East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG, Surrey Heath CCG, Crawley CCG, Horsham & Mid-Sussex CCG

Evidence review for Surrey and North West Sussex Area Prescribing Committee

Medicine details	
Name, brand name	Glycopyrronium Bromide 1mg/5ml Oral Solution (Colonis)
Manufacturer	Colonis Pharma Ltd
Proposed indication	For use in children and adolescents aged 3 years and older with chronic neurological disorders as symptomatic treatment of severe sialorrhoea, and for "off-label" use in Adults for the treatment of severe sialorrhoea.
Requested by	APC members on behalf of its users, following ePACT interrogation of prescription habits

SUMMARY

Clinical Effectiveness

NICE Evidence Summary ES5 - Severe sialorrhoea (drooling) in children and young people with chronic neurological disorders: oral glycopyrronium bromide. Published 14 February 2017[1].

A literature search was conducted by NICE which identified 62 references (see search strategy for full details). These references were screened using their titles and abstracts and 11 references were obtained and assessed for relevance. Two randomised controlled trials (RCTs) identified from the search (Mier et al. 2000 and Zeller et al. 2012a) were included in this evidence summary.

- This evidence summary 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. The majority of participants had cerebral palsy.
- 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. The most commonly reported adverse effects include dry mouth, constipation, urinary retention, reduced bronchial secretions and flushing. The SPC advises that glycopyrronium bromide can cause thickening of secretions, which may increase the risk of respiratory infection and pneumonia. Glycopyrronium bromide should be used with caution in people with heart problems due to its potential increase in heart rate, blood pressure and rhythm disorders (SPC: glycopyrronium).
- There is a lack of long-term safety data for glycopyrronium bromide, and the SPC 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, the effectiveness of glycopyrronium bromide should be balanced against the adverse effects associated with treatment.

The remaining 8 references were excluded. These are listed under excluded studies in the NICE paper with reasons for their exclusion.

Comment: There are no randomised controlled comparative studies, so prescribers should consider evidence for effectiveness, potential side effects and available routes of administration when choosing between them. The absence of long-term studies means that there is no evidence for continued effectiveness or safety if used continuously for long periods[6].

Safety

The SPC for Glycopyrronium bromide 1mg/5ml oral solution states that adverse effects are common with glycopyrronium bromide due to its anticholinergic action. The most common adverse reactions include dry mouth, constipation, diarrhoea, urinary retention, flushing and nasal congestion[4].

The SPC advises that anticholinergic adverse effects may be dose dependent and difficult to assess in a child with disabilities. Treatment should be stopped in the event of constipation, urinary retention or pneumonia[4].

Due to the lack of long term safety data, glycopyrronium bromide 1mg/5ml oral solution is recommended for short-term intermittent use only[4].

Summary of Product Characteristics (SPC) for this product[4] specifically states the following:

- **Mild to moderate sialorrhoea:** Due to the low likelihood of benefit and the known adverse effect profile, glycopyrronium bromide 1mg/5ml oral solution should not be given to children with mild to moderate sialorrhoea.

• **Contraindications:** Hypersensitivity to the active substance or to any of the excipients listed in [SPC]. Pregnancy and breast-feeding. Glaucoma. Urinary retention. Severe renal impairment eGFR<30ml/min/1.73m^2 including those with end-stage renal disease requiring dialysis. History of intestinal obstruction, GORD, ulcerative colitis, paralytic ileus, pyloric stenosis and myasthenia gravis. Concomitant treatment with potassium chloride solid oral dose; anticholinergics; and cardiac conditions.
Glycopyrronium bromide was associated with more adverse effects and discontinuations because of adverse effects than placebo[1].

Patient factors

• Glycopyrronium bromide was associated with more adverse effects and discontinuations because of adverse effects than placebo[1].
• The SPC recommends that glycopyrronium bromide should be taken at least one hour before or at least two hours after meals or at consistent times with respect to food intake[1].
• Most children in the clinical trials had cerebral palsy. Glycopyrronium has not been extensively tested in children with other neurological conditions[1].

