New Medicine Assessment

Oral Glycopyrronium
Indication Treatment of: hypersalivation in adults and children

Following the review of glycopyrronium bromide in patients with hypersalivation in Parkinson's disease (Appendix 1), the LSCMMG requested that glycopyrronium use in other indications be considered. Due to the paucity of clinical evidence a review summary rather than a full review has been conducted to supplement the initial review in Appendix 1.

Recommendation: Amber0

Oral glycopyrronium bromide is recommended in adults and children with neurological conditions and hypersalivation following assessment by a specialist experienced in the treatment of patients with neurological conditions.

The long-term safety of oral glycopyrronium has not been confirmed therefore treatment is recommended for short-term intermittent use with frequent reviews of efficacy and adverse effects.

- Suitable for prescribing in primary care following recommendation or initiation by a specialist.
- Little or no specific monitoring required.
- Patient may need a regular review, but this would not exceed that required for other medicines routinely prescribed in primary care.
- Brief prescribing document or information sheet may be required.

Primary care prescribers must be familiar with the drug to take on prescribing responsibility or must get the required information.

Summary of supporting evidence:

NICE evidence summaries:

Two NICE evidence summaries relating to glycopyrronium have been published. The first evidence summary "Hypersalivation: oral glycopyrronium bromide" [1] was published in 2013 and described the efficacy and safety of oral preparations of glycopyrronium when used to treat hypersalivation in adults, children and young people. This evidence summary concluded the following:

> "There is moderate evidence that oral glycopyrronium bromide (tablets and solution or suspension) reduces hypersalivation (sialorrhoea) or drooling in children and young people with a neurological condition, and adults with Parkinson's disease, compared with placebo. There is also limited evidence of its efficacy in adults with schizophrenia and clozapine-induced hypersalivation. The most commonly reported adverse effects of oral glycopyrronium bromide are antimuscarinic, for example dry mouth. There is no evidence of its long-term efficacy or safety in treating hypersalivation."

The second evidence summary "Severe sialorrhoea (drooling) in children and young people with chronic neurological: oral glycopyrronium bromide." [2] published in 2017 discusses 2 small randomised controlled trials (RCTs) that compared glycopyrronium bromide with placebo for the treatment of severe sialorrhoea in children and young people with chronic neurological conditions disorders. NICE states the following:

- In both RCTs, participants treated with glycopyrronium bromide had statistically significantly improved drooling after 8 weeks, (measured using the modified Teacher's Drooling Scale [mTDS]), compared with placebo.
- Adverse effects were common with glycopyrronium bromide, mostly due to its anticholinergic action.
- There is a lack of long-term safety data for oral glycopyrronium bromide, and the SPC for Sialanar[a] recommends that the total treatment duration should be kept as short as possible.
- It is not possible to determine the relative effectiveness of glycopyrronium bromide compared with other treatments for severe sialorrhoea because glycopyrronium has only been compared to placebo. Because Sialanar[b] is not bioequivalent to other formulations of glycopyrronium bromide, switching to Sialanar should only be conducted under supervision to ensure that efficacy and side effects are balanced. The effectiveness of glycopyrronium bromide should be balanced against the adverse effects associated with treatment.

Associated NICE guidelines

NICE guidelines NG62 – "Cerebral palsy in under 25s: assessment and management," recommend considering anticholinergic medication to reduce the severity and frequency of drooling in children and young people with cerebral palsy. The guideline recommends glycopyrronium bromide (oral or by enteral tube), transdermal hyoscine hydrobromide or trihexyphenidyl hydrochloride (for children with dyskinetic cerebral palsy, but only with input from specialist services). [3]

Scottish Medicines Consortium (SMC)

The SMC has completed an assessment of glycopyrronium (Sialanar). [3] Glycopyrronium has been accepted for use in Scotland within its licensed indication (symptomatic treatment of severe sialorrhoea in children and adolescents aged 3 years and older with chronic neurological disorders). Following an abbreviated submission, the SMC concluded that:

> "The availability of glycopyrronium (Sialanar®) provides a licensed alternative to an existing generic preparation used outwith the terms of its marketing authorisation, at a small additional cost."

