Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2419

solriamfetol 75mg and 150mg film-coated tablets (Sunosi®)

Jazz Pharmaceuticals

4 February 2022

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission

solriamfetol (Sunosi®) is not recommended for use within NHSScotland.

Indication under review: to improve wakefulness and reduce excessive daytime sleepiness (EDS) in adult patients with obstructive sleep apnoea (OSA) whose EDS has not been satisfactorily treated by primary OSA therapy, such as continuous positive airway pressure (CPAP).

Solriamfetol, compared with placebo, reduced EDS in adults with OSA who were currently using or had previously tried a primary OSA therapy.

The submitting company did not present a sufficiently robust clinical and economic analysis to gain acceptance by SMC.

Chairman
Scottish Medicines Consortium

Indication

Solriamfetol is indicated to improve wakefulness and reduce excessive daytime sleepiness (EDS) in adult patients with obstructive sleep apnoea (OSA) whose EDS has not been satisfactorily treated by primary OSA therapy, such as continuous positive airway pressure (CPAP).[1]

Dosing Information

The recommended starting dose is solriamfetol 37.5mg orally once daily with or without food, upon awakening. Depending on clinical response, the dose can be titrated to a higher level by doubling the dose at intervals of at least 3 days, with a recommended maximum daily dose of 150mg once daily. Taking solriamfetol less than 9 hours before bedtime should be avoided as it may affect night time sleep. The need for continued treatment and the appropriate dose should be periodically assessed during extended treatment in patients prescribed solriamfetol.

Blood pressure and heart rate should be assessed before initiating solriamfetol and should be monitored periodically during treatment, especially after increasing the dose. Pre-existing hypertension should be controlled before initiating solriamfetol and caution should be exercised in treating patients at higher risk of major adverse cardiovascular events, particularly patients with pre-existing hypertension, patients with known cardiovascular or cerebrovascular disease and elderly patients. If a patient has increases in blood pressure or heart rate that cannot be managed with dose reduction of solriamfetol or other appropriate medical intervention, discontinuation of solriamfetol should be considered. Caution should be exercised when using other medicinal products that increase blood pressure and heart rate.

Treatment should be initiated by a healthcare professional experienced in the treatment of OSA. Solriamfetol is not a therapy for the underlying airway obstruction in patients with OSA. Primary OSA therapy should be maintained in these patients.[1]

Product availability date

1 September 2020

Summary of evidence on comparative efficacy

Solriamfetol is a dopamine and norepinephrine reuptake inhibitor. Its mechanism of action to improve wakefulness in patients with EDS associated with OSA has not been fully characterised.[1]

The submitting company has requested that SMC considers solriamfetol when positioned for use in patients with EDS due to OSA who have an Epworth Sleepiness Scale (ESS) score >12.

A double-blind phase III study (TONES 3) recruited adults (18 to 75 years old) with OSA and EDS despite current or prior primary therapy for OSA, including CPAP, mandibular advancement device or surgical intervention. They had an ESS score ≥10, sleep latency less than 30 minutes (average of first four of a five-trial 40-minute Maintenance of Wakefulness Test [MWT]), usual nightly sleep ≥6

hours and body mass index (BMI) between 18 and <45kg/m^2. Randomisation was stratified by adherence to primary OSA therapy and patients were assigned in 2:1:1:2:2 ratio to 12 weeks oral once daily (within one hour of awakening) placebo, solriamfetol 37.5mg, 75mg, 150mg or 300mg, with the latter two groups receiving 75mg and 150mg, respectively, for days 1 to 3. The co-primary outcomes were change from baseline to week 12 in MWT and ESS score. These were compared with placebo in a hierarchy that included the key secondary outcome percentage of patients with improvement on Patient Global Impression of Change (PGI-C) commencing at the highest solriamfetol dose. Efficacy was assessed in the modified intention to treat (mITT) population, which comprised all randomised patients who received at least one dose of study drug and had baseline and at least one post-baseline efficacy evaluation of MWT and ESS.[2,3]