Cost implications

• Glycopyrronium bromide tablets and oral solution are available on prescription, but previously these have been imported or prepared by "specials" manufacturers at fluctuating and uncontrolled cost to the NHS.
• From Aug-15 to Jul-16, prescribing costs for oral Glycopyrronium bromide (all formulations, all indications, all patient groups) was as follows:-

Commissioner	Actual Cost	Cost per 100,000 pop.
EAST SURREY CCG	£61,215.38	£34,152.74
GUILDFORD AND WAVERLEY CCG	£39,390.83	£17,647.11
NORTH WEST SURREY CCG	£45,168.85	£12,326.06
SURREY DOWNS CCG	£105,689.02	£34,936.67
SURREY HEATH CCG	£10,262.71	£10,827.36
CRAWLEY	£41,900.55	£32,297.03
HORSHAM AND MID SUSSEX	£189,918.85	£81,143.17

It should be noted, that since Sialanar 320 micrograms/ml oral solution (glycopyrronium bromide 400 microgram/ml oral solution) was approved for use as a BLUE drug by the PCN on 5th April 2017, the current cost of prescribing Glycopyrronium bromide from Mar-18 to Mar-19 is now as follows:-

Commissioner	Actual Cost	Cost per 100,000 pop.
EAST SURREY CCG	£86,887.09	£47,292.69
GUILDFORD AND WAVERLEY CCG	£54,573.70	£24,137.29
NORTH WEST SURREY CCG	£34,143.66	£9,154.01
SURREY DOWNS CCG	£108,360.11	£35,194.88
SURREY HEATH CCG	£5,585.55	£5,769.42
CRAWLEY	£40,632.85	£30,449.82
HORSHAM AND MID SUSSEX	£123,714.27	£51,263.95

• Glycopyrronium bromide 1mg/5 ml oral solution (Colonis) costs £91 per 150 ml bottle (part VIIIa Drug Tariff).
• Once opened the bottle has a shelf life of 28 days. Any liquid remaining after this time should be discarded[4].
• NICE Evidence Summary ES5 states that the manufacturer (Sialanar) estimates that there are approximately 1,500 children in England who may be eligible for treatment with glycopyrronium bromide[4].
• Unfortunately, current prescribing data within the APC is not specific to indication or patient group, so generalisations of cost pressures/savings have been made.

It should be noted, that it is thought that the majority of current prescribing of glycopyrronium bromide is for adult patients.

Relevant guidance / reviews

1. **Severe sialorrhoea (drooling) in children and young people with chronic neurological disorders: oral glycopyrronium bromide (NICE Evidence Summary 5)[1]**

This evidence summary 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. The majority of participants had cerebral palsy.

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. The most commonly reported adverse effects include dry mouth, constipation, urinary retention, reduced bronchial secretions and flushing. The SPC advises that glycopyrronium bromide can cause thickening of secretions, which may increase the risk of respiratory infection and pneumonia. Glycopyrronium bromide should be used with caution in people with heart problems due to its potential increase in heart rate, blood pressure and rhythm disorders (SPC: glycopyrronium).

There is a lack of long-term safety data for glycopyrronium bromide, and the SPC 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. The effectiveness of glycopyrronium bromide should be balanced against the adverse effects associated with treatment.

Sialanar 320 micrograms/ml oral solution was the first formulation of glycopyrronium bromide to be licensed for this indication in the UK. In January 2019 Glycopyrronium bromide 1mg/5ml oral solution (Colonis) was approved to have the same indication as Sialanar i.e. for the symptomatic treatment of severe sialorrhoea (chronic pathological drooling) in children and adolescents aged 3 years and older with chronic neurological disorders.

Likely place in therapy relative to current treatments

Sialanar 320 micrograms/ml oral solution was the first formulation of glycopyrronium bromide to be licensed in the UK for managing sialorrhoea and was approved as a BLUE drug without information sheet by the PCN on 5th April 2017(PCN 260-2017).

Other medicines that have been used to manage sialorrhoea include the following (Specialist Pharmacy Service, 2015):
- other antimuscarinic medicines (for example hyoscine hydrobromide, amitriptyline, atropine and trihexyphenidyl hydrochloride)
- botulinum toxin[1].

None of these medicines are currently recommended for use in sialorrhoea within Surrey APC.

In line with the guidance from the General Medical Council (GMC), unlicensed or off-label medicines should be used only where there is no suitably licensed medicine that will meet the patient's need.

