

# Tyrosine kinase inhibitors for the treatment of Chronic Myeloid Leukaemia (CML)

## Drug utilisation sub-committee (DUSC)

*February 2014*

### Abstract

#### Purpose

The DUSC requested an analysis of the utilisation of PBS-listed tyrosine kinase inhibitors (TKIs), imatinib, dasatinib and nilotinib, for the treatment of CML. This analysis is a part of the routine analyses conducted by the DUSC investigating how the current utilisation of PBS medicines compares with the use as recommended by the PBAC.

#### Background

Imatinib, dasatinib and nilotinib inhibit the activity of the abnormal tyrosine kinase created by the Philadelphia chromosome abnormality in patients with chronic myeloid leukaemia.

The PBS restrictions for the TKIs for CML have evolved over time. The current PBS restrictions, when used in accordance with certain criteria, include:

- imatinib, dasatinib and nilotinib as first line therapy in the treatment of the chronic phase of CML. Patients can switch between the three drugs within first line if intolerant, but not if they have failed;
- imatinib in accelerated or blast phase;
- dasatinib, after failure of first line imatinib or nilotinib, in any phase; and
- nilotinib, after failure of first line imatinib or dasatinib, in the chronic or accelerated phase.

Authority applications are managed by the Department of Human Services (DHS) Medicare Specialised Drugs area. Initial applications require prior written approval. Subsequent applications for imatinib can be made by telephone.

#### Date of listing on PBS

For CML:

Imatinib: December 2001;

dasatinib: August 2007;

nilotinib: August 2008.

## **Data Source**

The DHS Medicare prescription database provided supplied R/PBS prescription data and associated expenditure. The DHS Medicare Authority Approval database provided supplementary data on the phase of the disease and whether use was initial or continuing treatment.

## **Key Findings**

- The number of patients on treatment, number of prescriptions and expenditure of TKIs for CML has increased steadily (i.e. linear trend) over a 12 year period from 2001 to 2013. This reflects the increasing prevalence of CML as mortality from CML declines and patients continue on treatment. Utilisation is expected to continue to increase in the future.
- The DUSC considered that the steadily increasing expenditure for TKIs in CML is explicable entirely on the basis of increased survival.
- The number of new patients commencing treatment has remained stable. This trend is consistent with incidence of CML reported by the AIHW.
- Listing of dasatinib and nilotinib for chronic phase CML after failure of imatinib, and subsequently as first line therapy, has not had a noticeable impact on the steady upward trend in prevalent patients, prescription utilisation and expenditure for CML drugs.

## Purpose of analysis

The DUSC requested an analysis of the utilisation of PBS-listed tyrosine kinase inhibitors (TKIs), imatinib, dasatinib and nilotinib, for the treatment of CML. This analysis is a part of the routine analyses conducted by the DUSC investigating how the current utilisation of PBS medicines compares with the use as recommended by the PBAC.

## Background

### Pharmacology

Imatinib, dasatinib and nilotinib are protein-tyrosine kinase inhibitors that inhibit the activity of the BCR-ABL tyrosine kinase, the constitutive abnormal tyrosine kinase created by the Philadelphia chromosome abnormality in patients with CML.<sup>1,2,3</sup>

### TGA approved indications

**Imatinib (Glivec®)** is indicated for the treatment of patients with CML.

**Dasatinib (Sprycel®)** is indicated for the treatment of:

- adults aged 18 years or over with newly diagnosed Philadelphia chromosome positive (Ph+) CML in the chronic phase; and
- adults aged 18 years or over with chronic, accelerated or myeloid or lymphoid blast phase CML with resistance or intolerance to prior therapy including imatinib.

**Nilotinib (Tasigna®)** is indicated for the treatment of:

- adult patients with newly diagnosed Ph+ CML in chronic phase; and
- adults with chronic phase and accelerated phase Ph+ CML resistant to or intolerant of prior therapy including imatinib.

Imatinib and dasatinib are registered for indications other than CML. For more information, see the Product Information for details (<http://tga.gov.au/hp/information-medicines-pi.htm>).

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<sup>1</sup> Glivec (imatinib) Product Information. Accessed 16 December 2013. Available from <https://www.ebs.tga.gov.au/>

<sup>2</sup> Sprycel (dasatinib) Product Information. Accessed 16 December 2013. Available from <https://www.ebs.tga.gov.au/>

<sup>3</sup> Tasigna (nilotinib) Product Information. Accessed 16 December 2013. Available from <https://www.ebs.tga.gov.au/>.

