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Year 2016
Products Approved For Additional Indication (DCA 299 – 28 April 2016)

NO	PRODUCT (ACTIVE INGREDIENT)	ADDITIONAL INDICATION	MARKETING AUTHORIZATION HOLDER
1.	1.1 **PERJETA 420 MG CONCENTRATE FOR SOLUTION FOR INFUSION** [Pertuzumab 30 mg/ml]	➢ Indication: *Neoadjuvant Treatment of Breast Cancer* *Perjeta is indicated in combination with trastuzumab and chemotherapy for the neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either >2cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer (see Dosage and Administration and Clinical Studies).* ➢ Posology: *The recommended initial dose of Perjeta is 840 mg administered as a 60 minutes intravenous infusion, followed by every 3 weeks thereafter by a dose of 420 mg administered over a period 30-60 minutes. When administered with Perjeta, the recommendation is to follow a 3-weekly schedule for trastuzumab administered as an IV infusion with an initial dose of 8 mg/kg followed every 3 weeks thereafter by a dose of 6 mg/kg. When administered with Perjeta, the recommended initial dose of docetaxel is 75 mg/m^2. The dose may be escalated to 100 mg/m^2 if the initial dose is well tolerated. The medicinal products should be administered sequentially. Perjeta and trastuzumab can be given in any order. When the patient is receiving docetaxel, the docetaxel should be administered after Perjeta and trastuzumab. An observation period of 30-60 minutes is recommended after each Perjeta infusion and before commencement of any subsequent infusion of trastuzumab or docetaxel (see section 2.4 Warnings and Precautions). Perjeta, trastuzumab and docetaxel should be administered as above as part of one of the following regimens:* • *For 3 cycles following FEC therapy* • *For 4 cycles prior to FEC therapy* • *For 6 cycles with carboplatin (escalation of docetaxel above 75mg/m^2 is not recommended)* *Following surgery, patients should be treated with adjuvant trastuzumab to complete 1 year of treatment.* *There is insufficient evidence to recommend concomitant administration of an anthracycline with Perjeta.* *The safety of Perjeta as part of a doxorubicin-containing regimen has not*	ROCHE (MALAYSIA) SDN. BHD. Level 21, The Pinnacle Persiaran Lagoon, Bandar Sunway 47500 Subang Jaya, Selangor

		been established. *Duration of treatment* *It is recommended that patients are treated with Perjeta for three to six cycles depending on the regimen chosen.* *The safety of Perjeta administered for greater than 6 cycles for the neoadjuvant treatment of breast cancer has not been established.*	
2	2.1 **Abraxane for Injectable Suspension 100mg** [Paclitaxel 100mg]	➢ Indication: *Abraxane in combination with gemcitabine is indicated for the first-line treatment of adult patients with metastatic adenocarcinoma of the pancreas.* *Abraxane in combination with carboplatin is indicated as first-line treatment of locally advanced or metastatic non-small cell lung cancer, in patients who are not candidates for curative surgery or radiation therapy.* ➢ Posology: *Pancreatic adenocarcinoma* The recommended dose of Abraxane in combination with gemcitabine is 125 mg/m^2 administered intravenously over 30 minutes on Days 1, 8 and 15 of each 28-day cycle. The concurrent recommended dose of gemcitabine is 1000 mg/m^2 administered intravenously over 30 minutes immediately after the completion of Abraxane administration on Days 1, 8 and 15 of each 28-day cycle. *Dose adjustments during treatment of pancreatic adenocarcinoma* **Table 1: Dose level reductions for patients with pancreatic adenocarcinoma** **Dose Level** | **Abraxane Dose (mg/m^2)** | **Gemcitabine Dose (mg/m^2)** Full dose | 125 | 1000 1st dose level reduction | 100 | 800 2nd dose level reduction | 75 | 600 If additional dose reduction required | Discontinue treatment | Discontinue treatment **Table 2: Dose modifications for neutropenia and/or thrombocytopenia at the start of a cycle or within a cycle for patients with pancreatic**	Celgene Sdn. Bhd. Lot 6.05, Level 6, KPMG Tower 8, First Avenue, Bandar Utama 47800 Petaling Jaya, Selangor.

