TECENTRIQ
atezolizumab

Roche

Dear Dr XXX

Roche Products (NZ) Limited is pleased to inform you that Tecentriq® (atezolizumab) in combination with nab-paclitaxel is now indicated for:[1]

the treatment of patients with unresectable locally advanced or metastatic triple-negative breast cancer (TNBC) whose tumors have PD-L1 expression ≥1%, and who have not received prior chemotherapy for metastatic disease.

The indication is based on the **IMpassion130** study.[2] This is a phase 3, randomised, double-blind placebo-controlled study evaluating the efficacy and safety of Tecentriq plus nab-paclitaxel compared with placebo and nab-paclitaxel in patients with unresectable locally advanced or metastatic TNBC who had not received prior chemotherapy for their metastatic disease. Of the 902 patients enrolled in the study, 41% had tumours with PD-L1 positive expression.
Co-primary endpoints were investigator-assessed progression-free survival (PFS) and overall survival (OS) in the intent-to-treat (ITT) and PD-L1 positive populations.

In the final PFS analysis, Tecentriq and nab-paclitaxel vs placebo and nab-paclitaxel significantly improved PFS in the PD-L1-positive population (hazard ratio [HR] 0.62; 95% CI, 0.49–0.78; p<0.001). Median PFS was 7.5 months in the Tecentriq arm vs 5 months in the placebo arm. There was also a significant improvement in PFS in the ITT population (HR=0.80; 95%CI, 0.69-0.92; p=0.0025).

At the first interim OS analysis, there was no significant difference in OS in the ITT population with Tecentriq and nab-paclitaxel compared with placebo and nab-paclitaxel (HR 0.84; 95% CI, 0.69–1.02; p=0.08). The median OS was 21.3 months vs 17.6 months, respectively. Median OS for the PD-L1-positive population was 25 months in the Tecentriq and nab-paclitaxel arm vs 15.5 months in the placebo and nab-paclitaxel arm. Kaplan-Meier estimates included a HR of 0.62 (95% CI 0.45–0.86). Overall survival at the first interim analysis was not formally tested due to the statistical hierarchy plan. One additional interim and 1 final OS analyses are planned.

Safety in the Tecentriq plus nab-paclitaxel arm appeared consistent with the known safety profiles of the individual medicines, and no new safety signals were identified with the combination.

For more information on dosing and adverse effects, please refer to the **Tecentriq Data Sheet**.

Tecentriq is not funded by PHARMAC. Roche have a Cost Share Programme for Tecentriq; for more information please contact **nz.costshare@roche.com**. For medical information enquiries, contact Roche Medical Information on **0800 276 243**.

PD-L1 testing

Roche in conjunction with Southern Community Laboratories Ltd and Roche Diagnostics have established a testing pathway for PD-L1 using the SP142 assay consistent with the assessment of PD-L1 expression by IHC in the IMpassion130 study.
There are two forms to complete:

1. PD-L1 (SP142) Triple Negative Breast Cancer Referral form.
2. Consent and payment form.

A copy of these are attached for your reference. Once the forms have been completed by the referrer and patient, please send to Southern Community Laboratories with the histology specimen.

Kind regards,

Sheree Clifton
Product Specialist
Roche Products NZ Ltd
Phone: +64 9 523 9412
Mobile: +64 21 883 187
Email: sheree.clifton@roche.com

Dr Michael Lau
Consultant Pathologist
Southern Community Laboratories Ltd
Phone: +64 3 474 8322
Email: michael.lau@sclabs.co.nz

Dr Fenella Devereux
Consultant Pathologist
Southern Community Laboratories Ltd
Phone: +64 3 474 8324
Email: fenella.devereux@sclabs.co.nz

Mark Kilgour
Marketing Manager
Roche Diagnostics NZ Ltd
Phone: +64 9 259 5133
Mobile: +64 21 946 530
Email: mark.kilgour@roche.com

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1. Tecentriq Data Sheet (March 2019). 2. Schmid, P et al. Atezolizumab and Nab-Paclitaxel in Advanced Triple-Negative Breast Cancer. N Engl J Med 2018; 379:2108-2121

Tecentriq® (atezolizumab)

Tecentriq (atezolizumab, 1200 mg/20mL concentrate for solution for infusion) is a **Prescription Medicine** for the treatment of: adult patients with locally advanced or metastatic non-small cell lung cancer after prior chemotherapy; adult patients with locally advanced or metastatic urothelial carcinoma who are considered cisplatin-ineligible and whose tumours have a PD-L1 expression ≥ 5%, or who are considered ineligible for any other platinum-containing chemotherapy regardless of level of tumour PD-L1 expression, or have disease progression during or following platinum-containing chemotherapy, or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy; in combination with nab-paclitaxel for patients with unresectable locally advanced or metastatic triple-negative breast cancer (TNBC) whose tumours have PD-L1 expression ≥ 1% and who have not received prior chemotherapy for metastatic disease.

Dose and Method of Administration: *2L NSCLC and urothelial carcinoma:* Recommended dosage is 1200 mg by IV infusion every three weeks. TNBC: Recommended dosage is 840mg Tecentriq by IV infusion on day 1 and 15, and nab-paclitaxel on days 1, 8 and 15 of a 28-day cycle.Please see Tecentriq Data Sheet and Abraxane Data sheet for further information.

Contraindications: Hypersensitivity to atezolizumab or to any excipient.