SPC: Glycopyrronium bromide (Sialanar®) is indicated for the symptomatic treatment of severe sialorrhea in children and adolescents aged 3 years and older with chronic neurological disorders (Sialanar is indicated for the paediatric population only). It should be prescribed by physicians experienced in the treatment of paediatric patients with neurological disorders. [5]

UKMI Q&A document

UKMI have produced an information document for the use of glycopyrronium in hypersalivation. [6] The document summarised the following:

- Benefits of using glycopyrronium include its long duration of action and it is less likely to cause central or cardiac adverse effects.
- Although oral absorption is poor, most of the published evidence of efficacy is for administration by the oral route, particularly in children and young adults with neurodevelopmental disabilities, where it has been used with some success in relatively small studies.

[a] Sialanar is indicated for symptomatic treatment of severe sialorrhoea (chronic pathological drooling) in children and adolescents aged 3 years and older with chronic neurological disorders

[b] Glycopyrronium 320 micrograms /ml oral solution. Each ml contains 400 micrograms glycopyrronium bromide equivalent to 320 micrograms of glycopyrronium.

- Recommended doses vary, and should be titrated carefully according to the patient's response and tolerance. As with other antimuscarinics, the side effects may limit chronic use of glycopyrronium.
- No efficacy data exist to compare different formulations of glycopyrronium or to compare its efficacy to other antimuscarinics used for treatment of hypersalivation.
- Data are also lacking for long-term efficacy and safety.

The UKMI document includes two randomised controlled trials.

A prospective double-blind, placebo-controlled, crossover, randomised dose-ranging study of oral glycopyrronium in 39 children (age range 4-19 years) with neurodevelopmental conditions and excessive drooling has been carried out [7]. After a 1-week baseline medication-free observation period, patients received either drug or placebo treatment for 8 weeks followed by a 2-week washout and observation period before crossover. Medication was given three times a day, although 4 children received twice daily doses at parental request. The dose of glycopyrronium was increased weekly for 4 weeks to a maximum dose, which was then continued for an additional 4 weeks, unless adverse effects occurred or desired dryness was achieved. 27 (69%) children completed the study and they all demonstrated improvement in drooling. The mean highest tolerated dose was 2.5mg (range 1.2mg – 3mg) which was given three times daily to most participants. Of 36 patients taking glycopyrronium, 25 (69%) experienced side effects. Of the 12 children who did not complete the study, 8 withdrew because of adverse effects, 1 of these while receiving placebo.

A randomised placebo-controlled trial investigated the efficacy of glycopyrronium oral solution (1mg/5ml) in 36 patients aged 3-16 with cerebral palsy, mental retardation, or another neurologic condition associated with problem drooling [8]. Patients were randomised to receive matching placebo or glycopyrronium 20 microgram/kg three times a day titrated over 4 weeks to a maximum dose of 100 microgram/kg or 1.5 - 3mg per dose (based on weight) three times a day, whichever was less, and remained on that dose for a further 4 weeks. Doses were administered at least one hour before or two hours after meals. The mean daily dose of glycopyrronium was 150 microgram/kg. At week 8, 14 of 19 patients (73.7%) in the glycopyrronium group and 3 of 17 (17.6%) in the placebo group showed at least a 3-point improvement in the modified Teacher's Drooling Scale (mTDS) score (p=0.0011). The most common adverse reactions were dry mouth, vomiting, nasal congestion and constipation. One patient in each treatment group withdrew from the study due to adverse effects.

Drug Tariff

Prices:

- Sialanar® 400 mcg per mL oral solution 250mL - £320
- Glycopyrronium bromide 1 mg of per 5 mL oral solution (Colonis® generic) 150 mL- £91
- Glycopyrronium bromide 1 mg tablets 30 - £250.39
- Glycopyrronium bromide 2 mg tablets 30 - £281.18

Costs based on MIMS list prices October 2021.

