

<b>Enclosure No:</b>	2a/AWMSG/0221
<b>Agenda item No:</b>	6 -Statements of advice issued between January 2015 and September 2020
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### **Action for AWMSG**

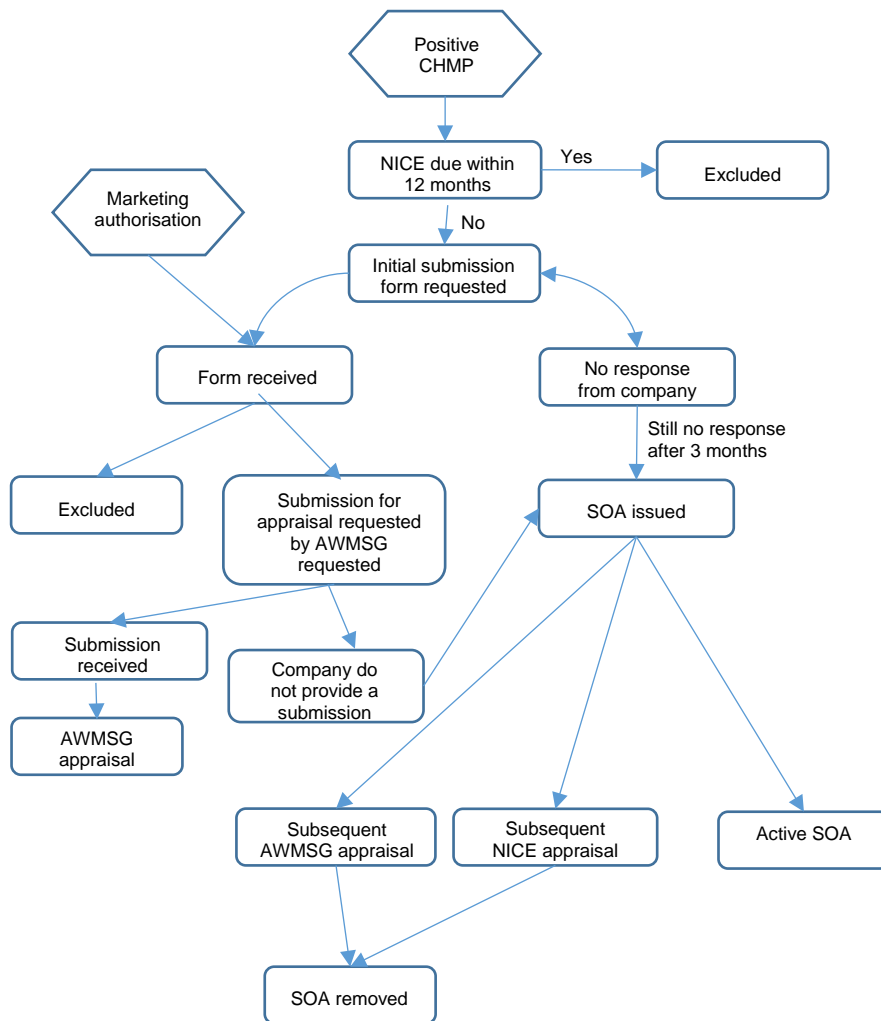
Members are invited to comment on this paper which reviews the statements of advice published by AWMSG over the last five years.

### **Purpose:**

To report on the trend and number of Statements of Advice (SOA) issued by the All Wales Medicines Strategy Group (AWMSG) over the last five years, detailing (where available) reasons for non-engagement. To also provide a comparison with the Scottish Medicines Consortium (SMC) as a similar organisation to AWMSG serving a comparable population size to Wales.

### **Background:**

This report has been produced to provide context to the SOAs issued by AWMSG and how they compare to a similar HTA body in Scotland. For new medicines which meet the criteria for appraisal by AWMSG where a submission is not forthcoming within three months of the marketing authorisation date, AWMSG issue a SOA which is posted on the AWMSG website. The SOA confirms that the medicine cannot be endorsed for use within NHS Wales and is ratified by Welsh Government. The SOA is interim to guidance subsequently published by AWMSG or the National Institute for Health and Care Excellence (NICE). A flow diagram which illustrates the new medicines decisions process is shown in Figure 1.



