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Drug and Form	TGA Indication	Current PBS Listing	Listing Requested by Sponsor	PBAC Outcome and Comments
Atomoxetine hydrochloride, capsules 10 mg, 18 mg, 25 mg, 40 mg, and 60 mg, Strattera® Eli Lilly Australia Pty Ltd Major submission	Treatment of Attention Deficit Hyperactivity Disorder (ADHD) as defined by DSM-IV criteria in children 6 years of age and older, adolescents and adults.	Not PBS listed		PBAC rejected the submission because of uncertain cost-effectiveness.
			Authority required listing for: Initial treatment of patients with attention-deficit hyperactivity disorder (ADHD) diagnosed between the ages of 6 and 18 years by a paediatrician or psychiatrist according to the DSM-IV criteria where: ·Treatment with dexamphetamine sulfate or methylphenidate 10mg poses an unacceptable medical risk due to the following contraindications to immediate-release stimulant treatment as specified in the TGA-approved product information: ·The patient has a history of substance abuse or misuse (other than alcohol); and/or ·The patient has comorbid motor tics or Tourette's Syndrome; and/or ·The patient has comorbid severe anxiety diagnosed according to the DSM-IV.	Accepted. PBAC considered that the requested restriction was appropriate.

			OR Treatment with dexamphetamine sulfate or methylphenidate 10mg has resulted in the development or worsening of a comorbid mood disorder (diagnosed according to the DSM-IV criteria i.e. anxiety disorder, obsessive compulsive disorder, depressive disorder) of a severity necessitating permanent stimulant treatment withdrawal; or where the combination of stimulant treatment with another agent would pose an unacceptable medical risk of a severity necessitating permanent stimulant treatment withdrawal. OR Treatment with dexamphetamine sulfate AND methylphenidate 10mg has resulted in the development of adverse reactions of a severity necessitating permanent treatment withdrawal: ·Adverse effects on growth and weight ·Adverse effects on sleep including insomnia ·Adverse effects on appetite including anorexia; and for: Continuing treatment where the patient has previously been issued with an authority prescription for this drug.	

			Comparator: ‘no pharmacological intervention’	Accepted
			Clinical claim: atomoxetine has significant advantages in effectiveness over the main comparator but is associated with more toxicity.	Accepted
			Economic claim: Cost-effectiveness - cost utility approach.	PBAC considered that most of its previous concerns had been addressed in this submission. The outstanding issues about the economic model, which led to uncertainty about the reliability of the base-case incremental cost-effectiveness ratio, concerned the assumption about the delayed response at 8 months of non-responders to atomoxetine at 10 weeks compared to non-responders to placebo at 10 weeks, the assumption about a difference in relapse rates between the atomoxetine and placebo arms of the model and utilities. PBAC noted that the model was less sensitive to assumptions about the relapse rates than those in relation to delayed response rates.
			Sponsor’s comments:	The sponsor needs to clarify the decision with the PBAC, but refers

				you to its own website (www.lilly.com.au) for further information.

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Drug and Form	TGA Indication	Current PBS Listing	Listing Requested by Sponsor	PBAC Outcome and Comments
Botulinum toxin type A purified neurotoxin complex, powder for injection, 100 units (Botox®) Allergan Australia Pty Ltd Major submission	Botulinum Toxin Type A Purified Neurotoxin Complex is indicated for: - Treatment of blepharospasm associated with dystonia, including benign blepharospasm and VII nerve disorders (specifically hemifacial spasm) in patients twelve years and over; Treatment of cervical dystonia (spasmodic torticollis); - Treatment of dynamic equinus foot deformity due to spasticity in juvenile cerebral palsy patients two years of age or older; - Treatment of severe primary hyperhidrosis of the axillae; - Treatment of glabellar lines associated with corrugator and/or procerus muscle activity; - Treatment of focal	Section 100, Botulinum Toxin Program: Treatment of blepharospasm associated with dystonia, including benign blepharospasm and VIIth nerve disorders (hemifacial spasm) in patients 12 years and older; Treatment of dynamic equinus foot deformity due to spasticity in ambulant paediatric cerebral palsy patients 2 years of age or older; Treatment of spasmodic torticollis, either as monotherapy or as adjunctive therapy to current standard care.		PBAC rejected the submission because of uncertainty in extrapolation of response in the clinical trial data to a quality of life measure, and a high and uncertain cost-effectiveness ratio.
			Section 100, Botulinum Toxin Program for the treatment of focal spasticity, as part of a sustained therapy program in adult patients: a) where there is no fixed muscle contracture to limit treatment efficacy, and b) where non-invasive physical therapies have failed, and c) where treatment is in conjunction with a therapy program designed to meet defined functional goal(s) of treatment. Treatment is limited to two injections in the first year and, if necessary to maintain functional goals, one injection per year in the second and subsequent years.	Accepted.