Prescribing for last 12 months (Sep20-Aug21)

BNFPresentation	Prescriber Act Cost	Prescriber Items	Prescriber Quantity X Items	Total mg prescribed	Cost per 1 mg dose
Glycopyrronium bromide 5mg/5ml oral suspension	£1,646.70	89	11372	11372	£0.14
Glycopyrronium bromide 5mg/5ml oral solution	£2,666.65	97	9700	9700	£0.27
Glycopyrronium bromide 500micrograms/5ml oral suspension	£985.68	18	6120	612	£1.61
Glycopyrronium bromide 2.5mg/5ml oral solution	£1,750.58	15	1500	750	£2.33
Glycopyrronium bromide 200micrograms/5ml oral solution	£10.95	1	100	4	£2.74
Glycopyrronium bromide 1mg/5ml oral solution sugar free	£252,541.61	1454	447150	89430	£2.82
Glycopyrronium bromide 400micrograms/ml soln sugar free	£35,404.02	169	29710	11884	£2.98
Glycopyrronium bromide 1mg/5ml oral liquid	£2,270.73	10	3496	699.2	£3.25
Glycopyrronium bromide 500micrograms/5ml oral solution	£913.28	28	2800	280	£3.26
Sialanar 320micrograms/ml oral solution	£32,601.44	136	27360	8755.2	£3.72
Glycopyrronium bromide 200micrograms/5ml oral suspension	£414.03	18	2700	108	£3.83
Glycopyrronium bromide 2mg tablets	£63,963.08	93	7796	15592	£4.10
Glycopyrronium bromide 1mg tablets	£65,048.29	103	8903	8903	£7.31
Total	**£460,217.04**	**2231**			

Dose

For Sialanar:

The dosing schedule for glycopyrronium is based on the weight of the child, starting with approximately 12.8 micrograms/kg per dose (equivalent to 16 micrograms/kg per dose glycopyrronium bromide), three times per day and increasing by the doses shown in Table 1 below, every 7 days. Dose titration should be continued until efficacy is balanced with undesirable effects and amended up or down as appropriate, to a maximum individual dose of 64 micrograms/kg body weight glycopyrronium or 6 ml (1.9 mg glycopyrronium, equivalent to 2.4 mg glycopyrronium bromide) three times a day, whichever is less. Dose titrations should be conducted in discussion with the carer to assess both efficacy and undesirable effects until an acceptable maintenance dose is achieved. [9]

For Glycopyrronium bromide tablets:

The dosing schedule for Glycopyrronium bromide tablets is based on the weight of the child with the initial dosing of 0.02 mg/kg to be given orally three times daily and titrate in increments of 0.02 mg/kg every 5-7 days based on therapeutic response and adverse reactions. The maximum recommended dosage is 0.1 mg/kg three times daily not to exceed 1.5-3 mg per dose based upon weight. [10]

Appendix 1

Lancashire & South Cumbria Medicines Management Group

New Medicine Assessment

Glycopyrronium Bromide Oral Solution

For Hypersalivation/ Sialorrhoea in Adults with Parkinson's Disease

Recommendation: Amber0

Glycopyrronium bromide oral solution is recommended for hypersalivation/ sialorrhoea in adults with Parkinson's disease if non-pharmacological management (for example, speech and language therapy) is not available or has not been effective.

- Suitable for prescribing in primary care following recommendation or initiation by a specialist.
- Little or no specific monitoring required.
- Patient may need a regular review, but this would not exceed that required for other medicines routinely prescribed in primary care.
- Brief prescribing document or information sheet may be required.

Primary care prescribers must be familiar with the drug to take on prescribing responsibility or must get the required information.

Prescribers should choose the product with the lowest acquisition cost where appropriate.

Summary of supporting evidence:

- NICE recommends considering glycopyrronium bromide to manage drooling of saliva in patients with Parkinson's disease when non-pharmacological management is not available or has not been effective. [3]
- Two RCTs have demonstrated efficacy of glycopyrronium bromide in the management of symptoms of drooling of saliva in patients with Parkinson's disease. [4] [6]
- Glycopyrronium bromide has a long duration of action and is less likely to cause central nervous system or cardiac adverse events than other antimuscarinics. [7]
- A significant proportion of Parkinson's disease patients experience excessive drooling of saliva (70-80% according to NICE NG71) and there are limited treatment options which have been investigated with RCTs.