## Dosage and administration

Table 1: TGA approved doses of TKIs for CML

Phase	Drug	Dose
Chronic	Imatinib	Standard: 400 mg/day Increased dose: 600–800 mg/day (disease progression, lack of response, loss of previous response)
	Dasatinib	100 mg/day Increased dose: 140 mg/day (lack of haematological or cytogenic response)
	Nilotinib	Newly diagnosed: 300 mg twice daily Resistant or intolerant to prior therapy: 400 mg twice daily
Accelerated	Imatinib	Standard: 600 mg/day Increased dose: 400 mg twice daily
	Dasatinib	Standard dose: 140 mg/day Increased dose: 180 mg/day (lack of haematological or cytogenic response)
	Nilotinib	400 mg twice daily
Blast	Imatinib	600 mg/day Increased dose: 400 mg twice daily
	Dasatinib	140 mg/day
	Nilotinib	-

\*On 1/4/2012 the PBS wording of the first-line restrictions was modified to include dose guidance. Patients should be commenced on a dose of imatinib mesylate 400mg (base) daily, dasatinib of at least 100mg (base) daily and nilotinib of 300mg twice daily. The current Product Information (PI) and Consumer Medicine Information (CMI) are available from <http://tga.gov.au/hp/information-medicines-pi.htm> and <http://www.tga.gov.au/consumers/information-medicines-cmi.htm>.

### PBS listing details (as at 1 November 2013)

The PBS restrictions for the TKIs for CML are complex and have evolved over time. The full restriction wording is available at [pbs.gov.au](http://pbs.gov.au). The restriction history is summarised in Appendix A.

PBS item codes for CML are shown in Table 2, Table 3 and Table 4. Some item codes have been superseded over time.

**Table 2: PBS item listing history for imatinib for CML**

Item Listing Date	PBS item code (stage)	Form and Strength	Maximum Quantity	Max. Repeats	DPMQ	Brand Name	Item End Date
1/12/2001	8549Y (AP/BP)	Capsules equivalent to 100 mg imatinib, 120	1	2	\$ 4,363.76	Glivec	31/01/2003
	8550B (AP/BP)	Capsules equivalent to 100 mg imatinib, 180	1	2	\$ 6,543.33	Glivec	31/01/2003
21/10/2002	6359Q (CP)	Capsules equivalent to 100 mg imatinib, 120	1	5	\$ 3,772.33	Glivec	30/11/2004
	6360R (CP)	Capsules equivalent to 100 mg imatinib, 180	1	5	\$ 5,658.50	Glivec	30/11/2004
	6361T (AP/BP)	Capsules equivalent to 100 mg imatinib, 120	1	2	\$ 3,772.33	Glivec	30/11/2004
	6362W (AP/BP)	Capsules equivalent to 100 mg imatinib, 180	1	2	\$ 5,658.50	Glivec	30/11/2004
1/05/2004	6444E (CP)	Tablet 100 mg (as mesylate)	60	5	\$ 1,886.17	Glivec	31/10/2007
	6445F (CP)	Tablet 400 mg (as mesylate)	30	5	\$ 3,772.33	Glivec	31/10/2007
	6446G (AP/BP)	Tablet 100 mg (as mesylate)	60	2	\$ 1,886.17	Glivec	31/10/2007
	6447H (AP/BP)	Tablet 400 mg (as mesylate)	30	2	\$ 3,772.33	Glivec	31/10/2007
1/11/2007	9113P (CP)	Tablet 100 mg (as mesylate)	60	5	\$ 2,005.19	Glivec	Current
	9114Q (CP)	Tablet 400 mg (as mesylate)	30	5	\$ 3,863.81	Glivec	Current
	9115R (AP/BP)	Tablet 100 mg (as mesylate)	60	2	\$ 2,005.19	Glivec	Current
	9116T (AP/BP)	Tablet 400 mg (as mesylate)	30	2	\$ 3,863.81	Glivec	Current

Source: PBS Item History file accessed 1 November 2013.

CP= chronic phase; AP = accelerated phase; BP = blast phase

**Table 3: PBS item listing history for dasatinib for CML**

Item Listing Date	PBS item code	Form and Strength	Maximum Quantity	Max. Repeats	DPMQ	Brand Name	Item End Date
1/08/2007	2478K	Tablet 20 mg	60	5	\$ 3,095.66	Sprycel	Current
	2482P	Tablet 50 mg	60	5	\$ 5,004.01	Sprycel	Current
	2485T	Tablet 70 mg	60	5	\$ 6,160.40	Sprycel	Current
1/11/2008	9282M	Tablet 20 mg	60	2	\$ 3,246.36	Sprycel	31/03/2012
	9283N	Tablet 50 mg	60	2	\$ 5,250.68	Sprycel	31/03/2012
	9284P	Tablet 70 mg	60	2	\$ 6,465.01	Sprycel	31/03/2012
1/05/2010	9341P	Tablet 100 mg	30	2	\$ 5,250.68	Sprycel	31/03/2012
	9342Q	Tablet 100 mg	30	5	\$ 5,004.01	Sprycel	Current
1/04/2012	1354G (CP)	Tablet 20 mg	60	5	\$ 3,095.66	Sprycel	Current
	1381Q (CP)	Tablet 50 mg	60	5	\$ 5,004.01	Sprycel	Current
	1415L (CP)	Tablet 70 mg	60	5	\$ 6,160.40	Sprycel	Current
	1416M (CP)	Tablet 100 mg	30	5	\$ 5,004.01	Sprycel	Current

Source: PBS Item History file accessed 1 November 2013. Shaded cells are for second line treatment in any phase.