The co-primary outcomes, change from baseline to week 12 in MWT and ESS score, and the key secondary outcome, percentage of patients with improvement on PGI-C, were significantly improved with all doses of solriamfetol versus placebo, except for PGI-C with solriamfetol 37.5mg. Results are detailed in Table 1 below for the licensed doses.[2,3]

Table 1: Primary and secondary outcomes of TONES 3 study.[2]

		Solriamfetol		
	Placebo (N=114)	**37.5mg (N=56)**	**75mg (N=58)**	**150mg (N=116)**
MWT, LS mean change (minutes)	0.21	4.74	9.08	10.96
MWT, LS mean difference (minutes) (95% CI) p-value	-	4.5 (1.2, 7.9) 0.009	8.9 (5.6, 12.1) <0.001	10.7 (8.0, 13.4) <0.001
ESS, LS mean change	-3.3	-5.1	-5.0	-7.7
ESS LS mean difference (95% CI) p-value	-	-1.9 (-3.4, -0.3) 0.016	-1.7 (-3.2, -0.2) 0.023	-4.5 (-5.7, -3.2) <0.001
PGI-C improved, n (%)	56 (49%)	31 (55%)	42 (72%)	104 (90%)
PGI-C improved, difference, % (95% CI) p-value	-	6.2% (-9.7, 22.2) 0.445	23% (8.6, 38.0) 0.004	40% (29.8, 51.2) <0.001

CI = confidence interval; LS mean change = least square mean change from baseline to week 12; MWT = Maintenance of Wakefulness Test; ESS = Epworth Sleepiness Scale; PGI-C = Patient Global Impression of Change.

There were LS mean differences in change from baseline to week 12 that favoured solriamfetol 150mg versus placebo in Functional Outcomes of Sleep Questionnaire 10-item (FOSQ-10); Work Productivity and Activity Impairment Questionnaire: Specific Health Problem (WPAI:SHP) impairment at work, and impairment of activity outside work; Short-Form 36 (SF-36) physical component summary, mental component summary. However, in general changes with lower doses of solriamfetol were smaller and not significantly different from placebo across all three questionnaires. Solriamfetol had limited effects on EuroQol 5-dimension 5-level (Euroqol EQ-5D-5L) with no differences from placebo and no effect on absenteeism on WPAI:SHP.[4,5]

Data to support the economic analyses were derived from a subgroup of patients in TONES 3 who had an ESS score >12. Clinical evidence in this subgroup was not provided.

A double-blind phase III withdrawal study (TONES 4) recruited patients to similar criteria as TONES 3. All patients had a 2-week titration phase commencing with once daily solriamfetol 75mg, then

gradually increasing to 300mg or to the maximum tolerated dose, which was continued for a further two weeks. Then 124 patients who had improvement on PGI-C, MWT and ESS were equally randomised, with stratification for adherence to OSA therapy, to continue solriamfetol or switch to placebo for 2 weeks. The co-primary outcomes were change from week 4 to week 6 in MWT and ESS score. These were assessed in a mITT population. There was fixed hierarchical testing of the key secondary outcome, worsening on PGI-C, after both primary outcomes. During the randomised withdrawal there was significantly less deterioration with solriamfetol compared with placebo in all of these outcomes as detailed in Table 2.[6]

Patients who completed TONES 3 or 4 could receive open-label solriamfetol in an extension study (TONES 5), which also recruited patients with OSA or narcolepsy who completed other phase II or III studies. Those who enrolled immediately after completing the phase III (TONES 2 or 3) studies received up to 40 weeks' treatment (Group A) and those who had previously completed the phase III study (TONES 4) or the phase II studies (TONES 1, ADX-N05, 15-004 or 15-005) received up to 52 weeks treatment (Group B). After 6 months a subset of patients were equally randomised (with stratification for condition) to double-blind continuation of solriamfetol or placebo for 2 weeks then they continued solriamfetol, with a blinded titration for those randomised to placebo. In the randomised withdrawal phase, the primary outcome was change in ESS over that 2-week period in the mITT population. After the primary analysis, there was fixed hierarchical testing for the secondary outcomes, worsening on PGI-C then Clinician Global Impression of Change (CGI-C). Descriptive statistics were used for analyses of efficacy during open-label treatment.[7,8]