This would mean that Glycopyrronium Bromide 1mg/5ml Oral Solution (Colonis) should be considered as an alternative first-line option for children and young people with sialorrhoea (as it is currently the cheapest available product with this specific licence).

Recommendation to APC

For consideration by the members:

- Recommend glycopyrronium bromide 1mg/5ml oral solution to be given a BLUE (without information sheet) traffic light status but must be initiated under recommendation from a specialist consultant in paediatric patients with severe drooling who have tried other antimuscarinic treatments but have found these therapies are inadequate or intolerable due to side effects. The specialist should provide care and prescription until the patient is at a stable dose, and clear instructions should be provided to the GP at point of transfer with regards to dose changes, and the monitoring and management of anticholinergic side-effects.

- APC members to make recommendation as to whether patients currently using Sialanar are to be switched to more cost effective preparation glycopyrronium bromide 1mg/5ml oral solution (noting that Sialanar is not bioequivalent to glycopyrronium bromide 1mg/5ml oral solution, switching from Sialanar should only be conducted under supervision to ensure that efficacy and side effects are balanced.)

- APC members to consider Hypersalivation Treatment Pathway for all treatments for pharmacological management

of hypersalivation in children and adults see separate Evidence Review Document.

Medicine details

Name and brand name

Glycopyrronium Bromide 1mg/5ml Oral Solution (Colonis)

Licensed indication, formulation and usual dosage

The dosing schedule for Glycopyrronium bromide oral solution 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. For greater detail, see Table 1.

During the four-week titration period, dosing can be increased with the recommended dose titration schedule while ensuring that the anticholinergic adverse events are tolerable. Prior to each increase in dose, review the tolerability of the current dose level with the patient's caregiver.

Younger children may be more susceptible to adverse events and this should be kept in mind when dose adjustments are carried out.

Table 1: Dosing tables for children and adolescents aged 3 years and older

Weight	**Dose Level 1**		**Dose Level 2**		**Dose Level 3**		**Dose Level 4**		**Dose Level 5**	
kg	**(~0.02 mg/kg)**		**(~0.04 mg/kg)**		**(~0.06 mg/kg)**		**(~0.08 mg/kg)**		**(~0.1 mg/kg)**	
13-17	0.3 mg	1.5 ml	0.6 mg	3 ml	0.9 mg	4.5 ml	1.2 mg	6 ml	1.5 mg	7.5 ml
18-22	0.4 mg	2 ml	0.8 mg	4 ml	1.2 mg	6 ml	1.6 mg	8 ml	2.0 mg	10 ml
23-27	0.5 mg	2.5 ml	1.0 mg	5 ml	1.5 mg	7.5 ml	2.0 mg	10 ml	2.5 mg	12.5 ml
28-32	0.6 mg	3 ml	1.2 mg	6 ml	1.8 mg	9 ml	2.4 mg	12 ml	3.0 mg	15 ml
33-37	0.7 mg	3.5 ml	1.4 mg	7 ml	2.1 mg	10.5 ml	2.8 mg	14 ml	3.0 mg	15 ml
38-42	0.8 mg	4 ml	1.6 mg	8 ml	2.4 mg	12 ml	3.0 mg	15 ml	3.0 mg	15 ml
43-47	0.9 mg	4.5 ml	1.8 mg	9 ml	2.7 mg	13.5 ml	3.0 mg	15 ml	3.0 mg	15 ml
≥48	1.0 mg	5 ml	2.0 mg	10 ml	3.0 mg	15 ml	3.0 mg	15 ml	3.0 mg	15 ml

Glycopyrronium Bromide oral solution is not recommended for use in children younger than 3 years.

Summary of mechanism of action, and relevant pharmacokinetics

The salivary glands are innervated by the sympathetic and parasympathetic nervous system. Parasympathetic postganglionic cholinergic nerve fibres stimulate the rate of salivary secretion[2].
Glycopyrronium bromide is an antimuscarinic drug that can potentially reduce salivary secretions.
Antimuscarinics are contra-indicated in GI obstruction, intestinal atony, myasthenia gravis (but some antimuscarinics may be used to decrease muscarinic side-effects of anticholinesterases), paralytic ileus, prostatic enlargement, pyloric stenosis, severe ulcerative colitis, significant bladder outflow obstructions, toxic megacolon and urinary retention[1].

