**Scottish Medicines Consortium**

**Guidance to Manufacturers for Completion of New Product Assessment Form (NPAF)**

**Supplement:**

**Submissions for medicines where the comparator is available through a confidential Patient Access Scheme (PAS)**

**August 2016**

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**1. Background**

This supplement provides guidance to manufacturers on the approach to submissionsfor products where the comparator medicine has been accepted for use in NHS Scotland on the basis of a confidential patient access scheme (PAS) previously accepted by the Patient Access Scheme Assessment Group (PASAG). (See [here](http://www.scottishmedicines.org.uk/Submission_Process/Submission_guidance_and_forms/Patient-Access-Schemes) for more information on the different types of PAS and the PASAG process).

Increasingly submissions to SMC involve a comparator medicine (defined in section 6.7.2 of the [Guidance for Manufacturers](http://www.scottishmedicines.org.uk/Submission_Process/Submission_guidance_and_forms/Templates-Guidance-for-Submission)) that has been accepted for use only on the basis of a confidential patient access scheme (PAS). The PAS price of the relevant comparator must be used in the economic case to provide a realistic estimate of cost effectiveness of the new medicine.

SMC does not take account of any other type of discount that may be applied to the list price of comparator products (e.g. local/hospital discounts) and these should not be included within the economic evaluation; only PAS discounts are relevant and are the focus of this supplement.

**Note - the following key terms are used in this supplement:**

**Key comparator** – the medicine most likely to be displaced in NHS Scotland.

**Multiple comparators** – where there is a range of relevant comparator medicines used in practice.

**Inter-company combination** **regimen** – where the medicine under review is given with another medicine as part of a combination regimen, and the other medicine is marketed by a different company.

**Later-line medicine** – a medicine that may be used in sequential therapy (after the submitted medicine is given).

Where a submission involves any of the above scenarios with a confidential PAS, the ‘with PAS’ prices will normally be relevant for SMC decision-making and should be taken into account in the pharmaco-economic case for the new medicine under review, as outlined in this document.

**Please refer to the appendix for examples of submission requirements for a range of potential scenarios.**

**2. Pharmaco-economic evaluation**

**2.1 Comparator medicines available under PAS**

If a key comparator medicine in the economic case is available through a simple discount PAS, the submitting company must model the cost effectiveness of their product against the comparator at list price as the base case and also using a range of potential discounts for the comparator between 5% and 95% in 5% increments (i.e. provide 20 base case estimates accompanied by sensitivity analysis for each 5% discount level). These additional analyses should be provided as an appendix within the New Product Assessment Form (NPAF). Note that it is not acceptable for companies to provide only a set of analyses using a single estimate of the anticipated PAS discount for the comparator product (unless the submitting company also owns the comparator product).

In recognition of the high volume of analyses requested, it is suggested that sensitivity analysis for the increments should focus on key variables only, for example, those that produce most upward uncertainty in the incremental cost effectiveness ratio (ICER). This should be included in the submission to SMC. During the assessment further sensitivity analysis on other variables may be requested and would require the analysis over the full range of discounts.

SMC will select the cost effectiveness results that use the 5% increment closest to the actual PAS discount in place for the comparator and will use these for decision-making purposes. However, only the results using the list price of the comparator medicine will be reported in the detailed advice document (DAD) issued to the submitting company following the New Drugs Committee (NDC) meeting and in the final SMC DAD. A standard statement will note that the results using the ‘with PAS’ price for the comparator medicine(s) cannot be reported.

If a comparator medicine is available through a complex PAS (defined in section 3 of [NHS Scotland Patient Access Scheme (PAS) Guidance](http://www.scottishmedicines.org.uk/Submission_Process/Submission_guidance_and_forms/Patient-Access-Schemes)), the mechanism of the PAS may be described in sufficient detail in the relevant DAD to allow a company to factor an approximation of the operation of the scheme into their economic model. Any assumptions used in this modeling should be fully described. Alternatively, if it is not possible to approximate the PAS discount based on the information in the relevant DAD, a range of potential equivalent discounts for the comparator may be applied as described above.