adenocarcinoma

Cycle Day	ANC count (cells/mm^2)		Platelet count (cells/mm^3)	Abraxane Dose	Gemcitabine Dose
Day 1	< 1500	OR	< 100,000	Delay dose until recovery	
Day 8	≥ 500 but < 1000	OR	≥ 50,000 but < 75,000	Reduce doses 1 dose level	
	< 500	OR	< 50,000	Withhold doses	
Day 15: If Day 8 doses were given without modification:					
Day 15	≥ 500 but < 1000	OR	≥ 50,000 but < 75,000	Treat with Day 8 dose level and follow with WBC Growth Factors OR Reduce doses 1 dose level from Day 8 doses	
	< 500	OR	< 50,000	Withhold doses	
Day 15: If Day 8 doses were reduced:					
Day 15	≥ 1000	AND	≥ 75,000	Return to the Day 1 dose levels and follow with WBC Growth Factors OR Treat with same doses as Day 8	
	≥ 500 but < 1000	OR	≥ 50,000 but < 75,000	Treat with Day 8 dose levels and follow with WBC Growth Factors OR Reduce doses 1 dose level from Day 8 doses	
	< 500	OR	< 50,000	Withhold doses	
Day 15: If Day 8 doses were withheld:					
Day 15	≥ 1000	AND	≥ 75,000	Return to Day 1 dose levels and follow with WBC Growth Factors OR Reduce doses 1 dose level from Day 1 doses	
	≥ 500 but < 1000	OR	≥ 50,000 but < 75,000	Reduce 1 dose level and follow with WBC Growth Factors OR Reduce doses 2 dose levels from Day 1 doses	
	< 500	OR	< 50,000	Withhold doses	

Abbreviations: ANC=Absolute Neutrophil Count; WBC=white blood cell

Table 3: Dose modifications for other adverse drug reactions in patients with pancreatic adenocarcinoma

Adverse Drug Reaction (ADR)	Abraxane Dose	Gemcitabine Dose
Febrile Neutropenia: Grade 3 or 4	Withhold doses until fever resolves and ANC ≥ 1500; resume at next lower dose level[a]	
Peripheral Neuropathy: Grade 3 or 4	Withhold dose until improves to ≤ Grade 1; resume at next lower dose level[a]	Treat with same dose
Cutaneous Toxicity: Grade 2 or 3	Reduce to next lower dose level[a]; discontinue treatment if ADR persists	
Gastrointestinal Toxicity: Grade 3 mucositis or diarrhoea	Withhold doses until improves to ≤ Grade 1; resume at next lower dose level[a]	

[a]See Table 1 for dose level reductions

Non-Small Cell Lung Cancer

The recommended dose of ABRAXANE is 100 mg/m^2 administered as an intravenous infusion over 30 minutes on Days 1, 8, and 15 of each 21-day cycle. Administer carboplatin on Day 1 of each 21 day cycle immediately after ABRAXANE.

Dose adjustments during treatment of non-small cell lung cancer

Do not administer ABRAXANE on Day 1 of a cycle until absolute neutrophil count (ANC) is at least 1500 cells/mm^3 and platelet count is at least 100,000 cells/mm^3.

In patients who develop severe neutropenia or thrombocytopenia withhold treatment until counts recover to an absolute neutrophil count of at least 1500 cells/ mm^3 and platelet count of at least 100,000 cells/ mm^3 on Day 1 or to an absolute neutrophil count of at least 500 cells/ mm^3 and platelet count of at least 50,000 cells/ mm^3 on Days 8 or 15 of the cycle. Upon resumption of dosing, permanently reduce
ABRAXANE and carboplatin doses as outlined in Table 4.

Withhold ABRAXANE for Grade 3-4 peripheral neuropathy. Resume ABRAXANE and carboplatin at reduced doses (see Table 4) when peripheral neuropathy improves to Grade 1 or completely resolves.