Special warnings and precautions for use: See Data Sheet for dose modification and treatment advice for the following immune-releated events. ***Immune-related pneumonitis:*** Monitor for signs and symptoms of pneumonitis. Withhold Tecentriq for grade 2; permanently discontinue for grade 3 or 4 pneumonitis. ***Immune-related hepatitis:*** Monitor for signs and symptoms of hepatitis. Monitor AST, ALT and bilirubin prior to, and periodically during, treatment. Appropriate management of patients with abnormal LFTs at baseline should be considered. Withhold Tecentriq for persistent grade 2; permanently discontinue for grade 3 or 4 events. ***Immune-related colitis:*** Monitor for signs and symptoms of colitis. Withhold Tecentriq for grade 2 or 3 diarrhoea or symptomatic colitis; permanently discontinue for grade 4 diarrhoea or colitis. ***Immune-related endocrinopathies:*** Monitor for clinical signs and symptoms of endocrinopathies, including hypothyroidism, hyperthyroidism, adrenal insufficiency, hypophysitis and type 1 diabetes mellitus. Monitor thyroid function prior to, and periodically during, treatment. Appropriate management of patients with abnormal thyroid function tests at baseline should be considered. Withhold Tecentriq for grade 2 or 3; permanently discontinue for grade 4 hypophysitis. Withhold Tecentriq for grade 3 or 4 type 1 diabetes mellitus. Withhold Tecentriq for symptomatic hypothyroidism, hyperthyroidism or adrenal insufficiency. ***Immune-related meningoencephalitis:*** Monitor for clinical signs and symptoms of meningitis or encephalitis. Permanently discontinue treatment for any grade of meningitis or encephalitis. ***Immune-related neuropathies:*** Monitor for symptoms of motor and sensory neuropathy, including myasthenic syndrome/myasthenia gravis or Guillain-Barré syndrome. Permanently discontinue treatment for any grade of these events. ***Immune-related pancreatitis:*** Closely monitor for signs and symptoms suggestive of acute pancreatitis. Withhold Tecentriq for grade 3 or 4 serum amylase or lipase levels increased or grade 2 or 3 pancreatitis. Permanently discontinue for grade 4 or any grade of recurrent pancreatitis. ***Immune-related myocarditis:*** Monitor for signs and symptoms of myocarditis. Withhold Tecentriq for grade 2; permanently discontinue for grade 3 or 4 myocarditis. ***Immune-related nephritis:*** Monitor for signs and symptoms of nephritis. Withhold Tecentriq for Grade 2; permanently discontinue for grade 3 or 4 nephritis. ***Infusion-related reactions (IRRs):*** Reduce infusion rate or interrupt infusion for grade 1 or 2 IRRs. Tecentriq may be continued with close monitoring; consider premedication with antipyretic and antihistamines. Permanently discontinue treatment for grade 3 or 4 IRRs. ***Patients with autoimmune disease:*** Patients with autoimmune disease were excluded from clinical trials; use with caution after assessment of the potential risk versus benefit. ***Renal impairment:*** No dose adjustment required. ***Hepatic impairment:*** No dose adjustment required for mild impairment. No data in moderate or severe impairment. ***Use in the elderly:*** No overall differences in safety or efficacy were observed between patients ⩾ 65 years of age and those < 65 years. ***Use in pregnancy – Category D:*** Tecentriq poses a risk to the human foetus, including embryo lethality. Pregnant women should be advised of the potential risk to the foetus. Women of childbearing potential should use highly effective contraception during treatment and for at least 5 months after the last dose. Safety during labour and delivery has not been established. ***Breastfeeding:*** Either discontinue breastfeeding or discontinue Tecentriq. ***Fertility:*** Tecentriq may impair fertility in females of reproductive potential while receiving treatment.

Undesirable effects: See Data Sheet for full list. Fatal cases of pneumonitis and hepatitis have been observed. ***Blood and lymphatic system:*** thrombocytopenia, neutropenia. ***Cardiac disorders:*** myocarditis. ***Endocrine:*** hypothyroidism; hyperthyroidism; adrenal insufficiency; hypophysitis; diabetes mellitus. ***Gastrointestinal:*** diarrhoea; dysphagia; colitis; nausea; vomiting; abdominal pain; pancreatitis; amylase increased; lipase increased; oropharyngeal pain. ***General:*** chills; fatigue; asthenia; influenza-like illness; pyrexia; infusion-related reactions. ***Hepatobiliary:*** ALT increased; AST increased; hepatitis. ***Immune system:*** hypersensitivity. ***Infections and Infestations:*** urinary tract infection. ***Metabolism and nutrition***: decreased appetite; hypokalaemia; hyponatraemia; hyperglycaemia. ***Musculoskeletal and connective tissue:*** arthralgia; back pain; musculoskeletal. ***Nervous system:*** Guillain-Barré syndrome; non-infective encephalitis; non-infective meningitis; myasthenic syndrome, peripheral neuropathy. ***Renal and Urinary:*** nephritis. ***Respiratory, thoracic and mediastinal:*** cough; dyspnoea; hypoxia; nasal congestion; pneumonitis (including bronchiolitis, interstitial lung disease); nasopharyngitis. ***Skin and subcutaneous tissue:*** pruritus; rash (including skin exfoliation, skin ulcer, skin toxicity, palmar-plantar erythrodysaesthesia syndrome, toxic skin eruption, folliculitis, furuncle). ***Vascular:*** hypotension.

Tecentriq is not a PHARMAC-funded medicine.

Before prescribing, please review the Tecentriq Data Sheet available at www.medsafe.govt.nz.
Roche Products (New Zealand) Limited, Auckland. Ph 0800 276 243. www.roche.co.nz

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