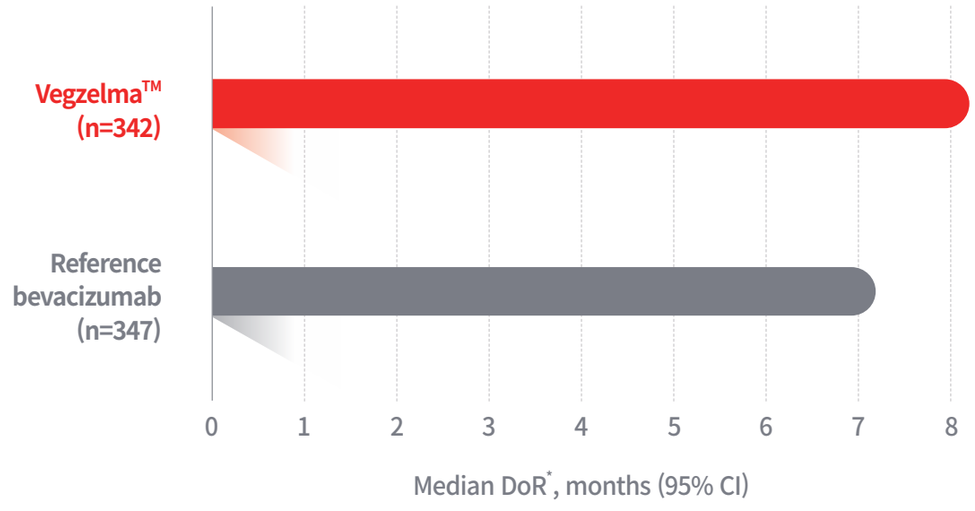


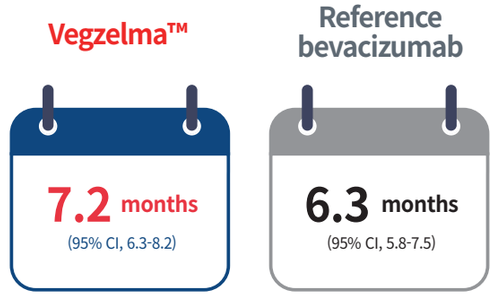
ORR, objective response rate; **CI,** confidence interval; **ITT,** intention-to-treat

Vegzelma™ was comparable to reference bevacizumab with respect to median DoR.*[3]

ITT population

- The median DoR* was similar between the two treatment groups [7.2 (95% CI, 6.3-8.2) months and 6.3 (95% CI, 5.8-7.5) months for the Vegzelma™ and reference bevacizumab treatment groups].[3]



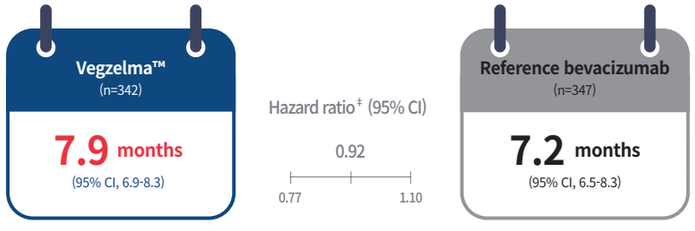


DoR: the time between the initial response (CR or PR) that is confirmed by the subsequent assessment after study treatment administration and PD/recurrence or death from any cause.

CI, confidence interval; **CR,** complete response; **PD,** progressive disease; **PR,** partial response; **DoR,** duration of response; **ITT,** intent-to-treat

Vegzelma™ was comparable in terms of PFS† to reference bevacizumab.[3]

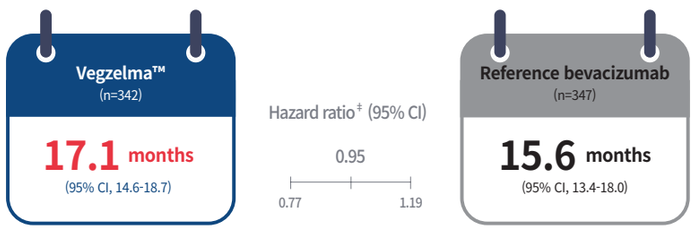
Median PFS†



- The median PFS† was similar between the two treatment groups [7.9 (95% CI, 6.9-8.3) months and 7.2 (95% CI, 6.5-8.3) months for the Vegzelma™ and reference bevacizumab treatment groups].[3]