Details of Review

Name of medicine (generic & brand name)**:**

Glycopyrronium Bromide (Sialanar® or Colonis® generic)

Strength(s) and form(s):

Oral solutions

400 mcg of glycopyrronium bromide per mL (Sialanar®) [1]

1 mg of glycopyrronium bromide per 5 mL (Colonis® generic) [2]

Dose and administration:

Unlicensed use

Based on dosing used in the trials the median dose is 1 mg three times a day.

BNF therapeutic class / mode of action:

Anticholinergic/antimuscarinic.

Licensed indication(s):

Symptomatic treatment of severe sialorrhoea (chronic pathological drooling) in children and adolescents aged 3 years and older with chronic neurological disorders. [1] [2]

Proposed use (if different from, or in addition to, licensed indication above):

Symptomatic treatment of hypersalivation/ sialorrhoea in adults with Parkinson's disease.

Course and cost:

Sialanar® 400 mcg per mL oral solution 250mL - £320

Glycopyrronium bromide 1 mg of per 5 mL oral solution (Colonis® generic) 150 mL- £91

For a course of 1 mg three times a day the cost is as follows:

Sialanar® costs £3.20 per 1 mg therefore the monthly cost is £288 with an annual cost of £3,456.

Generic costs £3.03 per 1 mg therefore the monthly cost is £273 with an annual cost of £3,272

Costs based on MIMS list prices June 2021.

Current standard of care/comparator therapies:

The most likely comparators are alternative antimuscarinics

- Procyclidine 5 mg tablets x 28 - £1.98
  Usual maintenance dose of 15 – 30 mg
  Annual cost = £77

- Trihexyphenidyl hydrochloride 5 mg x 84 - £20.62
  Usual maintenance dose of 10 – 15 mg
  Annual cost = £269

- Atropine 1% eye drops Minims x 20 (unlicensed application to the tongue twice daily) - £15.10
  Three packs would be required to cover one month of treatment.
  Annual cost = £ 544

Doses based on the BNF
Costs based on MIMS list prices June 2021.

Relevant NICE guidance:

Parkinson’s Disease in Adults NICE guideline NG 71 [3]

1.5.26 Only consider pharmacological management for drooling of saliva in people with Parkinson's disease if non-pharmacological management (for example, speech and language therapy) is not available or has not been effective. [2017]

1.5.27 Consider glycopyrronium bromide to manage drooling of saliva in people with Parkinson's disease. [2017]

1.5.28 If treatment for drooling of saliva with glycopyrronium bromide is not effective, not tolerated or contraindicated (for example, in people with cognitive impairment, hallucinations or delusions, or a history of adverse effects following anticholinergic treatment), consider referral to a specialist service for botulinum toxin A. [2017]

1.5.29 Only consider anticholinergic medicines other than glycopyrronium bromide to manage drooling of saliva in people with Parkinson's disease if their risk of cognitive adverse effects is thought to be minimal. Use topical preparations if possible (for example, atropine) to reduce the risk of adverse events. [2017]

Background and context

Parkinson's disease is a progressive neurodegenerative condition resulting from the death of dopamine-containing cells of the substantia nigra in the brain. Parkinson's disease is one of the most common neurological conditions. It is estimated to affect up to 160 people per 100,000, with an annual incidence in the UK of 15 to 20 per 100,000. People with Parkinson's disease classically present with the symptoms and signs described as 'parkinsonism': these include bradykinesia (slow movements), rigidity, rest tremor (shaking) and postural instability (loss of balance). [3]