In the subgroup of patients with OSA after the initial two-week titration LS mean ESS decreased from baseline of 15.2 to 6.2 in Group A and from 15.0 to 6.7 in Group B; the proportion reporting improvement in PGI-C was 95% and 96% in the respective groups. These benefits were generally maintained in patients who continued treatment over 40 and 52 weeks, respectively.[7] During the randomised withdrawal, there was significantly less deterioration in ESS, PGI-C and CGI-C with solriamfetol in the total study population, as detailed in Table 2.[7,8]

Table 2: Results from randomised withdrawal: TONES 4 and TONES 5.[6-8]

	TONES 4, mITT		TONES 5, mITT	
	Solriamfetol	**Placebo**	**Solriamfetol**	**Placebo**
ESS, change	-0.1*	4.5	1.6*	5.3
MWT, change	-1.0*	-12.1	-	-
PGI-C worse, %	20%*	50%	28%*	64%
CGI-C worse, %	22%	59%	29%*	64%

ESS = Epworth Sleepiness Scale; MWT = Maintenance of Wakefulness Test; PGI-C = Patient Global Impression of Change; CGI-C = Clinician Global Impression of Change. * Differences significant versus placebo, p<0.001.

*Other data were also assessed but remain confidential.**

Summary of evidence on comparative safety

The European Medicines Agency (EMA) review noted that the overall safety data for solriamfetol was mainly characterised by psychiatric disorders (symptom complex of anxiety, feeling jittery and irritability), nervous system disorders (headache, dry mouth and dizziness), gastrointestinal disorders (nausea, decreased appetite and diarrhoea) and effects on vital signs (blood pressure and heart rate increase). In most cases a clear dose-response or tendency towards higher incidence with increasing doses was observed.[2]

In the TONES 3 study within the placebo, solriamfetol 37.5mg, 75mg and 150mg groups adverse events were reported by 48% (57/119), 64% (37/58), 48% (30/62) and 71% (83/117) of patients, respectively. These were serious in 1.7%, 3.4%, 0 and 0.9% of patients and led to study drug discontinuation in 3.4%, 5.2%, 3.2% and 4.3% of patients, respectively. In the respective groups common adverse events included headache (8.4%, 6.9%, 8.1% and 8.5%), nausea (5.9%, 5.2%, 4.8%, and 8.5%), decreased appetite (0.8%, 1.7%, 4.8% and 7.7%), diarrhoea (0.8%, 1.7%, 4.8%, and 4.3%), dry mouth (1.7%, 1.7%, 1.6% and 4.3%), anxiety (0, 1.7%, 3.2% and 5.1%), insomnia (1.7%, 1.7%, 0 and 2.6%), feeling jittery (0, 5.2%, 4.8% and 0.9%) and irritability (0, 5.2%, 0 and 3.4%).[3]

Adverse events of special interest included cardiovascular events.[2] Solriamfetol increases blood pressure and heart rate in a dose-dependent fashion. Epidemiological data show that chronic elevations in blood pressure increase the risk of major adverse cardiovascular event (MACE), including stroke, heart attack and cardiovascular death. Many patients with OSA have multiple risk factors for MACE, including hypertension, diabetes, hyperlipidaemia and high BMI.[1] Patients with significant cardiovascular disease were excluded from the solriamfetol studies. Therefore, solriamfetol is contra-indicated in patients with unstable cardiovascular disease, serious heart arrhythmias and other serious heart problems.[1,2]

The solriamfetol studies excluded patients with a history of psychosis or bipolar disorders and the SPC notes that caution should be exercised when treating these patients due to psychiatric adverse reactions that could exacerbate symptoms of pre-existing psychiatric disorders.[1]