**Figure 1. Example of new medicines decision process**

The All Wales Therapeutics and Toxicology Centre (AWTTC) horizon scanning team identify new medicines likely to be available in the UK within a subsequent 12 to 18 month period. The UK PharmaScan database is the main source of this information; if information is missing or out of date the horizon scanning team will contact the company directly. The next point of contact with the company occurs on granting of a positive Committee for Human Medicinal Products (CHMP) when the company is sent an initial submission form. In the absence of an initial response AWTTC will make repeated efforts to make contact by email or telephone. In cases where there may be an unmet clinical need for the medicine in Wales advice from clinical experts is sought in addition to company engagement. If no response is received from the company an SOA is due for issue at three months post licence date. At this point further attempts are often made to contact the company and gather intelligence. Only where the best efforts of AWTTC have failed to encourage a submission from the company is the SOA issued.

Several updates to the health technology assessment (HTA) process have been completed in recent years which will have had a positive impact on company engagement. These include new policies for the appraisal of orphan and ultra-orphan medicines and reviews of the exclusion criteria. Earlier in 2020 changes were made to the wording on standard submission requests to further encourage dialogue

between the marketing authorisation (MA) holder and AWTTTC. Where reasons for non-engagement were provided by the MA holder they are now recorded on the AWTTTC database. The system has been updated retrospectively (where information exists) for all SOAs issued and still in place since January 2015.

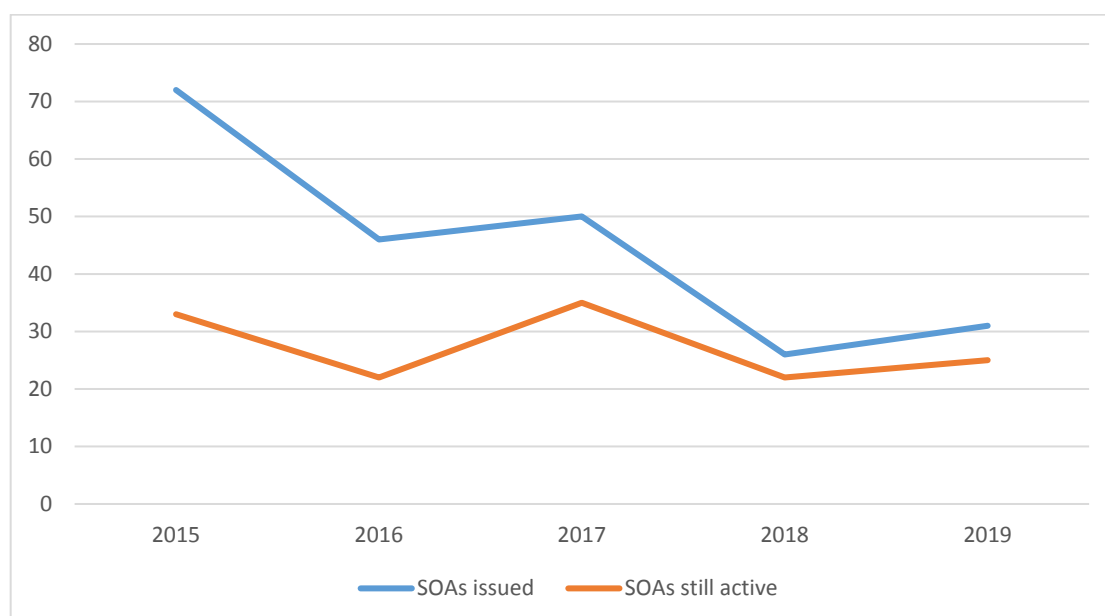
This report has been compiled to provide information on the numbers of SOAs issued by AWMSG over the past five years, how many are subsequently superseded or no longer apply, and how this compares with the Scottish HTA body (SMC).

**Methods:**

The AWTTTC HTA database was interrogated to gain as much information as possible in order to provide meaningful insight into SOAs issued by AWMSG. Data were compiled on the reasons for non-engagement and the status in relation to corresponding NICE appraisals. AWMSG SOAs were compared with 'Non-recommendations due to non-submission' issued by SMC. Data cut off was the end of September 2020.