Table 4: Permanent Dose Reductions for Hematologic and Neurologic Adverse Drug Reactions in NSCLC

Adverse Drug Reaction	Occurrence	Weekly ABRAXANE Dose (mg/m^2)	Every 3-Week Carboplatin Dose (AUC mg•min/mL)
Neutropenia Fever (ANC less than 500/mm^3 with fever >38°C) OR Delay of next cycle by more than 7 days for ANC less than 1500/mm^3 OR ANC less than 500/mm^3 for more than 7 days	First	75	4.5
	Second	50	3
	Third	Discontinue Treatment	
Platelet count less than 50,000/mm^3	First	75	4.5
	Second	Discontinue Treatment	
Severe sensory Neuropathy – Grade 3 or 4	First	75	4.5
	Second	50	3
	Third	Discontinue Treatment	

Special populations

Patients with hepatic impairment
For patient with mild hepatic impairment (total bilirubin > 1 to ≤ 1.5 x ULN and aspartate aminotransferase [AST] ≤ 10 x ULN), no dose adjustments are required, regardless of indication.
Treat with same doses as patients with normal hepatic function.

For metastatic breast cancer patients with moderate to severe hepatic impairment (total bilirubin > 1.5 to ≤ 5 x ULN and AST ≤ 10 x ULN), a 20% reduction in dose is recommended. The reduced dose may be escalated to the dose for patients with normal hepatic function if the patient is tolerating the treatment for at least two cycles.

For patients with metastatic adenocarcinoma of the pancreas and non-small cell lung cancer patients that have moderate to severe hepatic impairment, there are insufficient data to permit dosage recommendations.

For patients with total bilirubin > 5 x ULN or AST > 10 x ULN, there are insufficient data to permit dosage recommendations regardless of indication.

Patients with renal impairment
Adjustment of the starting Abraxane dose is not required for patients with mild to moderate renal impairment (estimated creatinine clearance ≥30 to <90 ml/min).

There are insufficient data available to recommend dose modifications of Abraxane in patients with severe renal impairment or end stage renal disease (estimated creatinine clearance <30 ml/min).

Older people
No additional dosage reductions, other than those for all patients, are recommended for patients 65 years and older.

Of the 229 patients in the randomized study who received Abraxane monotherapy for breast cancer, 13% were at least 65 years of age and < 2% were 75 years or older. No toxicities occurred notably more frequently among patients at least 65 years of age who received Abraxane. However, a subsequent analysis in 981 patients receiving Abraxane monotherapy for metastatic breast cancer, of which 15% were ≥ 65 years old and 2% were ≥ 75 years old, showed a higher incidence of epistaxis, diarrhoea, dehydration, fatigue and peripheral oedema in patients ≥ 65 years.

Of the 421 patients with pancreatic adenocarcinoma in the randomized study who received Abraxane in combination with gemcitabine, 41% were 65 years and older and 10% were 75 years and older. In patients aged 75 years and older who received Abraxane and gemcitabine, there was a higher incidence of serious adverse reactions and adverse reactions that led to treatment discontinuation. Patients with pancreatic adenocarcinoma aged 75 years and older should be carefully assessed before treatment is considered.

Of the 514 patients in the randomized study who received ABRAXANE and carboplatin for the first-line treatment of non-small cell lung cancer, 31% were 65 years or older and 3.5% were 75 years or older. Myelosuppression, peripheral neuropathy, and arthralgia were more frequent in patients 65 years or older compared to patients younger than 65 years old. No overall difference in effectiveness, as measured by response rates, was observed between patients 65 years or older compared to patients younger than 65 years old.

Pharmacokinetic/pharmacodynamics modelling using data from 125 patients with advanced solid tumours indicates that patients ≥ 65 years of age may be more susceptible to development of neutropenia within the first treatment cycle.

Paediatric population
The safety and efficacy of Abraxane in children and adolescents aged 0-17 years has not been established. There is no relevant use of Abraxane in the paediatric population in the indication of metastatic breast cancer, pancreatic adenocarcinoma or non-small cell lung cancer.

Method of administration

Administer reconstituted Abraxane suspension intravenously using an infusion set incorporating a 15 µm filter. Following administration, it is recommended that

		the intravenous line be flushed with sodium chloride 9 mg/ml (0.9%) solution for injection to ensure administration of the complete dose. For instructions on reconstitution of the medical product before administration, see section 6.5.	