	spasticity in adults; - Treatment of spasmodic dysphonia; - Treatment of strabismus in children and adults.		Comparator: Placebo for standard medical management	Accepted.
			Clinical claim: Botulinum toxin has significant advantages in effectiveness over placebo and has similar toxicity.	Accepted. However, PBAC noted there was uncertainty regarding the duration of the effectiveness of treatment as the numbers requiring permanent treatment were not reported.
			Economic claim: Cost effectiveness – cost-utility approach	PBAC considered the major uncertainty of the submission was the utility study, which mapped Ashworth scores to health states. The PBAC considered that this approach failed to capture the underlying varied causes of focal spasticity and the complexity of the clinical conditions.
			Sponsor's comments:	

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Drug and Form	TGA Indication	Current PBS Listing	Listing Requested by Sponsor	PBAC Outcome and Comments
Cetuximab, injection 100 mg in 50mL, vial Erbitux® Alphapharm Pty Ltd Minor submission	Treatment of patients with metastatic colorectal cancer that has been demonstrated to be epidermal growth factor receptor (EGFR) positive and whose disease has progressed or is refractory to irinotecan based therapy. Cetuximab can be used at the doses recommended either in combination with irinotecan or as a single agent.'	Not PBS listed		The PBAC rejected the submission because of uncertain clinical benefit and unacceptable and uncertain cost-effectiveness.
			Authority required listing for initial PBS–subsidised treatment, in combination with irinotecan, of metastatic colorectal cancer in patients with a WHO performance status of 2 or less, who have received and failed 5-fluorouracil or capecitabine, received and failed an irinotecan-based therapy, and received and failed or are considered unsuitable for, an oxaliplatin-based therapy. Continuing PBS-subsidised treatment, in combination with irinotecan, of metastatic colorectal cancer in patients with a WHO performance status of 2 or less, where 1) the patient has been previously issued with an authority prescription for cetuximab; and 2) a response to treatment of stable response or better has been observed. Subsequent continuing PBS-subsidised treatment, in combination with irinotecan, of metastatic colorectal cancer in patients with a WHO	The PBAC considered the proposed continuation rule requiring patients to have regular scans in the last weeks of life to be too onerous for the patient. It was not clear whether the cost of scanning had been included in the cost-effectiveness ratios.

			performance status of 2 or less, where 1) the patient has been previously issued with an authority prescription for cetuximab; and 2) a response to treatment of partial response or better has been observed.	
			Comparator: 'Usual care', comprising best supportive care and the chemotherapy agents currently used 3rd line.	Accepted.
			Clinical claim: Cetuximab is significantly more effective than usual care and has similar or less toxicity.	PBAC considered the submission was unable to address the uncertainty that arose from the claim of a survival gain over the comparators based on a comparison across single arm studies.
			Economic claim: Cost-effectiveness – cost utility approach.	Rejected, in view of the uncertainty over the clinical claim.
			Sponsor's comments:	The sponsor disagrees with the decision and refers you to its website for further information: www.alphapharm.com.au

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Drug and Form	TGA Indication	Current PBS Listing	Listing Requested by Sponsor	PBAC Outcome and Comments
Cinacalcet hydrochloride, tablets, 30 mg, 60 mg, and 90 mg (Sensipar®) Amgen Australia Pty Ltd Major submission	Cinacalcet may be used to treat the biochemical manifestations of secondary hyperparathyroidism in patients with end stage renal disease, receiving dialysis. Cinacalcet should be used as adjunctive therapy. Cinacalcet is indicated for the treatment of hypercalcemia in patients with parathyroid carcinoma. Cinacalcet may be used to treat the biochemical manifestations of primary hyperparathryoidism in patients for whom parathryoidectomy is not a treatment option.	Not PBS listed		PBAC rejected the submission because of uncertain clinical benefit and uncertain cost-effectiveness.
			Section 100 Highly specialised Drug - Private Hospital Authority Required for initial treatment by a nephrologist of patients with end stage renal disease receiving dialysis who, despite conventional therapy, have uncontrolled secondary hyperparathyroidism, as demonstrated by an iPTH value > 53.0 pmol/L (> 500 pg/mL) (described as the “53+ subgroup”). Continuing treatment by a nephrologist at the effective dosage determined during the titration phase.	The PBAC noted some of the comparisons in the 53+ subgroup and the all-patient population were not statistically significant. This led to uncertainty about the interpretation of the data for the requested sub-group.
			Comparator: Placebo for add-on to standard care.	Accepted.
			Clinical claim: Cinacalcet has significant advantages over	There was uncertainty in the estimates of treatment effects,

			standard care and similar or less toxicity.	which make it difficult to conclude a treatment benefit in mortality in the 53+ subgroup compared to the all patient analysis. PBAC thus considered there was uncertainty about the estimate of the hazard ratio for mortality.
			Economic claim: Cost effectiveness – cost utility approach.	There was uncertainty about the economic model, in particular the mortality benefit, which was the main driver of the model. An additional uncertainty was the use of “clinical practice dosing” for cinacalcet rather than dosing based on the trials.
			Sponsor’s comments:	Although disagreeing with the recent recommendation, the sponsor intends to work collaboratively with the PBAC to find a way to move forward with reimbursement of cinacalcet, please refer to Amgen Australia website <http://www.amgen.com.au/public/contact/Sensipar.jsp> for further information.