CP= chronic phase; AP = accelerated phase; BP = blast phase

**Table 4: PBS item listing history for nilotinib for CML**

Item Listing Date	PBS item code	Form and Strength	Maximum Quantity	Max. Repeats	DPMQ	Brand Name	Item End Date
1/08/2008	9171Q (CP/AP)	Capsule 200 mg (as hydrochloride monohydrate)	120	5	\$ 5,872.35	Tasigna	Current
1/11/2008	9285Q (CP/AP)	Capsule 200 mg (as hydrochloride monohydrate)	112	2	\$ 5,490.42	Tasigna	31/03/2012
1/04/2012	1309X (CP)	Capsule 150 mg (as hydrochloride monohydrate)	120	5	\$ 4,468.08	Tasigna	Current

Source: PBS Item History file accessed 1 November 2013. Shaded cells are for second-line treatment.  
CP= chronic phase; AP = accelerated phase; BP = blast phase

All these drugs are Complex Authority Required (CAR) drugs, which means that the authority approval needs to be in writing and contain supplementary information. Second and subsequent applications for imatinib can be made by telephone. The CAR authority application forms for CML can be accessed from the DHS Medicare web site at: [www.medicareaustralia.gov.au/provider/pbs/drugs1/cml-glivec.jsp](http://www.medicareaustralia.gov.au/provider/pbs/drugs1/cml-glivec.jsp).

Current PBS listing details are available from [www.pbs.gov.au](http://www.pbs.gov.au)

## **Issues considered by the PBAC**

In July 2011, the PBAC noted that the availability of dasatinib and nilotinib as first-line therapy for CML would change the current treatment algorithm. The PBAC considered that it was unlikely that imatinib would be used after failure of dasatinib due to resistance, or after failure of nilotinib, as there is little evidence for this use. The PBAC considered it possible that imatinib might be used after dasatinib in cases of intolerance to dasatinib but the most likely scenario after failure of dasatinib is second-line nilotinib; and the most likely scenario after failure of nilotinib, after dose escalation to 400 mg twice daily, is second-line dasatinib. The PBAC considered that the PBS listings for TKIs in the second-line setting would need reviewing due to the change in the treatment algorithm. The PBAC also considered that, in future, it would be critical to distinguish between the need to change the TKI because of intolerance and because of inadequate response. Second-line therapy after dasatinib or nilotinib should refer to the situation where there has been failure of response and should not include failure due to toxicity. Changes between TKIs should be possible in first-line therapy where there is intolerance to the first initiated TKI. The PBAC noted that further discussion would be needed with the sponsors and Stakeholders before finalisation of the restrictions for first and second-line treatment settings.

A copy of the Public Summary Document from the July 2011 PBAC meeting is available at [www.health.gov.au/internet/main/publishing.nsf/Content/pbac-psd-dasatinib-july11](http://www.health.gov.au/internet/main/publishing.nsf/Content/pbac-psd-dasatinib-july11)

## **Previous reviews by DUSC**

DUSC reviewed imatinib utilisation for CML at its August 2003 meeting for the period December 2001 to April 2003. At that time, actual usage was slightly lower than that estimated in the submission. The DUSC considered that the trend indicated that the number of imatinib prescriptions could continue to increase and if so could result in slightly higher utilisation than estimated in the submission. Neither dasatinib nor nilotinib have been reviewed by DUSC previously.

## **Methods**

The number of PBS/RPBS prescriptions and benefits paid for imatinib, dasatinib and nilotinib for CML (see item codes in Tables 2–4) were extracted from the DHS Medicare Prescription database for the period 1 December 2001 to 30 June 2013. Data were extracted based on

