

Dear Sir/Madam,

## **RE: POST-MARKET REVIEW OF AUTHORITY REQUIRED PBS LISTINGS**

GlaxoSmithKline (GSK) Australia is committed to ensuring the appropriate use and access of its medicines and appreciates the opportunity to engage as a stakeholder in this review. We are committed to working with the Government to achieve the stated objective of this review 'improving patient safety and care by reducing red tape and administrative burden for health professionals'. We have made comments on specific Authority Required listing as indicated in the Authority Required medicines list to suggest areas of simplification of the current administrative processes for prescribing, which may be adversely affecting patient care and or access. As indicated in the Post-market Review of Authority Required List we would like to comment regarding on the following GSK medicines:

### **Tranche 1 Medicine List (Authority Required)**

- Tafinlar® (Dabrafenib) (PBS items 02846T, 02954L, 02963Y, 10003L)
- Tykerb® (Lapatinib) (PBS item 09148L)
- Votrient® (Pazopanib) (PBS items 2029T, 2030W, 2034C, 2035D, 2201W, 2232L): Renal Cell Carcinoma (RCC)
- Votrient® (Pazopanib) (PBS items 10041L, 10042M, 10043N, 10047T, 10052C, 10054E): Soft Tissue Sarcoma (STS)

### **Tranche 2 Medicine List (Authority Required)**

- Revolade® (Eltrombopag) (PBS items 05825N, 05826P, 05827Q, 05828R)
- Flolan Kit® (Epoprostenol) (PBS items 05030R, 05035B, 05036C, 05042J)
- Volibris® (Ambrisentan) (PBS items 05607D, 05608E, 09648T, 09649W)
- Avandamet® (Rosiglitazone + metformin) (PBS items 09059T, 09060W, 09061X, 09062Y)
- Avandia® (Rosiglitazone) (PBS items 08689H, 08690J)

An improved process for this review would have been to first consult and agree criteria and then to consult on individual listings; however, GSK has attempted to address both issues (criteria; and GSK's individual listings subject to this review) in this submission.

GSK proposes that medicines could be considered for prescribing as Authority Required (STREAMLINED) if they meet the following broad principles which are largely consistent with the original principles when the Authority Required (STREAMLINED) listing category were first implemented in July 2007. Authority Required items include short-term-use items, Section 100 items, and items with an increased potential for misuse, abuse or adverse effects (Pharmaceutical Benefits Scheme (PBS) - Fact Sheet Streamlined Authorities).

Authority Required (STREAMLINED) items were previous Authority Required items that were not short-term-use items, Section 100 items, and items with an increased potential for misuse, abuse or adverse effects. The PBS - Fact Sheet Streamlined Authorities clearly state that these streamlined authority items cannot be prescribed more readily than Authority Required items and that prescribers are still required to prescribe in accordance with the PBS restriction criteria and keep evidence of compliance and patient eligibility on patient records.

GSK also suggests that an additional criterion should be considered whether items should require Authority Required (written) or whether they should be Authority Required / Authority Required (STREAMLINED). This criterion should be whether there is some urgency in the commencement of treatment, for example, if a patient had progressive metastatic cancer requiring a change in therapy. In these cases, the commencement of their new treatment should not be delayed due to a system reliant on Australia Post and the associated delays in receipt of the necessary Authority to prescribe.

For some more complex authorities that require submission of additional documentation, an alternative to requiring written authority approvals could be an on-line approval an online secure portal for data capture of PBS restriction requirements that allows for appropriate documentation to be submitted for review by Medicare Australia.

GSK agrees with the suggestions contained in the post-market reviews submissions to the Terms of Reference that there should be consideration of the risk that changing the criteria for determining whether a medicine should be recommended as an Authority Required or Authority Required (STREAMLINED) could adversely impact the PBAC's ability to provide a positive recommendation for inclusion of new items on the PBS.

Therefore, if changing the criteria would propose a risk to PBAC confidence and results in a potential delay to a positive recommendation and to the PBS listing of important new medicines, then this should be fully explored as a potential unintended consequence of the review. Though as new medicines often have 'tight' financial controls and managed through, strict PBS criteria, deeds of agreement and special pricing arrangements, this should give some solution to some comments around the potential for unintended consequences, such as potential for over utilisation and/or inappropriate prescribing.