**Results:**

Figure 2 shows the number of SOAs published annually and the number that still apply as of September 2020. The total number of active SOA stands at 158. The number issued on an annual basis has steadily decreased over the five year period from 72 in 2015 to 31 in 2019 (whole years only). As SOAs are superseded by HTA advice, either through appraisal by AWMSG or NICE, the number that still apply is more consistent year on year with a range from 22 to 33.



**Figure 2. All SOAs issued and SOAs still active by year**

Since January 2015 88 (36%) SOAs have subsequently been excluded or superseded by AWMSG or NICE appraisal advice. Table 1 provides a breakdown by year of the numbers of SOAs subsequently superseded or excluded. There are currently 23 appraisals either proposed or in progress with NICE which are expected to supersede active SOAs on publication of advice.

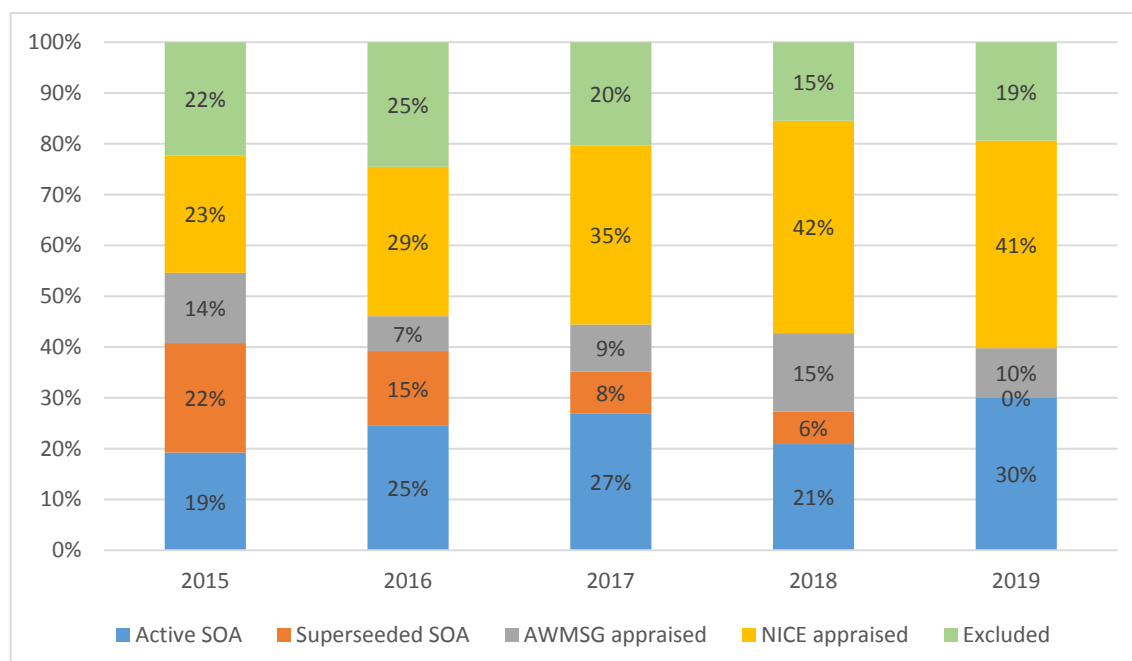
**Table 1. All SOAs issued by year since January 2015**

Calendar year	All SOAs issued	SOAs superseded by AWMSG advice or in progress	SOAs superseded by NICE advice	SOAs subsequently excluded for other reasons	SOAs which still apply
2015	72	26 (36%)	12 (17%)	1 (1%)	33 (46%)
2016	46	10 (22%)	8 (17%)	6 (13%)	23 (48%)
2017	50	7 (14%)	3 (6%)	5 (10%)	35 (70%)
2018	26	2 (8%)	1 (4%)	1 (4%)	22 (85%)
2019	31	6 (19%)	0	0	25 (81%)
2020*	21	0	0	0	21 (100%)
<b>Total</b>	<b>246</b>	<b>51 (21%)</b>	<b>24 (10%)</b>	<b>13 (5%)</b>	<b>158 (64%)</b>

\*to end September 2020

The number of new medicines considered by the new medicines decisions process was 137 in 2015 and 104 in 2019 (each new medicine has an entry on the HTA database). The reduction in the number of new medicines being considered by AWTTTC may be on part a reflection of improved horizon scanning processes and advance intelligence, as well as a variation in the number of products licensed. A number of medicines are routinely excluded without requiring database entries or an initial submission form due to information gathered by the horizon scanning team. It is also likely that continued revision of the AWMSG exclusion criteria has contributed to the gradual increase in the number of medicines not considered appropriate for HTA.