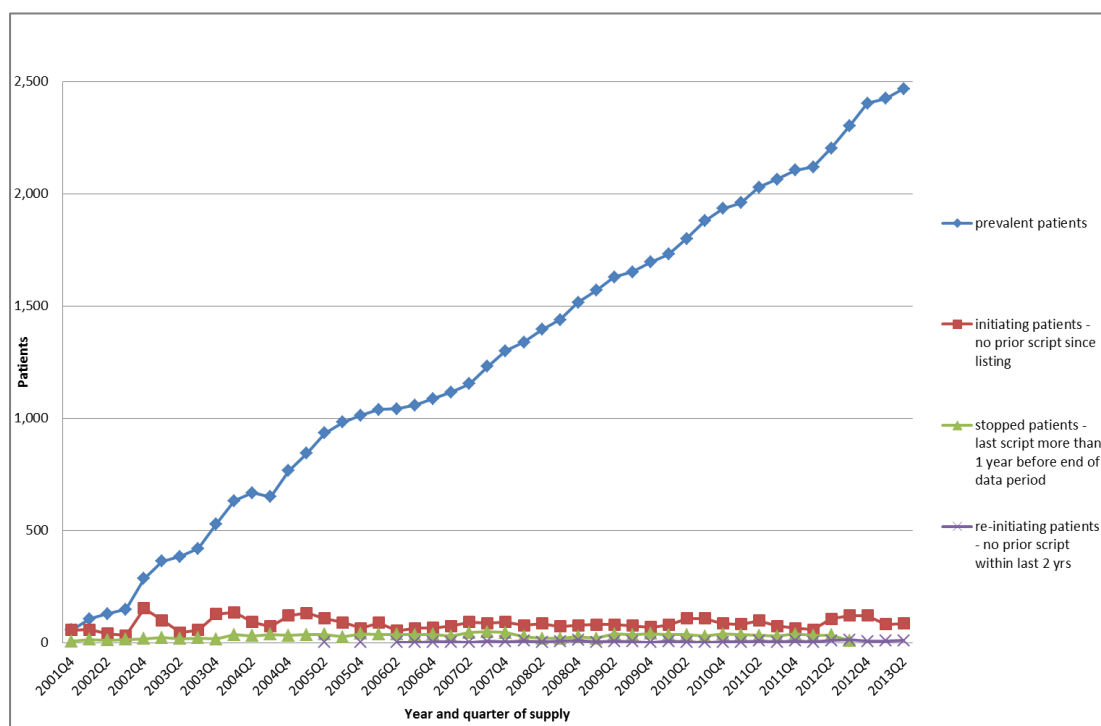
the date of supply of the prescription to the patient. The number of patients treated was determined by counting the number of individual de-identified personal identification numbers in the specified time period. New patients were defined as those with no prior prescription of a TKI since 1 December 2001.

The DHS Medicare Authority Approval database was used as a supplementary data source to classify approvals by disease phase and whether the approval was for initial or continuing treatment.

## Results

### Analysis of drug utilisation

#### *Number of patients treated with TKIs for CML*



**Figure 1: Number of CML patients treated – prevalent, initiating, stopped and re-initiating**

Note: the number of stopped patients cannot be estimated for the last year of the data period

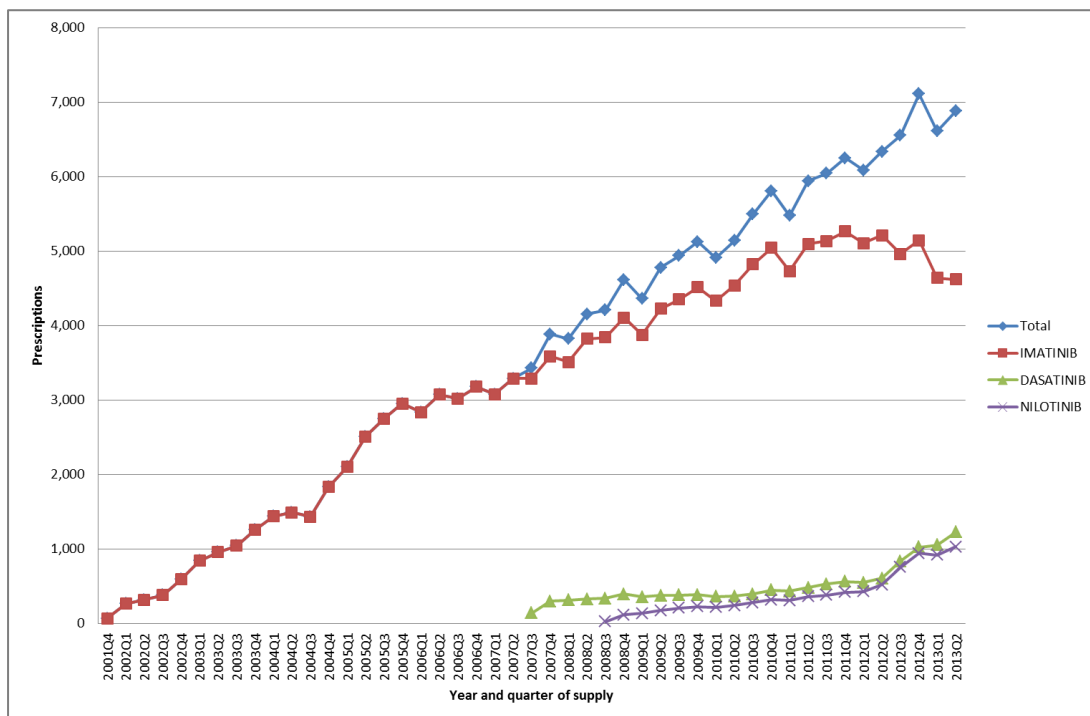
As shown in Figure 1, on average 84 new patients started treatment with a TKI each quarter (338 patients/year). The relatively stable trend in the number of new patients treated over the past 12 years is consistent with incidence trends reported by the Australian Institute of Health and Welfare (AIHW),<sup>4</sup> but the total number of patients starting TKIs (338) is higher than the reported incidence of CML of about 280 patients per year.