### **Tranche 1: GSK oncology Medicines**

The Tranche 1 medicine list identified groups of medicines that create the greatest regulatory burden with the first priority area being Authority Required listings related to the use of drugs in cancer. This includes the following GSK oncology medicines (Table 1).

GSK notes inconsistencies in Authority Required with the following oncology medicines:

- Tykerb® (lapatanib): Authority Required (**written**);
- Votrient® (pazopanib) [Soft tissue sarcoma]: Authority Required (**written**) for initial treatment and Authority Required (**telephone**) for continuing treatment; and
- Tafinlar® (dabrafenib) & Votrient® (pazopanib) [Renal cell carcinoma]: Authority Required;

Whilst, there are similarities in PBS restriction criteria (i.e. testing necessary to identify eligible patients, monotherapy or combination use, WHO performance status of 2 or less, must have stable or responding disease) across dabrafenib, lapatanib and pazopanib, there are inconsistencies in how each medicine is prescribed by oncologists and accessed by patients. GSK requests that these

oncology medicines are considered for Authority Required (STREAMLINED) for initial and continuing treatment PBS Restriction criteria.

**Table 1. Tranche 1: GSK Oncology Medicines - Lapatanib, Dabrafenib and Pazopanib (RCC and STS)**

GSK Oncology Medicines Tranche 1	PBS item(s)	Source	Current Authority Required PBS Listing			Requested
			Authority Required	Initial treatment (Written/Phone)	Continuing treatment (Written/Phone)	Authority Required (Streamlined)
1. Tafinlar® (dabrafenib)	02846T, 02954L, 02963Y, 10003L	General Schedule (Section 85)	Yes	Yes (phone)	Yes (phone)	Yes - Initial and continuing treatment
2. Tykerb® (Lapatanib)	09148L	General Schedule (Section 85)	Yes	<b>Yes (written)*</b>	<b>Yes (written)*</b>	Yes - Initial and continuing treatment
3. Votrient® (Pazopanib) RCC	02029T, 02030W, 02034C, 02035D, 02201W, 02232L	General Schedule (Section 85)	Yes	Yes (phone)	Yes (phone)	Yes - Initial and continuing treatment
4. Votrient® (Pazopanib) STS	10041L, 10042M, 10043N, 10047T, 10052C, 10054E	General Schedule (Section 85)	Yes	<b>Yes (written)</b>	Yes (phone)	Yes - Initial and continuing treatment

Abbreviations: RCC=Renal Cell Carcinoma, Sarcoma = Soft tissue Sarcoma

\*Current criteria for lapatanib notes that under no circumstances will phone approvals be granted for complete authority applications, or for treatment that would otherwise extend the treatment period.

**1. Tafinlar® (Dabrafenib) (PBS items 2846T, 2954L, 2963Y, 10003L)**

**GSK recommends the Review Panel should consider dabrafenib for movement to an Authority Required (STREAMLINED) listing.**

Dabrafenib is a chronic therapy for the treatment of BRAF (V600) mutation positive metastatic melanoma. Dabrafenib is listed in Section 85 (not Section 100) and has limited/no potential for misuse or abuse. It is prescribed by oncologists that are highly trained and familiar with its adverse event profile and the PBS restriction criteria. These attributes suggest it meets the criteria for Authority Required (STREAMLINED) for initial and continuing treatment criteria. This is consistent with the suggestions contained in the post-market review submissions from Icon and Private Cancer Physicians of Australia.

## **2. Tykerb® (Lapatanib) (PBS item 9148L)**

**GSK recommends the Review Panel should consider lapatanib for movement to an Authority Required (STREAMLINED) listing.**

This PBS item for lapatanib covers its indication for HER2 positive metastatic breast cancer which is currently a Authority Required restriction requiring written approval. This is listed in Section 85 (not Section 100) and has limited/no potential for misuse or abuse. Lapatanib was PBS listed on May 2008 and has been on the market for a number of years; therefore, oncologists have substantial experience and familiarity using lapatanib. These attributes suggest it meets the criteria for Authority Required (STREAMLINED). This is consistent with the suggestions contained in the post-market reviews submissions from Icon and Private Cancer Physicians of Australia.