Vegzelma™ was comparable to reference bevacizumab in OS.*,[3]

Median OS*,[3]



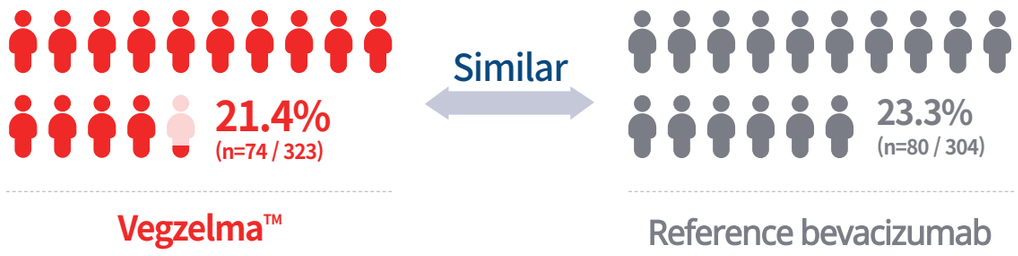
- The median OS* was similar between the two treatment groups [17.1 (95% CI, 14.6-18.7) months and 15.6 (95% CI, 13.4-18.0) months for the Vegzelma™ and reference bevacizumab treatment groups].[3]

†**PFS:** the time from randomization to determined PD/recurrence or death from any cause, whichever occurred first.[3] ‡**Hazard ratio:** a measure of how often a particular event happens in one group compared to how often it happens in another group, over time.[14] *__OS:__ the time from randomization to death from any cause[3]

CI, confidence interval; **OS,** overall survival; **PD,** progressive disease; **PFS,** progression-free survival

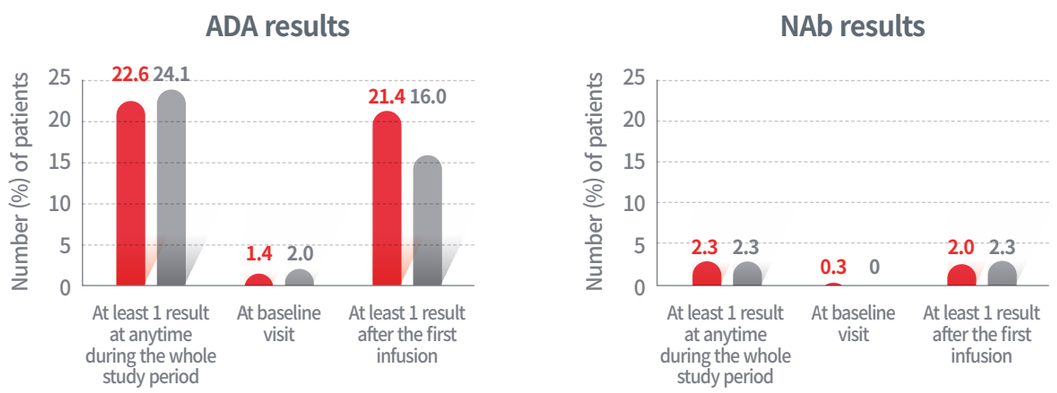
Vegzelma™ proved its immunogenicity similarity to reference bevacizumab in terms of ADA and NAb results.[3]

Proportion of patients with at least 1 positive ADA after the first infusion*



- The majority of patients had negative ADA test results at each time point.
- In general, the proportion of patients with positive ADA and NAb results at any time was similar in the Vegzelma™ and reference bevacizumab treatment groups.