Parkinson's disease has historically been recognised as a primary movement disorder; however, other symptoms (commonly referred to as non-motor symptoms) may be prominent. One type of non-motor symptoms is excessive drooling of saliva. Excessive saliva or drooling occurs in 70–80% of people with Parkinson's disease and may be more common in men. Drooling is thought to result from oropharyngeal dysfunction, including reduced swallowing frequency. NICE recommends non-pharmacological management of drooling of saliva such as speech and language therapy as the first line treatment. Pharmacological management such as antimuscarinics and botulinum toxin A may be considered if non-pharmacological interventions are not available or have not been effective. Glycopyrronium bromide is an antimuscarinic agent that reduces salivary secretions and does not cross the blood–brain barrier. Glycopyrronium bromide was prioritised for review for hypersalivation in adults with Parkinson's disease following a request by a Parkinson's disease specialist clinician at Blackpool teaching hospitals.

Summary of evidence

Summary of efficacy data in proposed use:

Arbouw et al RCT 2010 [4]

This double-blind, placebo-controlled, crossover trial evaluated oral glycopyrronium bromide for treating drooling in 23 adults with Parkinson's disease. Participants had Parkinson's disease and moderate-to-severe drooling (assessed as a score of 5 or above on a 9-point scale, with higher scores indicating more severe drooling). Mean baseline drooling score was 6.5±1.3, indicating severe drooling. Adults were excluded from the trial if they had drooling caused by factors other than Parkinson's disease; previous treatment or hypersensitivity to glycopyrronium bromide; medical conditions that would contraindicate antimuscarinic agents; or concomitant use of potassium chloride tablets, digoxin, or oral corticosteroids. [5]

Participants were randomised to a baseline week without study treatment, then 1 week of oral glycopyrronium bromide 1 mg/5 ml oral solution 3 times daily or placebo, followed by a 1-week washout, and a crossover to 1 week of the alternative. Allocation appeared to be concealed. The primary outcome was the difference in responder rates based on the change in severity and frequency of drooling between treatments. This was assessed by the participant or carer 3 times daily before administration of the study treatment using a 9-point scale, which ranged from 1 'dry: never drools' to 9 'profuse: clothing, hands, tray and objects become wet frequently'. Response to treatment was pre-defined as a mean score improvement of at least 30% from baseline, which the investigators suggested could be clinically relevant. Secondary outcomes were difference in mean scores between treatments and adverse effects. [5]

After 1 week of treatment, drooling responded to treatment in statistically significantly more people when they were taking glycopyrronium bromide (9 of 23; 39.1%) compared with when they were taking placebo (1 of 23; 4.3%) (mean difference in responder rate 34.8%, CI 95% 13.0; 56.5%, p=0.021). Mean drooling score after 1 week of glycopyrronium bromide as 3.8±1.6 compared with 4.6±1.7 with placebo (mean difference 0.8 points, CI95% 0.02; 1.4, p=0.011). A score of 4 on the drooling scale corresponds to 'moderate, wet on the lips and chin, occasionally', and a score of 5 to 'moderate, wet on the lips and chin, frequently'. [5]

Mestre et al RCT 2020 [6]

This was a 12-week, double-blinded, randomised, placebo-controlled, parallel study in patients with PD and Movement Disorder Society–Unified Parkinson's Disease Rating Scale > 2 (on item 2.2 of the scale). The intervention was glycopyrrolate up to 4.5 mg/d; the primary outcome was sialorrhea related disability (Radboud Oral Motor Inventory for Parkinson's Disease Saliva [ROMP-Saliva]).

Twenty eight individuals diagnosed with Parkinson's Disease (United Kingdom PD Society Brain Bank criteria) with moderate-to-severe sialorrhea defined by the Movement Disorder Society– Unified Parkinson's Disease Rating Scale (MDSUPDRS) > 2 (on item 2.2 of the scale), received oral glycopyrrolate capsules (or identical placebo) administered 3 times daily (TID) with an initial dose of 0.5 mg TID for four days, increased by 0.5 mg TID every four days during a 2-week titration phase followed by a 10-week maintenance phase.