Clinician feedback have indicated that receipts of approval for this item currently commonly takes 2 weeks and has been known to take up to 4 weeks. The lapatanib authority application for initial treatment must be made in writing and must include a signed patient acknowledgement; these particular criteria in addition to the complex Streamlined Authority can in some instances lead to clinicians continuing to prescribe medicines on which patients have experience disease progression and therefore may be an unintended barrier to patient access.

Lapatanib has similar PBS restriction requirements to dabrafenib (see above). For example:

- limited use beyond progression;
- targeting of eligible patients (i.e. HER2 positive as demonstrated by ISH [lapatanib] versus BRAF test [dabrafenib]); and
- the use of lapatanib in combination with capecitabine (not PBS subsidised for use in combination with trastuzumab [Herceptin®]) versus the use of dabrafenib as the sole PBS-subsidised therapy for this condition.

In consideration of these PBS restriction similarities the complex Authority Required restriction for lapatanib appears to be inconsistent with other oncology medicines currently listed on the PBS.

The current Authority Required mentions that under no circumstances will phone approvals be granted for complete authority prescriptions, or for treatment that would otherwise extend the treatment period. GSK suggest that if the PBAC does not consider that lapatanib could be listed as a streamlined authority, it should consider amending its listing to Authority required; which would allow the timely commencement of treatment.

## **3. Votrient® (Pazopanib) (PBS items 2029T, 2030W, 2034C, 2035D, 2201W, 2232L): Renal Cell Carcinoma (RCC)**

**GSK recommends the Review Panel should consider pazopanib (RCC) for movement to an Authority Required (STREAMLINED) listing.**

These PBS items for pazopanib cover its indication for metastatic renal cell carcinoma which is currently an Authority Required restriction. This is a Section 85 listing for a chronic therapy with limited/no potential for misuse or abuse and acceptable adverse event profile. These attributes suggest it meets the criteria for a Streamlined Authority. This is consistent with the suggestions for a similar product (sunitinib) with the same PBS listing by Icon and the Private Cancer Physicians of Australia.

GSK is supportive of the DUSC recommendation that the PBS listings of pazopanib and sunitinib be referred to the Post-Market Review of Authority Required PBS Listings for consideration of changing to Streamlined Authority. GSK believes that this will reduce the administrative burden associated with the current Authority Required listings.

**4. Votrient® (Pazopanib) (PBS items 10041L, 10042M, 10043N, 10047T, 10052C, 10054E): Soft Tissue Sarcoma (STS)**

***GSK recommends the Review Panel should consider pazopanib (STS) for movement to an Authority Required (STREAMLINED) listing.***

These PBS items for pazopanib cover its indication for metastatic soft tissue sarcoma (STS) which is currently an Authority required (written) restriction for initial treatment. Applications for continuing therapy may be made by telephone. This is a Section 85 listing (not Section 100) for a chronic therapy with limited/no potential for misuse or abuse and acceptable adverse event profile. These attributes suggest it meets the criteria for a Streamlined Authority.

Clinician feedback has indicated that receipt of approval for this item currently commonly takes 2 weeks and has been known to take up to 4 weeks. Patients with metastatic STS have very poor prognosis with median overall survival around 12 months. Pazopanib is indicated and reimbursed for second line treatment after treatment failure with an anthracycline. Hence, it is paramount to ensure that there are no delays in timely access to patients. Four weeks is a significant period of time for patients with progressive metastatic cancer and few to no treatment options to access a treatment with proven benefits in progression free survival and consequently quality of life.

GSK suggests that if the PBAC does not consider that this product could be listed as a streamlined authority, it should consider amending its listing to Authority required (for initial and continuing treatment) which would allow the timely commencement of treatment.