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Drug and Form	TGA Indication	Current PBS Listing	Listing Requested by Sponsor	PBAC Outcome and Comments
Methylphenidate hydrochloride, extended release tablets, 18 mg, 36 mg and 54 mg, Concerta® Janssen-Cilag Pty Ltd Minor submission	Treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents aged 6-18 years.	Not PBS listed		PBAC rejected the submission because of uncertain clinical benefit and uncertain cost-effectiveness at the price proposed.
			Authority required listing for the treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents aged 6-18 years who have demonstrated a response to immediate release methylphenidate hydrochloride with no emergence of serious adverse events, and who require continuous coverage over 12 hours, in accordance with State and Territory law.	Accepted
			Comparator: Methylphenidate immediate release (MPH-IR) tablet	Accepted
			Clinical claim: Concerta (MPH-CR) is significantly more effective than immediate release methylphenidate and has similar or less toxicity.	Rejected. Uncertainty still remained about the results of the randomised controlled open-label pragmatic trial showing a benefit, while the blinded randomised controlled registration trials showed no difference

				between immediate release (MPH-IR) methylphenidate tablet and the extended release (MPH-CR) tablets.
			Economic claim:	Rejected. PBAC agreed that a MPH-CR may have a benefit over MPH-IR, based on the likelihood of improved compliance, reduced stigmatisation and diversion. However, the PBAC considered that the extent of any benefit was uncertain and thus the cost-effectiveness was uncertain at the price requested by the sponsor.
			Sponsor's comments:	Janssen-Cilag will continue discussions with the PBAC to clarify and address the issues raised.

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Drug and Form	TGA Indication	Current PBS Listing	Listing Requested by Sponsor	PBAC Outcome and Comments
Risedronate sodium, tablet, 5 mg, (Actonel®); risedronate sodium, tablet 35 mg (Actonel Once-A-Week®); risedronate sodium with calcium carbonate, tablet, 35 mg -1250 mg (Actonel Combi®) Sanofi Aventis Pty Ltd Major submission	Treatment of osteoporosis; Treatment of glucococorticoid-induced osteoporosis; Preservation of bone mineral density in patients on long term corticosteroid therapy.	<u>Authority required</u> Initial and continuing treatment as the sole PBS-subsidised anti-resorptive agent for established osteoporosis in patients with fracture due to minimal trauma. The fracture must have been demonstrated radiologically and the year of plain x-ray or CT-scan or MRI scan must be included in the authority application. A vertebral fracture is defined as a 20% or greater reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body, or, a 20% or greater reduction in any of these heights compared to the vertebral body above or below the affected vertebral body.		PBAC rejected the submission because of uncertain benefit in the clinically relevant outcomes of non-vertebral fracture and hip fracture in the requested subgroup population: 75 years or older of age and with a BMD of -3.0 or less, and uncertain cost effectiveness.
			Add to the authority required listing to allow initial and continuing treatment of patients with osteoporosis at a high risk of fracture in those with a bone mineral density (BMD) T-score of –3.0 or less in a patient aged 75 years or older. The initial authority application must state patient's age and date of birth and the date, site (femoral neck or lumbar spine) and score of the qualifying BMD measurement.	Accepted
			Comparator: Placebo or 'watchful waiting' (patient monitoring and standard management with calcium and vitamin D).	Accepted

			Clinical claim: Risedronate has significant advantages in effectiveness over placebo and has similar or less toxicity.	Partially accepted. Although the reduction in morphometric fractures was statistically significant, the result for other fractures in the requested subgroup population of 75 years or older of age and with a BMD of -3.0 were not significantly different from placebo.
			Economic claim: Cost effectiveness – cost utility approach.	Rejected. PBAC noted that there were a number of uncertainties with the economic model leading to uncertainty in the comparison of risedronate with placebo. The relative risks applied in the model were applied for hip and other fractures for which there was no statistically significant difference from placebo in the requested subgroup population: 75 years or older of age and with a BMD of -3.0 or less.
			Sponsor's comments:	Sanofi-aventis disagrees with this decision and will seek all options available to ensure access to risedronate for the prevention of first fracture.