**2.2 Multiple comparators available under PAS**

Where an economic evaluation presents multiple relevant comparators and where simple or complex PAS apply to more than one of these medicines, the submitting company should present the analysis at list price for each comparator as the base case (i.e. using pairwise comparisons) and also over the 5% increments as above for each comparator. Analysis using the actual discount levels for each medicine can be very complex, so further analysis may be requested during the course of the assessment.

**2.3 Combination regimens**

Where a submission involves the medicine under review being given as part of a combination regimen with another medicine that is available through a PAS and this medicine is also marketed by the sponsor company, it is acceptable to use the ‘with PAS’ price of this medicine in the base case.

Where a submission involves the medicine under review being given as part of a combination regimen with another medicine that is available on the basis of a simple PAS and this medicine is marketed by a different company **(i.e. an inter-company combination regimen)**, the above approach (outlined in section 2.1) using a range of potential discounts for the other medicine should be followed. Only the results using the list price of the other medicine will be reported in the DAD issued to the submitting company following the NDC meeting and in the final SMC DAD.

Please contact the SMC Secretariat for advice in complex situations involving both an inter-company combination regimen (where the other medicine is available under a PAS) and where a key comparator medicine is also available under a PAS.

**2.4 Later-line medicines available under PAS**

Where a later-line medicine (see above) is available through a PAS, the list price should generally be used, unless the use of the medicine varies significantly between the arms of the model. However, if a key comparator is available through a PAS and is also used in subsequent lines of treatment in the model, the analysis provided should use the price of this medicine varied over the 5% increments at all points in the treatment pathway (i.e. both as the key comparator and as a later-line medicine).

**2.5 Where a PAS is also proposed for the medicine under review**

Where the medicine submitted for review has a PAS then cost effectiveness estimates should normally be provided both with and without the PAS (refer to section 6.15 of the main [Guidance for Manufacturers](http://www.scottishmedicines.org.uk/Submission_Process/Submission_guidance_and_forms/Templates-Guidance-for-Submission)). However, in a submission where both the new medicine under review and the comparator (or another medicine in an inter-company combination regimen) has a PAS, the following should apply:

* If the medicine submitted for review has a proposed simple discount PAS then only cost effectiveness estimates with the PAS are required. This is in recognition of the high company workload associated with generating additional ‘without PAS’ estimates that are unlikely to be required for NDC or SMC decision-making. In this situation, the results using the list price of the comparator medicine will not be reported in the final SMC DAD i.e. no results will be presented.
* If the medicine submitted for review has a proposed complex PAS then cost effectiveness estimates should be provided both with and without the PAS. The ‘without PAS’ estimates should be presented as the base case analysis. Refer to section 6.15 of the main [Guidance for Manufacturers](http://www.scottishmedicines.org.uk/Submission_Process/Submission_guidance_and_forms/Templates-Guidance-for-Submission) for further information.

Note that the comparator, and/or other medicine PAS should still be modeled as described in section 2.1 using a range of potential discounts.

**3. Resource implications (Budget impact template)**

Where the comparator (displaced medicine) is available through a PAS and/or the medicine under review is given as part of an inter-company combination regimen and the other medicine is available through a PAS, the budget impact template should use the list price for these medicines. There is no requirement to provide templates using a range of possible discount levels for the comparator/other medicine.

Appendix

**Submission requirements for example confidential PAS scenarios**

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| **Scenario 1: new medicine with simple PAS, single comparator with simple PAS** | |
| **Medicine being submitted for assessment** | Simple PAS proposed |
| **Comparator medicine** | With simple PAS |
| **Submission requirements: base case** | ICER presented using PAS price for new medicine and list price for comparator treatment. |
| **Submission requirements: sensitivity analysis** | 1. For the base case ICER, the list price for the comparator medicine should be varied through a discount range of 5%-95% at 5% increments. 2. The base case ICER above should be tested using conventional sensitivity analysis. In addition, for the key variables identified, the results should also be presented to show the impact of assuming the 5% to 95% discounts for the comparator. |
| **Submission requirements:**  **budget impact templates** | Template with and without new medicine’s PAS. Both templates use only the list price for the comparator. |
| **Reporting of results in final SMC advice** | No ICERs would be presented. Statement added to explain this is due to commercial in confidence concerns. |