Summary of clinical effectiveness issues

In OSA sleep is repeatedly disturbed secondary to partial or complete obstruction of the upper airway, leading to persistent EDS, which can occur at inappropriate times, for instance while actively conversing, eating, working, and driving. Standard treatment is CPAP applied through a nasal, oral, or oronasal interface during sleep. However, pathological sleepiness often continues despite treatment of the airway obstruction with CPAP.[2] The August 2021 National Institute for Health and Care Excellence (NICE) clinical guideline (NG202) recommended CPAP as a treatment option for adults with moderate or severe symptomatic obstructive sleep apnoea/ hypopnoea syndrome (OSAHS) and in patients with mild OSAHS who have symptoms that affect their quality of life and usual daytime activities. For patients unable to tolerate or who decline CPAP, alternatives include a customised or semi-customised mandibular advancement splint for adults

with optimal dental and periodontal health or surgery. Consideration can be given to tonsillectomy for people with OSAHS who have large obstructive tonsils and BMI less than 35kg/m^2. Oropharyngeal surgery can be considered in people with severe OSAHS who have been unable to tolerate CPAP and a customised mandibular advancement splint despite medically supervised attempts.[9]

Solriamfetol is the first medicine licensed in the UK for treating EDS in patients with OSA.[2] Clinical experts consulted by SMC considers that there is unmet need in this therapeutic area due to the lack of treatment options.

In the TONES 3 study there were dose-dependent improvements with licensed solriamfetol doses (37.5mg to 150mg) over placebo of about 5 to 10 minutes in MWT and about 2 to 4.5 points in ESS. Also, about 6% to 40% more patients reported improvement on PGI-C with solriamfetol than with placebo. Benefits appear to be maintained up to one year in the TONES 5 study, which included a placebo-controlled randomised withdrawal after 6 months.[2,3,7,8] Data to support the economic analyses were from subgroup analyses of patients with ESS>12. However, clinical evidence in this subgroup was not provided.

Quality of life benefits were only observed with the highest solriamfetol dose (150mg). The clinical significance of these is unclear with average improvements over placebo in functioning and activity assessed on the FOSQ-10 of about 1 point (on a 30-point scale), WPAI:SHP impairment at work and impairment of activity outside work of around 10% and improvements of around 2 points (on a 100-point scale) for SF-36 physical component summary and mental component summary. For all solriamfetol doses there were no benefits over placebo in overall quality of life measured using EQ-5D-5L or in absenteeism (on WPAI:SHP).[2,4,5]

In the TONES 3 study the placebo response rates were substantial for subjective outcomes, with an average improvement in ESS of 3.3 and 49% of patients reporting improvement on PGI-C. In the placebo group patients achieving a normal ESS score (≤10) increased from 4.4% at baseline to 38% at week 12. Changes in the objective measure of wakefulness, MWT, were less pronounced with an average change at 12 weeks of 0.21 minutes and an increase in the proportion of patients achieving normal ≥20 minutes MWT from 18% at baseline to 23% at week 12.[2,3]

The pharmacology of solriamfetol, which is a dopamine and norepinephrine reuptake inhibitor, is typical of some anti-depressant medicines. Mood enhancing effects may have confounded the magnitude of effect for subjective outcomes, such as PGI-C. In the assessment of EDS, factors such as depression were not taken into account. However, as the proportions of patients with a history of depression was comparable across the treatment groups, bias may be unlikely.[2]

In TONES 3 at baseline the average ESS score was 14.8 to 15.6 and MWT was 12 to 13 minutes; most patients (90%) considered their condition at least moderately severe on Clinical Global Impression of Severity (CGI-S). However, within the placebo, solriamfetol 37.5mg, 75mg, 150mg and 300mg groups 4.4%, 5.4%, 5.2% and 7.8% of patients had normal ESS ≤10 and 18%, 15%, 16% and 14% had normal ≥20 minutes MWT at baseline.[2]