Figure 3 shows the outcomes of the new medicine decision process annually. The percentage of medicines issued with a SOA in a calendar year has decreased from 41% to 30%. This is likely due to an improvement in company engagement as a result of changes made to the horizon scanning and HTA processes.



**Figure 3. Outcomes for all medicines considered by the new medicines decision process by year**

For those SOAs which have been superseded (either by NICE or AWMSG) the average time to appraisal from issue of SOA was 16 months. There would therefore be earlier access to these medicines for patients in NHS Wales if companies had made a submission to AWMSG on first request. These data imply that the 2018 figures are unlikely to change very much; NICE appraisals are proposed or in progress for 13 of the SOAs issued in 2019 and 2020. However, delays due to the COVID-19 pandemic may lead to an increase in the average time for these SOAs to be superseded by NICE advice.

### Factors expected to impact SOA numbers

#### a. Suspended or terminated NICE appraisals

NICE appraisals which are not completed (usually due to non-submission from the company) are allocated suspended or terminated status and NICE are unable to make a recommendation. The current process is for AWMSG to routinely request a submission because, for example NICE advice is not always expected within 12 months of MA. Past experience suggests that companies do not provide a submission to AWMSG following suspended or terminated NICE advice. The subsequent lack of submission has resulted in an active SOA, where NICE have already effectively not endorsed the medicine. Table 2 shows that there are currently 26 SOAs which still apply where an appraisal has been suspended (8) or terminated (18) with NICE.

**Table 2. Number of SOAs which have corresponding NICE suspended or terminated status**

Calendar year	SOAs which still apply	NICE suspended	NICE terminated
2015	33	1	3
2016	22	1	4
2017	35	1	7
2018	22	1	1
2019	25	2	3
2020*	21	2	0
<b>Total</b>	<b>158</b>	<b>8</b>	<b>18</b>
<b>*to end September 2020</b>			

#### b. Paediatric licence extensions

There are 18 medicines which currently have SOAs which are licence extensions for use in paediatric patients. For seven of these medicines there is positive HTA advice (either AWMSG or NICE) for use in the adult population. For eight of the medicines there is no HTA advice for the same indication in adults and three of these medicines currently have an SOA or negative advice for the adult population. A new streamlined appraisal process for paediatric licence extensions was approved by AWMSG in December 2020. The new process is expected to improve engagement and ultimately reduce the number of SOAs issued for these medicines.

### c. Antimicrobials

A further 13 medicines with active SOAs are for antimicrobial medicines. NICE are currently collaborating with NHS England to develop a new programme for evaluating antimicrobial medicines. This is currently in the pilot stage. Further discussion is recommended to establish how AWMSG will manage antimicrobial medicines recommended in NHS England through the new process.

### d. Medicines not launched

There are 21 active SOAs where the company stated there were no plans to launch or market the medicine in the UK.

### e. Blood products

There are eight blood products that have current SOAs with AWMSG, all but one were issued in 2017 or earlier. The criteria which excludes blood products was revised in 2017 and subsequently newly licensed blood products have not met the criteria for appraisal by AWMSG.

By taking account of the factors outlined above and setting aside any SOAs which fall into these criteria, just 69 of the 158 active SOAs would remain.

### Reasons for non-engagement

The first formal opportunity for company engagement is the completion of the initial submission form (Form A). The number of SOAs issued in the absence of a Form A are shown in Table 3, including the percentage of all SOAs issued in that year. The figures show that for the majority of these medicines if a Form A is not submitted and an SOA is issued, it is unlikely to be superseded by HTA advice, reflecting an absence of engagement with AWMSG or NICE from the MA holder.