Immunogenicity results : Safety population



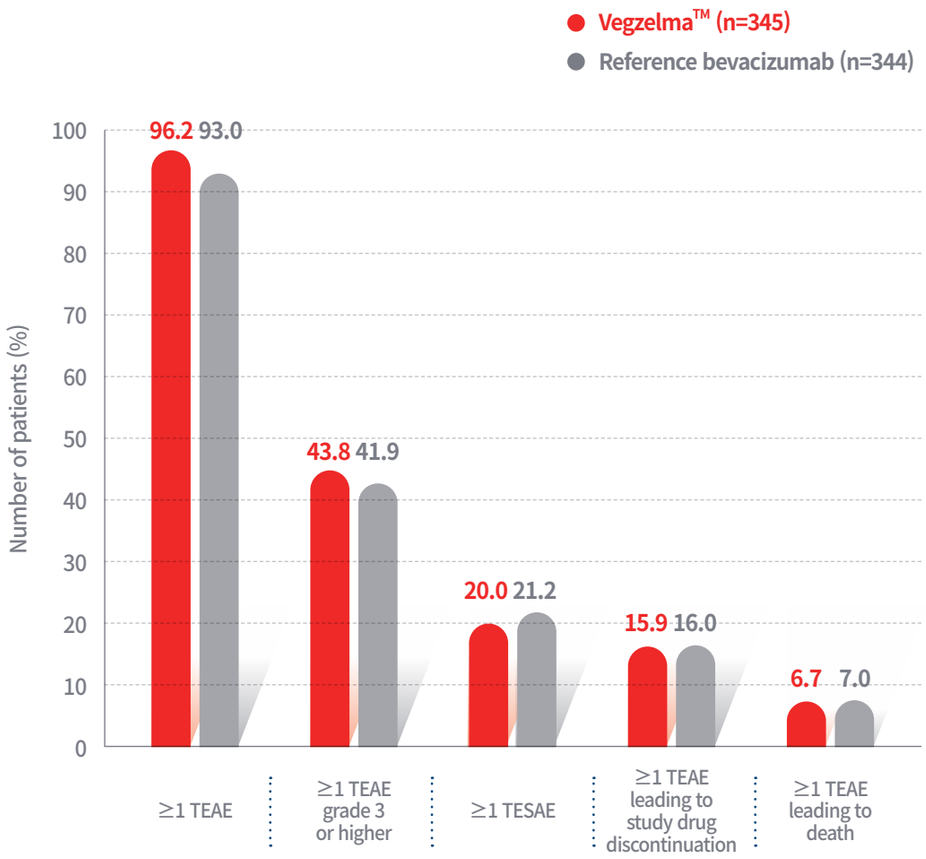
*The ADA test involves both screening and confirmatory assay to confirm positive results. Samples that are 'Potential Positive' in the screening assay would undergo further testing in the confirmatory assay to determine if patients are a true positive labeled 'Positive'. Only patients with a positive ADA result are included in the NAb summary.

ADA, antidrug antibody; **NAb,** neutralizing antibody

Vegzelma™ was well tolerated and showed a comparable safety profile to reference bevacizumab.[1]

Summary of TEAE during the whole study period : Safety population

- There was no notable difference between the two treatment groups for patients with any CTCAE grade in laboratory parameters.
- The majority of TEAEs were CTCAE grade 1 or grade 2 in severity.



CTCAE, Common Terminology Criteria for Adverse Events; **TEAE,** treatment-emergent adverse event; **TESAE,** treatment-emergent serious adverse event

Vegzelma™ has proven storage capability that lasts up to 48 months.[15]

Vegzelma™ (100mg/4mL)[15]

12 months X 4

Up to 48 months

(as of 2024)

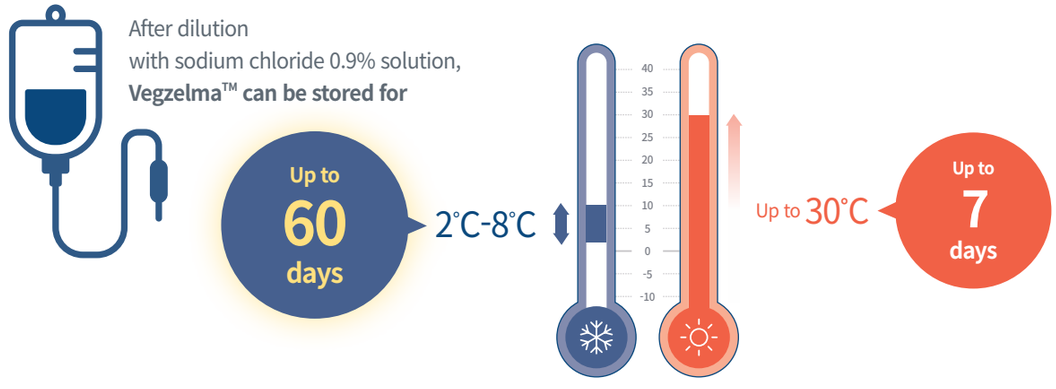
Vegzelma™ (400mg/16mL)[15]

12 months X 4

Up to 48 months

(as of 2024)

Vegzelma™ has shown improvement of in-use stability, which can be kept for up to 60 days at 2–8°C after dilution.[15,*]