## **Tranche 2: GSK Section 100 Medicines**

The three GSK medicines [(Revolade® (eltrombopag), Flolan® (epoprostenol), Volibris® (ambrisentan)] included in Tranche 2 of the special authority review are Section 100 items with Authority Required PBS restrictions requiring written approval. These types of medicines can be supplied through the PBS as authorised under Section 100 of the National Health Act 1953. *“Highly Specialised Drugs are medicines for the treatment of chronic conditions which, because of their clinical use or other special features, are restricted to supply through public and private hospitals having access to appropriate specialist facilities. To prescribe these drugs as pharmaceutical benefit items, medical practitioners are required to be affiliated with these specialist hospital units. A general practitioner or non-specialist hospital doctor may only prescribe Highly Specialised Drugs to provide maintenance therapy under the guidance of the treating specialist.”*

There are a number of criteria that patients must meet before being eligible for treatment with these medicines which may make them less suitable for a Streamlined Authority though should not exclude it becoming available as an Authority required item (e.g. phone authority) especially for continuing treatment criteria. Or alternatively, an online secure portal for data capture of PBS restriction requirements could be more efficient than the current process (i.e. an authority application for initial and continuing treatment must be made in writing). GSK suggests a workable system that keeps the integrity of the required PBS restriction data capture of Section 100 medicines would enable earlier access than a ‘written authority’ reliant on Australia Post and associated delays in receipt of the necessary Authority to prescribe.

Table 2 describes the GSK Section 100 medicines to be considered by the PBAC at the March 2015 meeting for Authority Required (STREAMLINED) for Tranche 2.

**Table 2. Tranche 2: Section 100 Medicines, Eltrombopag, Epoprostenol and Ambrisentan**

GSK Section 100 Medicines Tranche 2	PBS item(s)	Source	Current Authority Required PBS Listing			Requested Authority Required (Streamlined)
			Authority Required	Initial treatment (Written/Phone)	Continuing treatment (Written/Phone)	
5. Revolade® (Eltrombopag)	05825N, 05826P, 05827Q, 05828R	S100	Yes	Yes ( <i>written</i> )	Continuing 1*: Yes ( <i>written</i> ) Continuing 2+: Yes (phone)	Phone or online system could be more efficient than written especially for continuing criteria.
6. Flolan® (Epoprostenol)	05030R, 05035B, 05036C, 05042J	S100	Yes	Yes ( <i>written</i> )	Yes ( <i>written</i> )	Phone or online system could be more efficient than written especially for continuing criteria.
6. Volibris® (Ambrisentan)	05607D, 05608E, 09648T, 09649W	S100	Yes	Yes ( <i>written</i> )	Yes ( <i>written</i> )	Phone or online system could be more efficient than written especially for continuing criteria.

\*Continuing 1. Continuing treatment - first period of continuing treatment, or- re-initiation of interrupted treatment or

\*Continuing 2. Continuing treatment - second and subsequent applications for continuing treatment.

5. Revolade® (Eltrombopag) (PBS items 05825N, 05826P, 05827Q, 05828R)

**GSK recommends the Review Panel should consider that as eltrombopag patients must meet a number of criteria may make eltrombopag less suitable for a Streamlined Authority though should not exclude it becoming available as an Authority Required item (e.g. phone authority) especially for continuing treatment criteria. An online system could also be more efficient than a written authority.**

**GSK requests that as eltrombopag is in the PBS ATC code category 'B02BX - Other systemic hemostatics' with romiplostim that any potential changes are kept consistent between the two medicines.**

The PBS items for eltrombopag cover its indication for severe thrombocytopenia in an adult patient with severe chronic immune (idiopathic) thrombocytopenic purpura (ITP) in eligible patients; which is currently a Complex Authority Required restriction. Eltrombopag is a Section 100 medicine, part of the highly specialised drug program.

All patients must meet one of the three restrictions:

1. Initial treatment (**written**)
2. Continuing treatment - first period of continuing treatment, or re-initiation of interrupted treatment, (**written**) or
3. Continuing treatment - second and subsequent applications for continuing treatment (**phone**)

Currently, applications must be submitted in writing within one month of the date of the full blood count. Patients who fail to demonstrate a response to treatment with eltrombopag under the initial restriction will not be eligible to receive further PBS subsidised treatment. Under no circumstances would telephone approvals be granted for complete authority applications, or for treatment that would otherwise extend the treatment period.