In practice, solriamfetol would be dosed in accordance with the SPC, which recommends a starting dose of 37.5mg once daily that can be increased to a maximum of 150mg depending on clinical response.[1] Dosing in all the clinical studies was different. In TONES 3 patients were assigned to

fixed once daily doses (37.5mg, 75mg, 150mg or 300mg [unlicensed]) and it is possible that some patients may not have received the dose that they would require in practice. In TONES 4 and 5 patients received the maximum dose (up to 300mg) that they could tolerate in terms of adverse events and it is possible that some had higher doses than they would require in practice. A large proportion of patients received the unlicensed solriamfetol 300mg dose: 54% in TONES 4 and 58% in TONES 5.[2,3,6,7]

Subgroup analyses in TONES 3 indicated that there were no meaningful differences in response between the subgroups who were adherent and non-adherent to primary OSA therapy.[3,5]

The introduction of solriamfetol would provide the first medicine for treatment of EDS associated with OSA and it could be used in patients who had failed to adequately manage EDS with a primary OSA therapy, such as CPAP. Solriamfetol is a symptomatic treatment for EDS and has no effect on the OSA. Also, in the TONES 3 study it did not alter adherence to primary OSA therapy.[2,3]

*Other data were also assessed but remain confidential.**

Summary of comparative health economic evidence

The company submitted a cost-utility analysis for the comparison of solriamfetol (37.5 mg/75 mg/150 mg in a 40/40/20 split) in addition to standard of care (SoC) with SoC alone for the treatment of adult patients with OSA and ESS score greater than 12. This is a more severe patient population than the one presented in the clinical case.

A two-stage cohort-based model structure was used, comprising an initial 12-week decision tree followed by a Markov model with three health states (responders, non-responders and dead). In the decision-tree, dose-dependent treatment effects, defined as a reduction in ESS from baseline ≥3, were applied from week 1 in the solriamfetol arm and dose-specific response to treatment was assessed at 12 weeks as observed in the relevant sub-population in the TONES 3 study[3-5]. Responders maintained treatment effects and non-responders (including all patients in the SoC arm) assumed the baseline ESS score upon entering the Markov model. Transition to the non-responders state was via discontinuation as a result of lack of efficacy or treatment-emergent adverse events at dose-specific annual rates as observed in TONES 5.[6-8] General population all-cause mortality was assumed equal in all arms of the model. A lifetime time horizon and yearly cycle length was applied.

Clinical efficacy data from the TONES 3[3-5] study were modified, through the use of a centring method (Hawthorne effect) [14] to remove the placebo effect from the model. This was performed by subtracting the mean change in ESS from baseline to week 12 in the placebo arm from each individual ESS record in the IPD of the solriamfetol arms at week 12.

Utilities were obtained using a mapping algorithm, derived from a de novo analysis of National Health and Wellness Survey (NHWS)[16] data of 2,348 respondents across the EU5 (UK, France, Germany, Italy, and Spain) who self-reported experiencing OSA and/or narcolepsy in the past 12 months, self-reported a diagnosis of OSA and/or narcolepsy, and completed the ESS. The final NHWS mapping algorithm for estimating EQ-5D-3L utilities using a UK value set contained several

covariates, and as a result of the inclusion of age, allowed for utility values to be re-estimated using age adjustment in each cycle of the Markov model. In the Markov model, responders maintained their age-adjusted quality of life, while non-responders assumed the quality of life in the SoC arm.

Costs included in the model were medicine acquisition costs, hospital-based medical consultant contacts in the first year of treatment with solriamfetol, and a GP contact in the event of solriamfetol discontinuation. No costs were included in the SoC arm as solriamfetol would be an addition to SoC. A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a discount was offered on the list price of solriamfetol.

Table 3: Base-case results – weighted ICER at list price

Technologies	Total costs (£)	Total QALYs	Total LYG	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
Standard of care (SoC)	£0	11.524	30.213			
Solriamfetol (40/40/20- 37.5, 75, 150 mg)	£10,876	11.906	30.213	£10,876	0.382	£28,459

Abbreviations: ICER= incremental cost effectiveness ratio; LYG= life years gained; QALYs= quality adjusted life years.