<sup>4</sup> The average annual change in incidence rates for CML in Australia, 2002 to 2009, was 1.2%. Source: Australian Cancer Incidence and Mortality (ACIM) books, [www.aihw.gov.au/acim-books/](http://www.aihw.gov.au/acim-books/), accessed 17 December 2012.

The lower number of new patients commencing treatment in late 2011 and higher number in the second quarter of 2012 coincides with the listing of dasatinib and nilotinib as first-line therapies for chronic phase CML. This transient decrease and subsequent increase is probably due to patients transferring from patient access programs to PBS supply of dasatinib and nilotinib for first-line, chronic phase disease.

The total number of patients undergoing treatment with a TKI (prevalent patients) has increased steadily since 2001. In 2012/13 approximately 2,500 patients were treated with a TKI. Once TKI treatment has started, very few patients stop (or reinstate) treatment accounting for the increasing prevalent treated population over time.

### Number of prescriptions

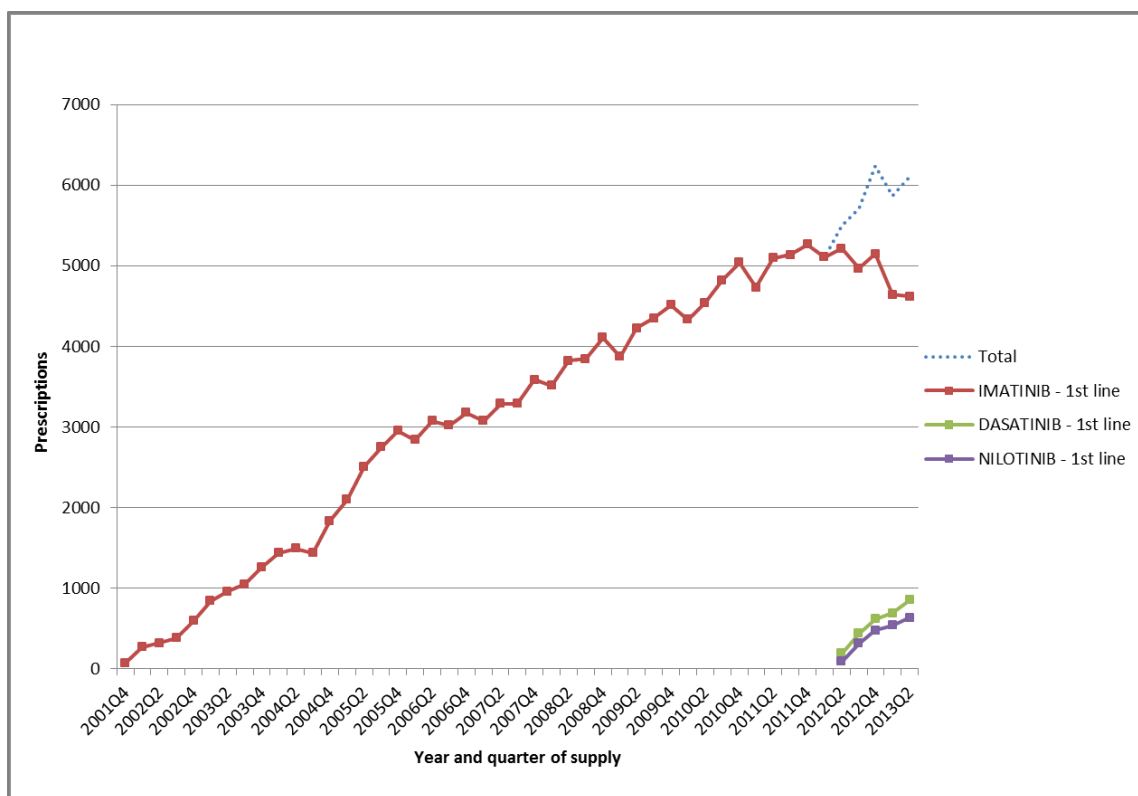


**Figure 2: PBS/RPBS prescriptions for TKIs in CML (all phases)**

Figure 2 shows the number of PBS/RPBS prescriptions supplied for imatinib, dasatinib and nilotinib in all phases of disease. Consistent with an increasing number of patients on treatment as shown in Figure 1, the number of prescriptions has increased steadily over time.