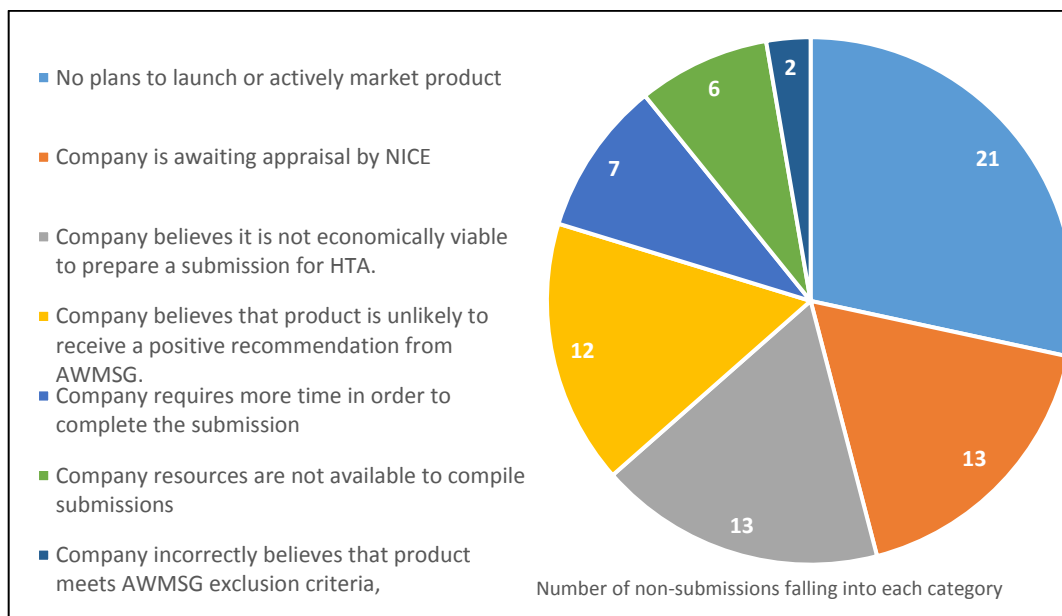
**Table 3. SOAs issued where no Form A received**

Calendar year	All SOAs issued (n = 246)	No Form A received (n = 119)	Still apply as of September 2020 (n = 104)
2015	72	26 (36%)	18 (69%)
2016	46	15 (33%)	13 (87%)
2017	50	28 (56%)	24 (86%)
2018	26	17 (65%)	16 (94%)
2019	31	16 (52%)	16 (100%)
2020*	21	17 (81%)	17 (100%)

\*to end September

Of the 158 active SOAs 55 submitted a Form A but subsequently failed to submit a full or limited submission, and 104 did not return a Form A. Setting aside those identified above (i.e. factors likely to have an impact on SOA numbers) over half of remaining active SOAs are those without a Form A (43 out of 69).

The reasons for non-engagement are now captured on the AWTTTC HTA database which has been updated retrospectively where possible for all SOAs issued since January 2015 and are still current (i.e. not superseded by HTA advice). Email communication with the company was examined to ascertain why the company had not submitted for HTA and the database record updated accordingly. Going forward the reasons for non-engagement are to be recorded routinely. The majority (60; 38%) of companies did not provide a reason as to why they did not intend to submit to AWMSG and in 25 (16%) cases there was no communication from the company. For current SOAs a summary of the reasons (where provided) is shown in Figure 4.



**Figure 4. Reasons for company non-engagement**

Where a reason for non-engagement has been provided, the majority were where the company had no plans to launch or actively market the medicine in the UK. For new medicines not already marketed for any other indications in the UK it may be that an alternative to the SOA process is more appropriate.

Where the company is awaiting appraisal by NICE, if the NICE appraisal is scheduled for publication more than 12 months post licence date then AWTTTC will request a submission. In 13 cases the company believed (wrongly) that an appraisal was not required even though NICE advice was expected outside of the 12 months. Of these: 5 are recorded as still in progress with NICE; 3 are not scheduled; 1 proposed; 1 suspended, 2 terminated and 1 on hold due to the Covid-19 pandemic.

In cases where the company do not think that appraisal is economically viable, this may be for various reasons, most commonly where the number of eligible patients in Wales is expected to be low.

For situations where the company do not expect to receive a positive recommendation from AWMSG, this may be due to insufficient clinical or cost effectiveness evidence. In some cases it may be that the company believe that the cost of the medicine is such that the most plausible Incremental Cost-Effectiveness ratio (ICER) per Quality Adjusted Life Year (QALY) would be unacceptable to AWMSG.