Key scenario analyses are presented below. The most substantial ICER increases came from alternative placebo adjustment mechanisms, dose split assumptions and mapping of utility scores.

Table 4: Selected Scenario Analyses at list price

	Base Case (Dose Split set to 40/40/20 for 37.5mg/75mg/150mg)	Scenario	ICER (£/QALY)
0	Base case	N/A	£28,459
1	Placebo effect assumed to be Hawthorne effect[14]	Alternate placebo mechanisms explored, assuming a 100% regression to mean placebo effect	£60,449
2	Placebo effect assumed to be Hawthorne effect[14]	Unadjusted treatment effects and modelling of placebo	Not provided
3	Proportion of patients on solriamfetol 150 mg dosage set to 20%	Disaggregated result for using only the solriamfetol 150mg dosage	£39,520
4	NHWS mapping - ESS Score: 12-24 coefficient	NHWS mapping - ESS Score: 12-24 coefficient using upper bound value	£40,481
5	Response is a reduction in ESS ≥3	Response is a reduction in ESS ≥2	£29,188
6	Response is a reduction in ESS ≥3	Response is a reduction in ESS ≥2 and dose split set to 33/33/33	£32,137

7	Response is a reduction in ESS ≥3	Response is a reduction in ESS ≥4	£27,071
8	Response is a reduction in ESS ≥3	Response is a reduction in ESS ≥4 and dose split set to 33/33/33	£29,722

Abbreviations: ICER= incremental cost effectiveness ratio; LYG= life years gained; QALYs= quality adjusted life years; NHWS = National Health and Wellness Survey; ESS= Epworth Sleepiness Scale.

Although the ICERs observed in the scenarios were generally consistent with the base case results, the analysis is subject to a number of limitations:

- Method of centring to remove the placebo effect: The adjustment performed led to a three state Markov model with no opportunity of accounting for ESS improvement over time, and eliminated the placebo effect in the SoC arm. In a sensitivity analysis on alternate placebo mechanisms, the ICER increased substantially (scenario 1). However, it still retained the three state Markov model, and held the SoC arm at a constant level of ESS. It is expected that the modelling of the placebo effect would lead to an even larger increase in the ICER. A request to the company was made to provide a model that used unadjusted treatment effects that could account for the ESS improvements over time by incorporating an additional health state (scenario 2). The company declined, noting the requirement of further assumptions to be made (e.g. discontinuation rates for SoC patients, treatment effects for non-responders, etc) which were deemed inappropriate. Statistical expert opinion sought by SMC, viewed the centring method used by the company as difficult to follow and built on many assumptions.
- 12-week time point to measure response: Responder classification and treatment continuation were based on baseline to week 12 reduction in ESS score. As OSA is a chronic condition this may not be a long enough time point to conduct an assessment. However, as TONES 3 was only a 12-week study, later data were not available. As the response rates for each of the three solriamfetol dose groups were the basis of the response for the duration of the economic model, they were integral to the cost-effectiveness analysis. Sensitivity analysis varying this was not available.
- Dose of solriamfetol: It is unclear what dose of solriamfetol will be used in Scotland long term and whether most patients will have to transition to the highest dose at some point in their treatment duration. As expected, using the highest dose would result in an increase in the ICER (scenario 3).
- ESS score reduction as a response measure: The company noted that clinicians may take a more holistic approach to assessing improvements in EDS, rather than an ESS reduction alone. Although a point reduction in ESS≥3 is a likely proxy for a patient subjectively noticing an improvement in their EDS, there was some uncertainty in base-case results as studies show that the ESS reduction required for a person to experience a subjective change in EDS is in the range of 2-4 points. [11-13] However, this was tested in sensitivity analysis, showing minimal impact on the ICERs. (scenarios 5-8).
- NHWS mapping algorithm: Although the mapping algorithm was validated using recommendations from the National Institute for Health and Care Excellence (NICE) Decision Support Unit[15], some uncertainty in the ICER remained. This was shown by an increased ICER in the sensitivity analysis of the ESS Score: 12-24 coefficient (scenario 4).