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| **Scenario 2: new medicine without a PAS, single comparator with simple PAS** | |
| **Medicine being submitted for assessment** | No PAS proposed |
| **Comparator medicine** | With simple PAS |
| **Submission requirements: base case** | ICER presented using list price for new medicine and list price for comparator treatment. |
| **Submission requirements: sensitivity analysis** | 1. For the base case ICER, the list price for the comparator medicine should be varied through a discount range of 5%-95% at 5% increments. 2. The base case ICER above should be tested using conventional sensitivity analysis. In addition, for the key variables identified, the results should also be presented to show the impact of assuming the 5% to 95% discounts for the comparator. |
| **Submission requirements:**  **budget impact templates** | Template using list price for new medicine and list price for the comparator. |
| **Reporting of results in final SMC advice** | ICERs using list price would be presented. |

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| **Scenario 3: new medicine with a PAS, multiple comparators with simple PAS** | |
| **Medicine being submitted for assessment** | Simple PAS proposed |
| **Comparator medicine** | More than one of the key comparators has a simple PAS |
| **Submission requirements: base case** | ICER presented using PAS price for new medicine and list price for comparator treatments, using pairwise comparisons. |
| **Submission requirements: sensitivity analysis** | 1. For the base case ICER, the list price for each of the comparator medicines should be varied through a discount range of 5%-95% at 5% increments. 2. The base case ICERs above against each comparator should be tested using conventional sensitivity analysis. In addition, for the key variables identified, the results should also be presented to show the impact of assuming the 5% to 95% discounts for each of the comparators. |
| **Submission requirements:**  **budget impact templates** | Template with and without new medicine’s PAS. Both templates use only the list price for the comparators |
| **Reporting of results in final SMC advice** | No ICERs would be presented. Statement added to explain this is due to commercial in confidence concerns. |

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| **Scenario 4: new medicine with a complex PAS, single comparator with simple PAS** | |
| **Medicine being submitted for assessment** | Complex PAS proposed |
| **Comparator medicine** | With simple PAS |
| **Submission requirements: base case** | ICER presented using list price for new medicine and list price for comparator treatment. |
| **Submission requirements: sensitivity analysis** | 1. ICER to be presented incorporating the complex PAS for the new medicine and the list price for the comparator medicine. 2. For the base case ICER using the list price for the new medicine, the list price for the comparator medicine should be varied through a discount range of 5%-95% at 5% increments. 3. For the base case ICER incorporating the complex PAS for the new medicine, the list price for the comparator medicine should be varied through a discount range of 5%- 95% at 5% increments. 4. The base case ICER above should be tested using conventional sensitivity analysis. In addition, for the key variables identified, the results should also be presented to show the impact of assuming the 5% to 95% discounts for the comparator. This analysis should also be provided assuming the complex PAS applies for the new medicine. |
| **Submission requirements:**  **budget impact templates** | Template with and without new medicine’s PAS. Both templates use only the list price for the comparator. |
| **Reporting of results in final SMC advice** | ICERs using list price would be presented. |

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| **Scenario 5: new medicine with a simple PAS and this medicine is used in combination with another medicine marketed by a different company with a simple PAS, comparator has no PAS.** | |
| **Medicine being submitted for assessment** | Simple PAS proposed, but is used in combination with a medicine from a different company that has a PAS |
| **Comparator medicine** | No PAS |
| **Submission requirements: base case** | ICER presented using PAS for the new medicine and list price for the medicine it is used in combination with. |
| **Submission requirements: sensitivity analysis** | 1. For the base case ICER, the list price for the other medicine used in the combination should be varied through a discount range of 5%-95% at 5% increments. 2. The base case ICER above should be tested using conventional sensitivity analysis. In addition, for the key variables identified, the results should also be presented to show the impact of assuming the 5% to 95% discounts for the other medicine used in the combination. |
| **Submission requirements:**  **budget impact templates** | Template with and without new medicine’s PAS. Both templates use only the list price for other medicine used in the combination. |
| **Reporting of results in final SMC advice** | No ICERs would be presented. Statement added to explain this is due to commercial in confidence concerns. |