The vast majority of prescriptions are for chronic phase disease as demonstrated in Figures 3 and 4. This is consistent with the natural history of the disease – an initially indolent, chronic phase followed by accelerated phase and blast crisis.

Figure 3 shows the number of PBS/RPBS prescriptions supplied for imatinib, dasatinib and nilotinib for first-line therapy in chronic phase CML.



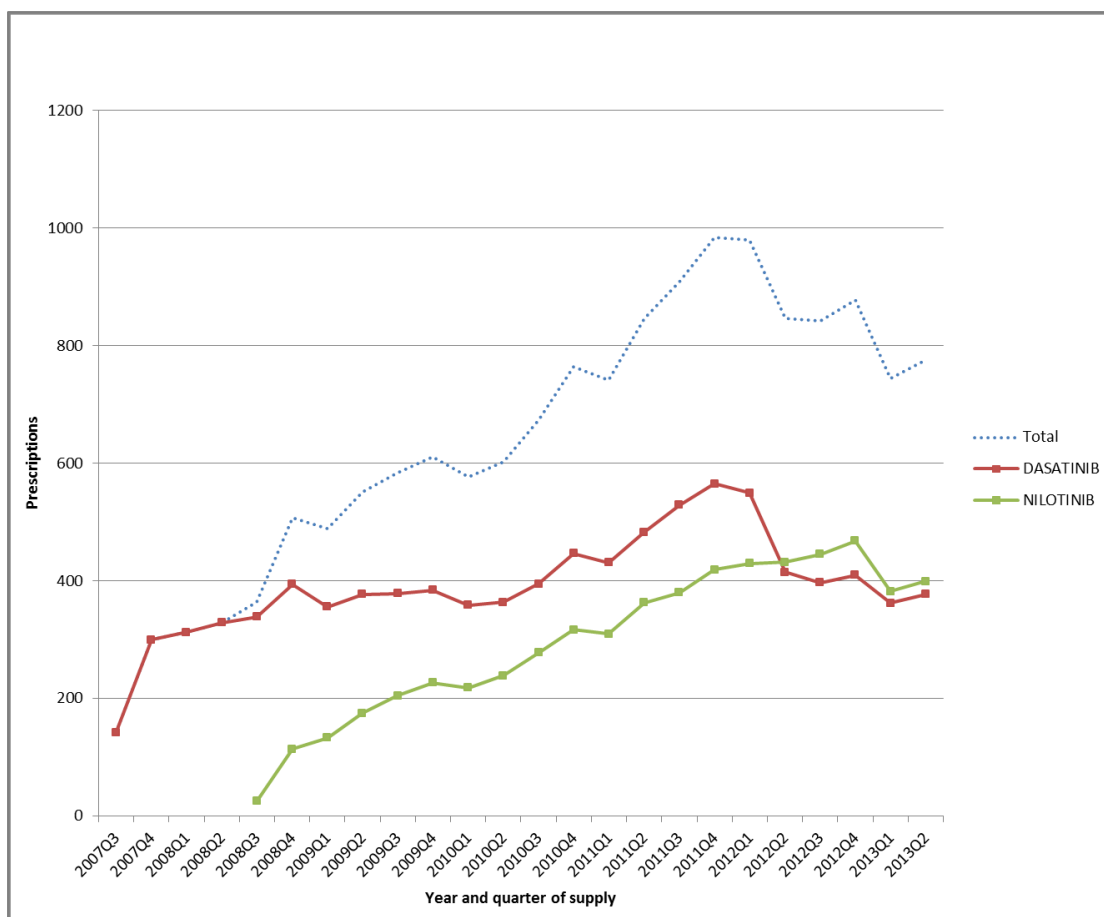
**Figure 3: Supplied prescriptions for TKIs in first line therapy for chronic phase CML**

Note: Data includes historical and current PBS item codes for first line chronic phase treatment: 1309X, 1354G, 1381Q, 1415L, 1416M, 6359Q, 6360R, 6444E, 6445F, 9113P and 9114Q. See Tables 2, 3 and 4 for item details

Following the extension to listing from April 2012 to include use of dasatinib and nilotinib as first-line therapy for chronic phase CML, utilisation of imatinib has declined. This is consistent with the basis of listing with dasatinib and nilotinib expected to substitute for imatinib.