#### **AWMSG compared with Scottish Medicines Consortium (SMC)**

We have compared the SOAs issued by AWMSG with 'Non-recommendations due to non-submission' issued by SMC shown in Table 4.

**Table 4. AWMSG SOAs compared with SMC Non-submissions**

Calendar year	SOAs which still apply	Of SOA that still apply number with SMC non submission	Of SOA that still apply number in progress or appraised by SMC	Of SOA that still apply number with no SMC status	SMC non submission that no longer have SOA with AWMSG	AWMSG appraisals not appraised by SMC
2015	33	12 (36%)	7 (21%)	14 (42%)	6	4
2016	22	15 (68%)	1 (5%)	6 (27%)	1	4
2017	35	24 (69%)	4 (11%)	7 (20%)	0	4
2018	22	8(36%)	2 (9%)	12 (55%)	0	3
2019	25	8 (32%)	2 (8%)	15 (60%)	2	2
2020*	21	2 (10%)	0	19 (90%)	0	5
<b>Total</b>	<b>158</b>	<b>69 (44%)</b>	<b>16 (10%)</b>	<b>73 (46%)</b>	<b>9</b>	<b>22</b>
*to end September						

Overall AWMSG issued a significantly higher number of SOAs compared with SMC and of the 158 SOAs which still apply, only 69 have a corresponding SMC non-submission status, 14 have been appraised by SMC of which 2 were not-recommended and a further 2 are now in progress.

It is unclear as to what status the remaining 73 medicines have within the SMC process. It is likely that the majority have been excluded from their appraisal process although this cannot be determined from the SMC website. However, this is supported by further interrogating the data. For these 73 medicines, when taking account of those factors already identified as influencing SOA numbers, then there are only 30 outstanding. Of these, 23 did not submit initial information to AWMSG i.e. no Form A. SMC does not request initial information from marketing authorisation holders in this way and it is unclear whether this has any impact on the number of medicines issued an SMC non-submission status. Other differences exist between the HTA processes of SMC and AWMSG which will also influence these results.

Furthermore, for the 69 medicines which also have a non-submission to SMC and then setting aside those already identified with factors likely to influence the number of SOAs, only 24 remain. Similarly, of the 16 medicines either appraised or in progress with SMC only 4 would likely warrant further investigation.

#### **Summary:**

This report provides a preliminary overview of the SOAs issued by AWMSG over a five year period. It demonstrates that SOAs are not necessarily finite in all cases and over time are often superseded by HTA advice. The report also shows an annual decrease in the number of SOAs issued. This decrease cannot be attributed a single cause but is likely the accrued effect of a number of factors. New policies are expected to have improved industry engagement for orphan and ultra-orphan medicines; continued review of the exclusion criteria and improved horizon scanning intelligence will have also led to a reduction in the number of SOAs issued annually.

Of the 158 active SOAs, this report has identified 69 which could require further investigation (43 of these did not submit a Form A). The other 89 account for medicines where the SOAs are either to be reviewed shortly under new and proposed policies or are identified as having other associated factors that would now not likely result in meeting the criteria for appraisal by AWMSG.



**Conclusion:**

The detail in this report provides insight into the reasons for which companies are not engaging with the AWMSG process and also how the numbers compare with SMC. We have been able to provide context to 89 of the 158 active SOAs and there is likely no value in revisiting these. It has allowed us to identify areas which warrant further investigation with a view to further improving the new medicines decision process and industry engagement. Several action points have been identified:

- Investigate ways to streamline the SOA process with consideration of circumstances where a NICE appraisal has been suspended or terminated and where medicines are not to be launched or marketed in the UK.
- Investigate discrepancies between AWMSG SOAs and SMC advice for medicines which could still potentially meet the criteria to appraise. In particular medicines for which SMC have received a submission. Also consider further the value in reviewing medicines with an AWMSG SOA and a non-submission statement with SMC, or where SMC status is unknown.
- Identify medicines with active SOAs which are available in NHS England through commissioning policies and consider investigating further.
- Review active paediatric SOAs once the revised AWMSG paediatric process is launched.

A second review of SOAs will be conducted after the next financial year, using data up to the end of March 2022, with this report serving as a baseline. It is anticipated that re-visiting this analysis and comparing with data one year on will show what impact any actions arising from this report will have on SOAs issued.