Important drug interactions

Concomitant use of the following medicinal products is contraindicated:
Potassium chloride solid oral dose: glycopyrronium may potentiate the risk of upper gastrointestinal injury associated with oral solid formulations of potassium chloride due to increased gastrointestinal transit time creating a high localized concentration of potassium ions. An association with upper GI bleeding and small bowel ulceration, stenosis, perforation, and obstruction has been observed.
Anticholinergics: concomitant use of anticholinergics may increase the risk of anticholinergic side effects. Anticholinergics may delay the gastrointestinal absorption of other anticholinergics administered orally and also increase the risk of anticholinergic side effects.
Concomitant use of the following medicinal products should be considered with caution:
Antispasmodics: glycopyrronium may antagonize the pharmacologic effects of

	gastrointestinal prokinetic active substances such as domperidone, metoclopramide. **Topiramate**: glycopyrronium may potentiate the effects of oligohidrosis and hyperthermia associated with the use of topiramate, particularly in paediatric patients; **Sedating antihistamines**: may have additive anticholinergic effects. A reduction in anticholinergic and/or antihistamine dosage may be necessary; **Neuroleptics/antipsychotics**: the effects of active substances such as phenothiazines, clozapine and haloperidol may be potentiated. A reduction in anticholinergic and/or neuroleptic/antipsychotic dose may be necessary; **Skeletal muscle relaxants**: Use of anticholinergics after administration of botulinum toxin may potentiate systemic anticholinergic effects; **Tricyclic antidepressants and MAOIs**: may have additive anticholinergic effects. A reduction in anticholinergic and/or tricyclic antidepressants and MAOIs dosage may be necessary. **Opioids**: active substances such as pethidine and codeine may result in additive central nervous system and gastrointestinal adverse effects, and increase the risk of severe constipation or paralytic ileus and CNS depression. If concomitant use cannot be avoided, patients should be monitored for potentially excessive or prolonged CNS depression and constipation; **Corticosteroids**: Steroid-induced glaucoma may develop with topical, inhaled, oral or intravenous, steroid administration. Concomitant use may result in increased intraocular pressure via an open- or a closed-angle mechanism; **Other Medicinal products with anticholinergic** properties (e.g. antihistamines, antidepressants) may cause cumulative parasympatholytic effects including dry mouth, urinary retention, constipation and confusion, and an increased risk of anticholinergic intoxication syndrome[4].
Monitoring requirements	Anticholinergic effects such as urinary retention, constipation and overheating due to inhibition of sweating may be dose dependent and difficult to assess in a disabled child. Monitoring by physicians and caregivers is required with adherence to the management instructions below: **Management of important anticholinergic side effects** 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[4].
Prescribing considerations	If the indication is sialorrhoea, then prescriptions should be made by generic name, i.e. Glycopyrronium Bromide 1mg/5ml Oral Solution There is potential for confusion and dosing error when prescribing, due to the way that the strength of Sialanar is expressed. On SystmOne Sialanar appears as Sialanar 320mcg/ml oral solution. Each ml of Sialanar contains 400 micrograms of glycopyrronium bromide. This is equivalent to 320 micrograms of glycopyrronium. Therefore, glycopyrronium bromide 400mcg/ml oral solution sugar free is the same as Sialanar 320mcg/ml oral solution (250ml costs £320). The dose is usually expressed as the salt glycopyrronium bromide, therefore, if a dose of 400mcg is required, this would be provided with 1ml volume of Sialanar 320 micrograms/ml.
Other considerations	Current practice to treat sialorrhoea in children is likely to be as recommended in NICE guideline NG62 (Cerebral palsy in under 25s: assessment and management)[6] and is believed to be the off-label use of oral anticholinergics, beta-blockers and botulinum toxin. It is to be noted that in line with the guidance from the General Medical Council (GMC), unlicensed or off-label medicines should be used only where there is no suitably licensed medicine that will meet the patient's need.

	Sialanar® and glycopyrronium bromide 1mg/5ml oral solution (Colonis) are the only licensed products available at this time.