The plateau in imatinib utilisation prior to April 2012 is probably due to use of dasatinib or nilotinib via patient familiarisation programs prior to PBS listing for first line chronic phase CML.

Figure 4 shows the number of PBS/RPBS prescriptions supplied for dasatinib and nilotinib for second-line therapy in CML.



**Figure 4: Supplied prescriptions for TKIs in second line therapy for CML**

Note: Data includes PBS item codes for second line therapy: see Tables 3 and 4 for item details

The reduction in prescriptions supplied for second-line treatment from the second quarter of 2012 onwards coincides with the listing of dasatinib and nilotinib for first line treatment. This could indicate that some patients were receiving first line dasatinib or nilotinib prior to listing for this indication.



Initial authority approvals, which represent initiating patients, demonstrate that a higher proportion of patients commenced on dasatinib and nilotinib in first line than was expected in the submissions.

**Table 5: Initial authority approvals for first line chronic phase CML treatment in the first year of nilotinib and dasatinib first-line listing**

Quarter of supply	NILOTINIB	IMATINIB	DASATINIB	TOTAL
2012Q2	71	109	88	
2012Q3	78	77	58	
2012Q4	79	103	76	
2013Q1	56	67	75	
<b>Total</b>	<b>284</b>	<b>356</b>	<b>297</b>	<b>937</b>
<b>Percentage of total</b>	<b>30%</b>	<b>38%</b>	<b>32%</b>	<b>100%</b>

## Analysis of expenditure

**Table 6: PBS/RPBS expenditure for CML by drug**

Year	IMATINIB	DASATINIB	NILOTINIB	Total
2002	\$8,888,805			\$8,888,805
2003	\$19,088,705			\$19,088,705
2004	\$27,734,255			\$27,734,255
2005	\$43,456,003			\$43,456,003
2006	\$50,203,375			\$50,203,375
2007	\$53,760,354	\$2,542,707		\$56,303,060
2008	\$63,373,230	\$7,745,640	\$766,496	\$71,885,365
2009	\$70,699,507	\$8,166,481	\$4,102,175	\$82,968,162
2010	\$77,530,026	\$8,416,912	\$5,809,359	\$91,756,299
2011	\$82,587,179	\$10,803,104	\$8,063,187	\$101,453,470
2012	\$81,934,299	\$15,446,820	\$14,156,871	\$111,537,991

The increasing expenditure aligns with the increasing number of prescriptions dispensed over time (Figure 3).

## Discussion

Utilisation and expenditure of the TKIs is steadily increasing. This is due, not to an increasing number of incident patients, but a high treatment continuation rate, leading to a steady increase in the number of prevalent patients. At the time of listing, continuation rates for first line TKI therapies in CML were expected to be high (greater than 80%). The DUSC considered that the steadily increasing expenditure for TKIs in CML is explicable entirely on the basis of increased survival.

Further growth in utilisation is expected into the future as mortality from CML declines<sup>5</sup> and the population ages. At some point utilisation will plateau, but this is may not be until at least 2050, based on prevalence projections from the US.<sup>6</sup> The DUSC considered that the average duration of treatment will be 20 to 30 years. This is because the median age at presentation is 50 to 60 years old and patients are unlikely to survive longer than the average life expectancy (i.e. approximately 80 years). Duration of treatment (in years) in a stable population is approximately equal to point prevalence divided by incidence (in a year), thus this ratio is unlikely to be greater than 20 to 30. This means that expenditure increase is likely to continue at the current rate for another 10 years (since it has already been increasing for 12 years) before a plateau begins to form.

Current Australian incidence of CML is approximately 300 patients and the prevalent treated population is approximately 2,500 patients.

While first line use of nilotinib and dasatinib is higher than what was predicted in the submission estimates, the total market utilisation has continued to increase in a steady linear trend. This implies that first line nilotinib and dasatinib have substituted within the imatinib market, and the extent of substitution for imatinib was greater than anticipated.

As the TKIs are complex authority required medicines, administered by the Specialised Drugs area of DHS Medicare, there is low risk of use outside of the restriction.

## DUSC Actions

- DUSC referred the report to the PBAC for information.
- DUSC requested information be provided on dosage in first and second line therapy for each drug, for the purpose of checking predicted versus actual dosing.

## Context for analysis

The DUSC is a Sub Committee of the Pharmaceutical Benefits Advisory Committee (PBAC). The DUSC assesses estimates on projected usage and financial cost of medicines.

The DUSC also analyses data on actual use of medicines, including the utilisation of PBS listed medicines, and provides advice to the PBAC on these matters. This may include outlining how the current utilisation of PBS medicines compares with the use as recommended by the PBAC.

The DUSC operates in accordance with the quality use of medicines objective of the National Medicines Policy and considers that the DUSC utilisation analyses will assist consumers and health professionals to better understand the costs, benefits and risks of medicines.