At the end of the 3-month treatment period, the ROMP-Saliva score was 16.5 (CI95% 13.5; 19.5) in the glycopyrrolate group and 21.8 (CI95% 18.8; 24.8) in the placebo group, with a between-group difference of 5.3 (CI95% 1.0; 9.6) in favour of glycopyrrolate. The between-group difference was 5.8 (CI95% 1.5; 10.2) after adjustment for maintenance dose and baseline MDS-UPDRS Part III score.

Summary of safety data:

In the placebo-controlled, crossover RCT by Arbouw et al. (2010), adverse effects were assessed using a questionnaire at the end of each treatment week. No serious adverse effects were reported in people taking glycopyrronium bromide or placebo, and there were no statistically significant differences between study treatments in non-serious adverse effects. Dry mouth was the most common adverse effect, experienced by 12 of 23 (52.2%) people while taking glycopyrronium bromide compared with 7 of 23 (30.4%) while taking placebo (p=0.18). A change in motor symptoms was reported among 13% of people in the glycopyrronium bromide group and 17.4% in the placebo group (p=1.0). The following adverse effects were reported equally among the groups: nervousness (21.7%), constipation (13%), vision problems (13%) and palpitations (4.3%). The participant that had 5 times the dosage of glycopyrronium bromide in the first 3 days of treatment experienced marked dryness of the mouth, which resolved within a day of stopping the trial. [5]

In the Mestre et al. placebo controlled trial, the reported adverse events were similar to those in the study by Arbouw et al. The most common adverse events were dry mouth, constipation, worsening cognition, and urinary retention. Constipation was the most common cause of participant drop out from the trial and there were no serious adverse events recorded. [6]

The SPC for Sialanar® (for paediatric use) lists the following contraindications which are in common with other antimuscarinics: [1]

- Hypersensitivity to the active substance or to any of the excipients
- Angle-closure glaucoma
- Myasthenia gravis (large doses of quaternary ammonium compounds have been shown to antagonise end plate nicotinic receptors)
- Pyloric stenosis
- Paralytic ileus
- Prostatic enlargement
- Urinary retention
- Severe renal impairment (eGFR <30 ml/min/1.73m^2), including those with end-stage renal disease requiring dialysis
- Intestinal obstruction
- Pregnancy and breast-feeding.
- Potassium chloride solid oral dose products
- Anticholinergic medicines

Caution is advised in patients with gastro-oesophageal reflux disease, ulcerative colitis, pre-existing constipation, hypertension, and conditions characterised by tachycardia (e.g. hyperthyroidism). Anticholinergic effects such as urinary retention, constipation and overheating due to inhibition of sweating are dose dependent. Monitoring by physicians and caregivers is required. The carer should stop treatment and seek advice from the prescriber in the event of:

- Constipation
- Urinary retention
- Pneumonia
- Allergic reaction
- Pyrexia
- Very hot weather

- Changes in behaviour

After evaluating the event, the prescriber will decide if treatment should remain stopped or if this should continue at a lower dose.

Strengths and limitations of the evidence:

Strengths

- NICE recommends considering glycopyrronium bromide to manage drooling of saliva in patients with Parkinson's disease when non-pharmacological management is not available or has not been effective. [3]
- Two RCTs have demonstrated efficacy of glycopyrronium bromide in the management of symptoms of drooling of saliva in patients with Parkinson's disease. [4] [6]
- Glycopyrronium bromide has a long duration of action and is less likely to cause central nervous system or cardiac adverse events. [7]
- A significant proportion of Parkinson's disease patients experience excessive drooling of saliva (70-80% according to NICE NG71) and there are limited treatment options which have been investigated with RCTs.

Limitations

- Glycopyrronium bromide is not licensed in the UK for the treatment of hypersalivation in adults with Parkinson's disease.
- There are no comparative studies comparing glycopyrronium bromide to alternative treatment options following failure of non-pharmacological treatments.
- Both RCTs were small (less than 30 participants), short term studies and do not provide evidence of long-term safety and efficacy.
- The doses used in the trials varied, although the median dose in Mestre et al. trials reflected the dosing regimen in Arbouw et al.
- The outcome measures used in the RCTs are subjective due to the difficulty and lack of methods for assessing saliva production.