Clinician feedback has indicated that receipts of approval for this item currently commonly takes 2 weeks and has been known to take up to 4 weeks (sometimes even longer when the application forms are not adequately completed). During this waiting period eligible patients wait for approval which can adversely affect patient care increasing the risk of patients requiring rescue medications whilst awaiting receipt of approval.

The requirement of all applications being submitted in writing within one month of the date of the full blood count and the patient and clinician acknowledgement to be signed and witnessed simultaneously can create a burden for health professionals and patients for the timings of appointments.

As previously mentioned, there are a number of criteria that patients must meet before being eligible for treatment with eltrombopag which may makes it less suitable for a Streamlined Authority though should not exclude it becoming available as an Authority required item (e.g. phone authority) especially for continuing treatment criteria. Or alternatively, an online secure portal for data capture of PBS restriction requirements (including patient and prescriber acknowledgement) could be more efficient than the current process. GSK requests that as Eltrombopag is in the PBS ATC code category 'B02BX - Other systemic hemostatics' with romiplostim that any potential changes are kept consistent between the two medicines.

**6. Flolan Kit® (Epoprostenol) (PBS items 05030R, 05035B, 05036C, 05042J), PAH / Volibris® (Ambrisentan) (PBS items 05607D, 05608E, 09648T, 09649W), PAH**

***GSK recommends the Review Panel should consider that as epoprostenol / ambrisentan patients must meet a number of criteria may make epoprostenol / ambrisentan less suitable for a Streamlined Authority though should not exclude it becoming available as an Authority Required item (e.g. phone authority) especially for continuing treatment criteria. An online system could also be more efficient than a written authority.***

***GSK requests that as epoprostenol / ambrisentan are in the PBS ATC code category 'C02KX' - Other systemic antihypertensives' with other PAH medicines with Special Authority requirements (i.e. iloprost, bosentan, sildenafil etc.), any potential changes are kept consistent between these medicines.***

The PBS items for epoprostenol / ambrisentan cover their use for pulmonary arterial hypertension (PAH) in eligible patients; which is currently an Authority Required restriction. Epoprostenol / ambrisentan are Section 100 medicines, part of the highly specialised drug program. Epoprostenol / ambrisentan must be prescribed by a small number of PAH designated centres across Australia with specialised expertise in the treatment of PAH patients.

All application must be in writing and must include:

- Sufficient information to determine the patients eligibility according to PBS criteria,
- Results of a right heart catheterisation (RHC) composite assessment,
- An echocardiography (ECHO) composite assessment, and
- A six minute walk test (6MWT).

Details of prior vasodilator therapy must be provided for patients with WHO functional Class III with mean right arterial pressure (mRAP) less than or equal to 8 mm Hg.

Clinician feedback has indicated that receipt of approval for these items currently commonly takes 2-4 weeks. Whilst, eligible patients wait for approval this can adversely affect patient care, where patients require clinical management whilst awaiting for receipt of approval. As previously mentioned, there are a number of criteria that patients must meet before being eligible for treatment; which may make it less suitable for a Streamlined Authority though should not exclude it becoming available as an Authority required item (e.g. phone authority) especially for continuing treatment criteria. Or alternatively, an online secure portal for data capture of PBS restriction requirements (including patient and prescriber acknowledgement) could be more efficient than the current process. Patients can often be on treatment for a prolonged period of time. Therefore, to simplify the continuing treatment criteria could be beneficial to specialists and nurses.

GSK requests that as epoprostenol / ambrisentan are in the PBS ATC code category 'C02KX' - Other systemic antihypertensives' with other PAH medicines with Special Authority requirements (i.e. iloprost, bosentan, sildenafil etc.), any potential changes are kept consistent between these medicines.

## **Tranche 2: Diabetes Medicines**

Table 3 describes the GSK diabetes medicines to be considered by the PBAC at the March 2015 meeting for Authority Required (STREAMLINED) for Tranche 2 (i.e. treatments for eye conditions and psychiatric conditions and cardiovascular disease).