*To reduce microbiological hazard, the product should be used as soon as practicable after preparation. If storage is necessary, in-use storage times and conditions are the responsibility of the user and would not be longer than 24 hours at 2-8°C.[16]

IMPORTANT INFORMATION ABOUT VEGZELMA (BEVACIZUMAB)

From 1 March 2025, Vegzelma will be funded under special authority criteria for: recurrent respiratory papillomatosis, ocular conditions, unresectable hepatocellular carcinoma (liver cancer) and advanced ovarian cancer. By 1 August 2025, all people with recurrent respiratory papillomatosis will need to have transitioned to the Vegzelma brand of bevacizumab. For people with ocular conditions, 'any brand' of bevacizumab will continue to be funded in Health New Zealand | Te Whatu Ora hospitals.

Before prescribing, please refer to the data sheet available on the Medsafe website at www.medsafe.govt.nz

Vegzelma (bevacizumab) is a Prescription Medicine containing 100mg or 400mg bevacizumab concentrate for solution for infusion.*

INDICATIONS: Treatment of Metastatic Colorectal Cancer in combination with fluoropyrimidine-based chemotherapy; Treatment of Advanced and/or metastatic Renal Cell Cancer in combination with interferon alfa-2a; Treatment of Advanced, metastatic or recurrent non-squamous Non-Small Cell Lung Cancer (NSCLC) in combination with carboplatin and paclitaxel for first-line treatment; Treatment of Metastatic Breast Cancer in combination with paclitaxel for first-line treatment in patients in whom an anthracycline-based therapy is contraindicated; Treatment of Relapsed high grade malignant Glioma as a single agent; Treatment of Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancer in combination with carboplatin and paclitaxel for first-line treatment of advanced (FIGO stages IIIB, IIIC and IV) disease, in combination with carboplatin and paclitaxel for recurrent, platinum-sensitive disease, in combination with paclitaxel, topotecan or pegylated liposomal doxorubicin for recurrent, platinum-resistant disease in patients who have received no more than two prior chemotherapy regimens and have not received any prior anti-angiogenic therapy including bevacizumab; Treatment of Cervical Cancer in combination with paclitaxel and cisplatin or paclitaxel and topotecan. **CONTRAINDICATIONS:** Vegzelma is contraindicated in patients with: known hypersensitivity to any components of the product; Chinese hamster ovary cell products or other recombinant human or humanised antibodies and NSCLC patients with recent pulmonary haemoptysis. **PRECAUTIONS:** Not for IV push, bolus administration; Vegzelma solutions should not be administered or mixed with dextrose or glucose solutions; gastrointestinal (GI) perforations and fistulae and non-GI fistulae: Discontinue for GI perforations, tracheo-esophageal fistula or any Grade 4 fistula. Consider discontinuation for internal fistula not arising in the GI tract; hypertension: Adequately control pre-existing hypertension before starting Vegzelma. Monitor and treat and discontinue if medically significant hypertension cannot be adequately controlled with antihypertensive therapy or if patient develops hypertensive crisis or hypertensive encephalopathy; wound healing complications: Do not initiate for at least 28 days following major surgery or until surgical wound is fully healed. Withhold treatment in patients who experience wound healing complications or are undergoing elective surgery; thromboembolism: Discontinue Vegzelma in patients who develop Arterial Thromboembolic Events (ATE). Exercise caution when treating patients receiving bevacizumab plus chemotherapy with a history of ATE, diabetes or ≥ 65 years. Discontinue Vegzelma in patients with Grade 4 Venous Thromboembolic Events (VTE) including pulmonary embolism. Monitor for ≤ Grade 3 VTE; haemorrhage: Discontinue in patients with Grade 3 or 4 bleeding during bevacizumab therapy. Monitor for signs and symptoms of CNS bleeding and discontinue in case of intracranial bleeding. Exercise caution before initiating Vegzelma therapy in patients with congenital bleeding diathesis, acquired coagulopathy or in patients receiving full dose of anticoagulants for the treatment of thromboembolism; pulmonary heamorrhage: Patients with recent pulmonary haemorrhage/haemoptysis should not be treated with bevacizumab; aneurysms and artery dissections: Before initiating bevacizumab carefully consider this risk in patients with risk factors such as hypertension or history of aneurysm; posterior reversible encephalopathy syndrome (PRES): Discontinue if patient develops PRES and treat specific symptoms including control of hypertension; proteinuria: Test for proteinuria prior to starting bevacizumab. Withhold until < 2 g/24h urine protein; congestive heart failure (CHF): Exercise caution when treating patients with significant cardiovascular disease or pre-existing CHF; neutropenia: Increased rates of severe neutropenia, febrile neutropenia or infection with severe neutropenia (including some fatalities) have