Given the limitations, the economic case has not been demonstrated.

*Other data were also assessed but remain confidential.**

Summary of patient and carer involvement

The following information reflects the views of the specified Patient Groups.

- We received patient group submissions from the Sleep Apnoea Trust Association (SATA) and The Sleep Charity, which are both charitable incorporated organisations.
- The Sleep Charity has received less than 1% pharmaceutical company funding in the past two years, with none from the submitting company. SATA has not received any pharmaceutical company funding in the past two years.
- Obstructive Sleep Apnoea (OSA) causes the throat muscles to relax sufficiently to cause a total (apnoea) or partial (hypopnea) blockage of the airway. A patient can stop breathing a hundred or more times throughout the night. The effort to breathe results in a partial awakening sufficient to allow breathing to restart. The excessive sleepiness experienced by those with OSA can have an impact on all aspects of their lives including; relationships, employment, physical wellbeing and mental health. Those with untreated OSA are at increased risk of accidents due to fatigue, for example they may fall asleep whilst driving or operating machinery.
- The standard treatment for Obstructive Sleep Apnoea, with or without daytime sleepiness, is a Continuous Positive Airway Pressure (CPAP) machine. Though CPAP therapy imposes some inconvenience, many patients regard the benefits of CPAP as life changing.
- For patients whose excessive daytime sleepiness cannot be controlled by CPAP, they may benefit from solriamfetol. An effective medicine that improves wakefulness and reduces excessive daytime sleepiness would improve the patient's quality of life in a number of ways including: improved concentration, better productivity at work, less likelihood of falling asleep at the wheel and improved mental health and relationships. However, many sleep apnoea patients have co-morbidities so it is possible that some of those patients would not be able to take solriamfetol.

Additional information: guidelines and protocols

In August 2021, NICE published a clinical guideline (NG202) on OSAHS and obesity hypoventilation syndrome in over 16s. This recommends CPAP as a treatment option for adults with moderate or severe symptomatic OSAHS and in patients with mild OSAHS who have symptoms that affect their quality of life and usual daytime activities. For patients who are unable to tolerate or decline CPAP, alternatives include a customised or semi-customised mandibular advancement splint for adults with optimal dental and periodontal health or surgery. Consideration can be given to tonsillectomy for people with OSAHS who have large obstructive tonsils and BMI less than

35kg/m^2. Oropharyngeal surgery can be considered in people with severe OSAHS who have been unable to tolerate CPAP and a customised mandibular advancement splint despite medically supervised attempts.[9]

Additional information: comparators

Standard of care.

Additional information: list price of medicine under review

Medicine	Dose Regimen	Cost per year (£)
Solriamfetol	37.5mg to 150mg orally once daily	1,154 to 3,232

Costs from BNF online on 10 November 2021. Costs do not take patient access schemes into consideration.

Additional information: budget impact

The submitting company estimated there would be 1,583 patients eligible for treatment with solriamfetol in each year, from year 1 to year 5. The estimated uptake rate was 5% in year 1 and 17% in year 5. This resulted in 79 patients estimated to receive treatment in year 1 rising to 369 patients in year 5.

At list prices, the gross impact on the medicines budget impact was estimated to be £178k in year 1 rising to £605k in year 5. As the medicine was an add-on therapy, no other medicines were displaced. Hence, the net medicines budget impact was equivalent to the gross impact. This assumed a 40/40/20 dose split for 37.5mg/75mg/150mg respectively.

*Other data were also assessed but remain confidential.**

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This assessment is based on data submitted by the applicant company up to and including 10 January 2022.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal: http://www.scottishmedicines.org.uk/About_SMC/Policy*

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.