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<sup>5</sup> Australian Cancer Incidence and Mortality (ACIM) books, <http://www.aihw.gov.au/acim-books/>, accessed 17 December 2012.

<sup>6</sup> Huang X, Cortes J, Katarjian H. Estimations of the Increasing Prevalence and Plateau Prevalence of Chronic Myeloid Leukemia in the Era of Tyrosine Kinase Inhibitor Therapy. *Cancer*. 2012: 3123-7.

The utilisation analysis report was provided to the pharmaceutical sponsors of each drug and comments on the report were provided to DUSC prior to its consideration of the analysis.

## **Sponsors' comments**

Bristol-Myers Squibb Australia Pty Ltd:

Bristol-Myers Squibb welcomes the findings of the analysis. The increasing prevalence of CML is reflective of a reduction in mortality, which is attributable to the availability of innovative and effective treatments, the first and second generation TKIs, on the Pharmaceutical Benefits Scheme.

Novartis Pharmaceuticals Australia Pty Limited:

The Sponsor thanks the DUSC for the opportunity to review and comment on this review and agrees that the prevalence of CML is increasing over time due to the clinical efficacy of these therapies.

## Appendix A

### *Restriction*

The restriction changes for the CML indications of the three drugs can be summarised as follows:

- On 1/12/2001 imatinib was listed (S85) for first line treatment of CML in the **accelerated** or **blast** phases.
- On 21/10/2002 this was extended to first line treatment in the **chronic** phase and the listing changed to S100, Special Authority Program.
- On 1/8/2007 dasatinib was listed (S85) for second line treatment (i.e. failed an adequate trial of imatinib) in **any** disease phase.
- On 1/11/2007 all the imatinib items were changed from S100 to S85 to be consistent with the dasatinib listings.
- On 1/8/2008 nilotinib was listed (S85) for second line treatment (i.e. failed an adequate trial of imatinib) in **chronic** or **accelerated** phases.
- On 1/4/2012 dasatinib and nilotinib restrictions were extended to first line treatment in **chronic** phase. Dasatinib retained the restriction for second line treatment (i.e. failed an adequate trial of imatinib or nilotinib) for **any** disease phase and nilotinib retained second line treatment (i.e. failed an adequate trial of imatinib or dasatinib) for **chronic** or **accelerated** phases.
- On 1/4/2012 the wording of the first line restrictions were modified to include dose guidance. Patients should be commenced on a dose of imatinib mesylate 400 mg (base) daily, dasatinib of at least 100 mg (base) daily and nilotinib of 300 mg twice daily.

# Tyrosine kinase inhibitors for the treatment of Chronic Myeloid Leukaemia (CML): Addendum

## Drug utilisation sub-committee (DUSC)

*October 2014*

### Abstract

#### Purpose

To assess the doses of imatinib, dasatinib and nilotinib for first and second line treatment of chronic myeloid leukaemia.

#### Background

At the February 2014 meeting, the DUSC considered an analysis of the utilisation of PBS-listed tyrosine kinase inhibitors (TKIs), imatinib, dasatinib and nilotinib, for the treatment of CML. The DUSC requested information be provided on dosage in first and second line therapy for imatinib, dasatinib and nilotinib in CML for the purpose of checking predicted versus actual dosing.

#### Data Source / methodology

The dosage information in this addendum comes from the quantity and strength information recorded in the Department of Human Services (DHS) Authorities Approval database for approvals from 2012 Q2 to 2013 Q3 inclusive.

The actual prescribed dose is not recorded in the database. The prescribed dose was estimated from the approval data by assuming the quantity prescribed on each prescription is intended to be for 30 days of treatment and summing the approvals for different strengths of a drug for a patient on a day, having regard to both the strength and the quantity requested.

Line of treatment (i.e. first or second line), disease phase and approval type (i.e. initial or continuing) were all defined from the analysis of the restriction text associated with the restriction codes recorded in the DHS Authorities Approval database.

#### Key Findings

The calculated dose relativities of imatinib versus dasatinib and imatinib versus nilotinib in the first line treatment of newly diagnosed patients are consistent with the values assumed by the PBAC when these drugs were recommended.

## **Disclaimer**

The information provided in this report does not constitute medical advice and is not intended to take the place of professional medical advice or care. It is not intended to define what constitutes reasonable, appropriate or best care for any individual for any given health issue. The information should not be used as a substitute for the judgement and skill of a medical practitioner.

The Department of Health (DoH) has made all reasonable efforts to ensure that information provided in this report is accurate. The information provided in this report was up-to-date when it was considered by the Drug Utilisation Sub-committee of the Pharmaceutical Benefits Advisory Committee. The context for that information may have changed since publication.

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