been observed in patients treated with myeolotoxic chemotherapy regimens plus bevacizumab in comparison to chemotherapy alone; hypersensitivity reactions and infusion reactions: Close observation of patient during and following administration of bevacizumab is recommended. Discontinue for anaphylactic reaction or Grade ≥3 infusion-related reaction; ovarian failure: New cases of ovarian failure were reported more frequently in patients receiving bevacizumab. After discontinuation of bevacizumab treatment, ovarian function recovered in a majority of women; Fertility, pregnancy and lactation: Women of childbearing potential should consider adequate contraception to prevent pregnancy and continue use for ≥ 6 months after last dose. Not recommended for use during pregnancy and lactation. Breastfeeding should be discontinued for ≥ 6 months following from last dose. Long term effects of treatment with bevacizumab on fertility are unknown. **INTERACTIONS:** In two clinical studies of metastatic renal cell carcinoma, microangiopathic haemolytic anaemia was reported in 7/19 patients treated with bevacizumab (10 mg/kg every two weeks) and sunitinib malate (50 mg daily) combination. All these findings were reversible upon discontinuation of bevacizumab and sunitinib malate. **ADVERSE EFFECTS:** Most common: febrile neutropenia, leucopenia, neutropenia, thrombocytopenia, anorexia, hypomagnesaemia, hyponatraemia, peripheral sensory neuropathy, dysgeusia, headache, dysarthria, eye disorder, lacrimation increased, hypertension, dyspnoea, epistaxis, rhinitis, cough, diarrhoea, nausea, vomiting, abdominal pain, constipation, stomatitis, rectal haemorhage, ovarian failure, exfoliative dermatitis, dry skin, skin discolouration, arthralgia, proteinuria, asthenia, fatigue, pyrexia, asthenia, pain, mucosal inflammation, weight decreased; Common: sepsis, abscess, cellulitis, infection, anaemia, lymphopenia, hypersensitivity, anaphylactic reactions, infusion-related reactions, dehydration, hyponatraemia, cerebrovascular accident, syncope, somnolence, headache, cardiac failure (congestive), supraventricular tachycardia, thromboembolism (arterial), deep vein thrombosis, haemorrhage, pulmonary embolism, dyspnoea, hypoxia, epistaxis, intestinal perforation (Ileus), intestinal obstruction, recto-vaginal fistulae, gastrointestinal disorder, stomatitis, proctalgia, palmar-plantar erythrodysaesthesia syndrome, muscular weakness, myalgia, arthralgia, back pain, proteinuria, urinary tract infection, pain, lethargy, mucosal inflammation, pelvic pain. **DOSAGE AND ADMINISTRATION:** Withdraw the necessary amount of Vegzelma and dilute to the required administration volume with 0.9% sodium chloride solution. The concentration of the final Vegzelma solution should be kept within the range of 1.4-16.5 mg/mL. The initial Vegzelma dose should be delivered over 90 minutes as an IV infusion. If the first infusion is well tolerated, the second infusion may be administered over 60 minutes. If the 60 minute infusion is well tolerated, all subsequent infusions may be administered over 30 minutes. Dose reduction of Vegzelma for adverse reactions is not recommended. Metastatic Colorectal Cancer*:* First-line treatment: 5 mg/kg every 2 weeks or 7.5 mg/kg every 3 weeks; Second-line treatment: 10 mg/kg every 2 weeks or 15 mg/kg every 3 weeks until disease progression. Advanced and/or Metastatic Renal Cell Cancer: 10 m/kg every 2 weeks until disease progression. Vegzelma should be given in combination with IFN alfa-2a (Roferon-A ®). Advanced, metastatic or recurrent non-squamous Non-Small Cell Lung Cancer (NSCLC)*:* 15 mg/kg every 3 weeks in combination with carboplatin and paclitaxel for up to 6 cycles of treatment followed by Vegzelma as a single agent until disease progression. Metastatic Breast Cancer: 10 mg/kg every 2 weeks or 15 mg/kg every 3 weeks until disease progression. Relapsed high grade malignant Glioma: 10 mg/kg every 2 weeks until disease progression. Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancer*:* Front-line treatment: 15 mg/kg every 3 weeks in combination with carboplatin and paclitaxel for up to 6 cycles of treatment followed by continued use of Vegzelma as a single agent for a total of 15 months therapy or until disease progression, whichever occurs earlier; Treatment of recurrent, platinum-sensitive disease: 15 mg/kg every 3 weeks in combination with carboplatin and paclitaxel for 6 cycles (up to 8 cycles) followed by continued use of Vegzelma as a single agent until disease progression; Treatment of recurrent, platinum-resistant disease: 10 mg/kg every 2 weeks in combination with one of the following agents - paclitaxel, topotecan (weekly) or pegylated liposomal doxorubicin. Alternatively, 15 mg/kg every 3 weeks in combination with topotecan given on days 1-5, every 3 weeks until disease progression. Cervical Cancer*:* 15 mg/kg every 3 weeks, in combination with paclitaxel and cisplatin or paclitaxel and toptecan until disease progression.
*not all dosage forms might be available at the same time.