Potential patient group (if appropriate to include)	
Brief description of disease	• Hypersalivation is the excessive production of saliva. This presents as drooling in children, young people and adults with a neurological condition, such as cerebral palsy, or Parkinson's disease. • Hypersalivation can also be an adverse effect of drug treatment (e.g. clozapine). • Chronic drooling can be defined as the unintentional loss of saliva from the mouth. Drooling is normal in infants and it usually stops by 15-18 months or age, but is considered pathological if present after 4 years. • Drooling is usually present due to neurological disturbance and less frequently to over production of saliva. Under normal circumstances, persons are able to compensate for increased salivation by swallowing. • However, sensory dysfunction may decrease a person's ability to recognise drooling and autonomic or motor dysfunction of swallowing may impede the ability to manage increased secretion[3]. • Drooling can result in perioral chapping, irritation, maceration and secondary infection of the skin. • Drooling is thought to result in oropharyngeal dysfunction, including reduced swallowing frequency[1]. • Bird et al (2011) reported that, second to sedation, hypersalivation is one of the most common adverse effects attributed to clozapine, occurring in 30-80% of people taking the drug[1].
Potential patient numbers per 100,000	The prevalence of moderate to severe drooling in children, young people and adults with neurological conditions, particularly cerebral palsy is estimated to be between 10 and 37%[1].
Outcomes required	Reduction on drooling and the resultant effects of drooling.

Summary of current treatment pathway

From NICE NG62 Cerebral palsy in under 25s: assessment and management[6]

Managing saliva control

1.11.1 Assess factors that may affect drooling in children and young people with cerebral palsy, such as positioning, medication history, reflux and dental issues, before starting drug therapy.

1.11.2 **To reduce the severity and frequency of drooling in children and young people with cerebral palsy, consider the use of anticholinergic medication:**

- **glycopyrronium bromide (oral or by enteral tube) or**
- transdermal hyoscine hydrobromide **or**
- trihexyphenidyl hydrochloride for children with dyskinetic cerebral palsy, but only with input from specialist services.

When choosing which medicine to use, take into account the preferences of the child or young person and their parents or carers, and the age range and indication covered by the marketing authorisations.

1.11.3 Regularly review the effectiveness, tolerability and side effects of all drug treatments used for saliva control.

1.11.4 Refer the child or young person to a specialist service if the anticholinergic drug treatments outlined in recommendations 1.11.2 and 1.11.3 are contraindicated, not tolerated or not effective, to consider other treatments for saliva control.

1.11.5 Consider specialist assessment and use of botulinum toxin A injections to the salivary glands with ultrasound guidance to reduce the severity and frequency of drooling in children and young people with cerebral palsy if anticholinergic drugs provide insufficient benefit or are not tolerated.

1.11.6 Advise children and young people and their parents or carers that high-dose botulinum toxin A injection to the salivary glands can rarely cause swallowing difficulties, and so they should return to hospital immediately if breathing or swallowing difficulties occur.

1.11.7 Consider referring young people for a surgical opinion, after an assessment confirming clinically safe swallow, if there is:

- a potential need for lifelong drug treatment or
- insufficient benefit or non-tolerance of anticholinergic drugs and botulinum toxin A injections.

A range of other pharmacological options are available to treat hypersalivation. Most of them are antimuscarinic drugs and all are unlicensed in the UK for the treatment of hypersalivation. There are no randomised controlled comparative studies, so prescribers should consider evidence for effectiveness, potential side effects and available routes of administration when choosing between them. The absence of long-term studies means that there is no evidence for continued effectiveness or safety if used continuously for long periods.

Evidence review

NICE Evidence Summary (ES5) - Severe sialorrhoea (drooling) in children and young people with chronic neurological disorders: oral glycopyrronium bromide
https://www.nice.org.uk/advice/es5/chapter/Key-points
As stated in summary above.