**Table 3. Tranche 2: Diabetes Medicines, Rosiglitazone + Metformin, Rosiglitazone,**

GSK Diabetes Medicines Tranche 2	PBS item(s)	Source	Current Authority Required PBS Listing			Requested
			Authority Required	Initial treatment (Written/Phone)	Continuing treatment (Written/Phone)	Authority Required (Streamlined)
7. Avandamet® (Rosiglitazone+ Metformin)	09059T, 09060W, 09061X, 09062Y	General Schedule (Section 85)	Yes	Yes (phone)	No	Yes
8. Avandia® (Rosiglitazone)	08689H, 08690J	General Schedule (Section 85)	Yes	Yes (phone)	No	Yes

### **7. Rosiglitazone + metformin (Avandamet®) (PBS items 09059T, 09060W, 09061X, 09062Y)**

**GSK recommends the Review Panel should consider rosiglitazone + metformin for movement to an Authority Required (STREAMLINED) listing.**

These PBS items for rosiglitazone + metformin cover its indication for Diabetes mellitus type 2; which is currently an Authority Required restriction. This is listed in Section 85 (not Section 100) and has limited/no potential for misuse or abuse. Rosiglitazone + metformin is listed in the PBS ATC Code category 'A10BD - Combinations of oral blood glucose lowering drugs' group of medicines (A10B BLOOD GLUCOSE LOWERING DRUGS, EXCL INSULINS). The other medicines in this category with similar indications are predominantly Authority Required (STREAMLINED) (i.e. the gliptins + metformin). Furthermore, rosiglitazone + metformin has been on the market for a number of years with its use declining considerably. Therefore, these attributes suggest the PBS items for rosiglitazone + metformin meet the criteria for Authority Required (STREAMLINED) and consideration as part of the post-market review for standardisation with the other combination products in this ATC category.

### **A10BD - Combinations of oral blood glucose lowering drugs'**

- **ROSIGLITAZONE + METFORMIN - Authority Required**
- VILDAGLIPTIN + METFORMIN - Authority Required (STREAMLINED)
- LINAGLIPTIN + METFORMIN - Authority Required (STREAMLINED)
- ALOGLIPTIN + METFORMIN - Authority Required (STREAMLINED)
- SAXAGLIPTIN + METFORMIN - Authority Required (STREAMLINED)
- SITAGLIPTIN + METFORMIN - Authority Required (STREAMLINED)

**8. *(Avandia® (Rosiglitazone) (PBS items 08689H, 08690J)***

**GSK recommends the Review Panel should consider rosiglitazone for movement to an Authority Required (STREAMLINED) listing.**

These PBS items for rosiglitazone cover its indication for Diabetes mellitus type 2 which is currently an Authority Required restriction. This is listed in Section 85 (not Section 100) and has limited/no potential for misuse or abuse. Rosiglitazone is listed in the PBS ATC Code category 'A10BG - Thiazolidinediones' group of medicines (A10B BLOOD GLUCOSE LOWERING DRUGS, EXCL INSULINS). The other medicine in this group is pioglitazone and is Authority Required (STREAMLINED). As above, has been on the market for a number of years and its use is declining considerably. These attributes suggest it meets the criteria for Authority Required (STREAMLINED) and consideration as part of the post-market review for standardisation with pioglitazone.

**General comments regarding the Post-Market Review process**

GSK acknowledges and welcomes ongoing improvements to the Post-Market Review programme processes, including those administered to date through the Post-Market Review of Authority Required PBS Listings. Transparent, predictable and robust processes are critical to ensure the programme draws on the expertise of a full range of stakeholders to deliver on stated objectives including improved patient safety and better targeting of medicines. In the context of the Post-Market Review of Authority Required PBS Listings, GSK acknowledges:

- the opportunity for stakeholders to comment on draft ToRs;
- the transparency of published information including the role and membership of the reference group;
- the inclusion of a wider range of expertise on the reference group (including industry, pharmacy, medical associations and health consumers); and
- clarity of next steps and future opportunities to engage in the review (e.g. stakeholder forum and draft report).

GSK strongly recommends the Department continue to work with stakeholders including the pharmaceutical industry to improve Post-Market Review programme processes. Further, GSK recommends the Department work with stakeholders to ensure programme outcomes are considered and interpreted appropriately in line with PBS and access to medicines policy settings, such as the separation of F1 and F2 and the available policy levers to drive the Quality Use of Medicines.