Date of preparation: Jan-2025 (based on Data Sheet last updated 3-Oct-2024). Material last updated 10-Feb-2025, TAPS BG4649, February 2025

References: 1. Ohe Y et al. Randomized Phase III Study Comparing the Efficacy and Safety of CT-P16, a New Biosimilar, to Reference Bevacizumab (Avastin®) In Patients With Metastatic or Recurrent Non-Small Cell Lung Cancer (NSCLC). Proceedings: American Association for Cancer Research (AACR) Annual Meeting 2022; April 8-13, 2022 New Orleans, Louisiana. **2.** Cho S et al., A Randomized, Double-Blind Trial Comparing the Pharmacokinetics of CT-P16, a Candidate Bevacizumab Biosimilar, with its Reference Product in Healthy Adult Males. BioDrugs. 2019. 33(2):173-181. **3.** Celltrion. Data on file. **4.** Celltrion. Facilities. Available at: https://www.celltrion.com/en-us/products/equipment. Accessed March 2022. **5.** Celltrion. homepage. Available at: <https://www.celltrion.com/en-us/AboutUs/Company Accessed April 2022> **6.** Morita A, et al. Safety, efficacy, and drug survival of the infliximab biosimilar CT-P13 in post-marketing surveillance of Japanese patients with psoriasis [published online ahead of print, 2022 Jul 7]. J Dermatol. 2022 **7.** Iannone F, et al. Subcutaneously-Administered Infliximab in the Management of Rheumatoid Arthritis: A Short Narrative Review of Current Clinical Evidence. J Inflamm Res. 2022;15:3259-3267. **8.** Henry D, et al. Pharmacoeconomics of Cancer Therapies: Considerations With the Introduction of Biosimilars. Semin Oncol. 2014;41:S13-S20. **9.** European Medicines Agency. Truxima® Summary of Product Characteristics. Available at : https://www.ema.europa.eu/en/documents/product-information/truxima-epar-product-information_en.pdf Accessed Mar 2022. **10.** U. S. Food and Drug Administration. Highlights of Prescribing Information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761088s009lbl.pdf. Accessed Mar 2022. **11.** Choi, D, et al. A Developer's Perspective on Clinical Evidence and Benefits for Rituximab Biosimilar Uptake, with a Focuson CT-P10. Clin Drug Investig. 2022. **12.** IQVIA Data: Trastuzumab Market in Europe as of 1st quarter of 2022. **13.** Businesswire. Celltrion Healthcare receives European Commission (EC) approval for the first high concentration, low-volume and citrate-free biosimilar adalimumab, Yuflyma™ (CT-P17). Available at: https://www.businesswire.com/news/home/20210215005195/en/Celltrion-Healthcare-receives-European-Commission-EC-approval-for-the-first-high-concentration-low-volume-and-citrate-free-biosimilar-adalimumab-Yuflyma™-CT-P17 Accessed Aug 2022 **14.** NIH National Cancer Institute. Hazard ratio. Available at http://www.cancer.gov/search/results?swKeyword=hazard+ratio Accessed July 2022 **15.** European Medicines Agency. Vegzelma™ Summary of Product Characteristics. **16.** Medsafe - Vegzelma New Zealand Data Sheet v04-0624

To allow for quick identification of new safety information, kindly report any side effects you may observe at the following contact channels.
Phone: 0800 838 899 or Email: medinfo-nz@celltrionhc.com

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