Summary of evidence on cost effectiveness:

N/A

Prescribing and risk management issues:

Prior to each increase in dose, prescribers should review the tolerability of the current dose level. If continuous treatment is needed or the treatment is repeated intermittently benefits and risks should be carefully considered on a case by case basis and treatment should be closely monitored. [2]

NICE recommends that pharmacological management for drooling of saliva in people with Parkinson's disease should only be considered if non-pharmacological management is not available or has not been effective. [3]

Commissioning considerations:

Comparative unit costs:

Drug	Example regimen	Pack cost	Cost per patient per year (ex VAT)
Glycopyrronium bromide 1 mg/5 mL oral solution (generic)	**1 mg three times daily**	**Generic – 150 mL costs £91** **Sialanar® – 250 mL costs £320**	**£3,272** **£3,456**

Glycopyrronium bromide 400 mcg/mL oral solution (Sialanar®)			
Procyclidine 5 mg tablets	15 – 30 mg daily	28 tablets costs £1.98	£77
Trihexyphenidyl hydrochloride 5 mg tablets	10 – 15 mg daily	84 tablets costs £20.62	£269
Atropine 1% preservative-free eye drops (Minims®)	Applied to the tongue twice daily	20 single dose vials costs £15.10	£544
Costs based on online Drug Tariff list prices June 2021 This table does not imply therapeutic equivalence of drugs or doses.			

Innovation, need and equity implications of the intervention:

A significant proportion of Parkinson's disease patients experience excessive drooling of saliva (70-80% according to NICE NG71) and there are limited treatment options which have been investigated with RCTs.

Financial implications of the intervention:

NICE estimates that Parkinson's disease has a prevalence of 160 people per 100,000 population. This equates to 2,800 Parkinson's disease patients in Lancashire and South Cumbria. Of those up to 80% are estimated to suffer with excessive drooling of saliva (2,240 patients).

As glycopyrronium bromide is a second line treatment option and is not effective in all patients, it anticipated that the number of patients being treated annually will be small. Assuming that 5% of the total eligible patients with symptoms of excessive drooling of saliva were initiated on to glycopyrronium bromide oral solution (112 patients across Lancashire and South Cumbria) the annual cost is estimated to be as follows:

> 112 x £3,272 (annual cost of generic glycopyrronium bromide oral solution) = **£366,464**

NICE states that the recommendations in NG 71 Parkinson's Disease in Adults are not anticipated to create a significant impact to NHS resources.

Service Impact Issues Identified:

Management of excessive drooling of saliva using glycopyrronium bromide would not be anticipated to generate additional outpatient appointments compared to non-pharmacological first line treatment options.

Equality and Inclusion Issues Identified:

Included with the paper to be considered at the meeting of the LSCMMG.

Cross Border Issues Identified:
Glycopyrronium bromide has a “Green” RAG classification for the treatment of hypersalivation in adults in Pan Mersey APC meaning it is considered suitable for non-specialist prescribing in primary and secondary care. In GMMMG, glycopyrronium bromide oral solution has a “Green” RAG following specialist initiation for treatment of severe sialorrhoea.
Legal Issues Identified:
N/A
Media/ Public Interest:
N/A

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Grading of evidence (based on SORT criteria):

Levels	Criteria	Notes
Level 1	Patient-oriented evidence from: • high quality randomised controlled trials (RCTs) with low risk of bias • systematic reviews or meta-analyses of RCTs with consistent findings	High quality individual RCT= allocation concealed, blinding if possible, intention-to-treat analysis, adequate statistical power, adequate follow-up (greater than 80%)
Level 2	Patient-oriented evidence from: • clinical trials at moderate or high risk of bias • systematic reviews or meta-analyses of such clinical trials or with inconsistent findings • cohort studies • case-control studies	
Level 3	Disease-oriented evidence, or evidence from: • consensus guidelines • expert opinion • case series	Any trial with disease-oriented evidence is Level 3, irrespective of quality

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