From NICE NG71, Parkinson's disease in adults[7], NICE recommends the use of glycopyrronium as a first line option in the treatment of drooling in Parkinson's disease. https://www.nice.org.uk/guidance/ng71

Drooling of saliva

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; see recommendation 1.7.8) is not available or has not been effective. **[2017]**

1.5.27 Consider glycopyrronium bromide[8] to manage drooling of saliva in people with Parkinson's disease. **[2017]**

1.5.28 If treatment for drooling of saliva with glycopyrronium bromide[8] 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[8]. **[2017]**

1.5.29 Only consider anticholinergic medicines other than glycopyrronium bromide[8] 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]**

Current APC Standard Operating Procedure for conducting evidence reviews states that if there is an up to date summary from a Trusted source e.g. NICE evidence summary, MTRAC, SMA, AWSMG, London Medicines Evaluation Network, then it is unnecessary to do an additional evidence review, and that NICE accredited guidelines should be given precedent over non NICE accredited guidance

Equity / Stakeholder views (if relevant)

Decisions of local Trusts DTCs and neighbouring APCs	Glycopyrronium bromide oral solution 400micrograms/mL (Sialanar® 320 micrograms/ml of glycopyrronium) approved for use on the following formularies: ➢ Brighton and Hove Clinical Commissioning Group, High Weald Lewes Havens Clinical Commissioning Group and Brighton and Sussex University Hospitals NHS Trust Joint Formulary: BLUE ➢ NHS Crawley and NHS Horsham and Mid Sussex CCG Formulary: BLUE ➢ East Sussex Health Economy Formulary- BLUE ➢ Surrey CCGs- BLUE (without information sheet) Glycopyrronium bromide 1mg/5ml oral solution sugar free (Colonis®) approved for use on the following formularies: ➢ NHS Coastal West Sussex CCG Formulary: Non-Formulary except GREEN for palliative care only.

	➢ East Sussex Health Economy Formulary- BLUE
Recommendations from national / regional decision making groups	**NICE NG62 Cerebral palsy in under 25s: assessment and management[6]** To reduce the severity and frequency of drooling in children and young people with cerebral palsy, consider the use of anticholinergic medication: • glycopyrronium bromide[3] (oral or by enteral tube) or • transdermal hyoscine hydrobromide[4]or • trihexyphenidyl hydrochloride[5] for children with dyskinetic cerebral palsy, but only with input from specialist services. When choosing which medicine to use, take into account the preferences of the child or young person and their parents or carers, and the age range and indication covered by the marketing authorisations. Scottish Medicines Consortium- Sialanar® is approved in accordance with license indication. Colonis® not yet reviewed All Wales Medicines Strategy Group- Sialanar® and Colonis® are both 'Not Recommended' for use in Wales.
Stakeholder views	No comments received from local stakeholders in response to consultation on this paper.
CCG priorities	• QIPP • Use of unlicensed medicines policy – preference to use a licensed drug for an unlicensed indication.

Health economic considerations

Cost per year per patient

• Glycopyrronium bromide 1mg/5 ml oral solution (Colonis®) costs £91 per 150 ml bottle (part VIIIa Drug Tariff).
• Once opened the bottle has a shelf life of 28 days. Any liquid remaining after this time should be discarded[4].
• NICE Evidence Summary ES5 states that the manufacturer (Sialanar®) estimates that there are approximately 1,500 children in England who may be eligible for treatment with glycopyrronium bromide[1].

Alternative treatments cost per patient per year

Costs of other treatments in comparison to Glycopyrronium Bromide 1mg/5ml oral solution

Medicine	Usual dose[a]	28-day cost (exc VAT)
Amitriptyline tablets[c]	50mg at night	28 tablets = £2.81
Atropine 1% eye drops[c]	2 drops 4 times daily	10ml = £131.87 minims 20 = £15.10
Glycopyrronium bromide oral solution 400micrograms/mL (Sialanar® 320 micrograms/ml of glycopyrronium)	1,600 micrograms (4ml) 3 times daily	250ml = £320.00 360ml = £460.80
Glycopyrronium bromide tablets (NB—not to be routinely used due to cost)[c]	1mg 3 times daily	30 tablets = £230.71 84 tablets = £645.99
Glycopyrronium bromide 1mg/5ml oral solution sugar free (Colonis®)	1mg 3 times daily	150ml = £91.00 450ml = £273.00
Hyoscine hydrobromide	150 micrograms 3	84 tablets = £12.88

	150micrograms tablets[c]	times daily	
	Hyoscine hydrobromide 300micrograms tablets[c]	300 micrograms 3 times daily	84 tablets = £12.88
	Hyoscine hydrobromide 100 microgram/mL oral solution (Special)[c]	300 micrograms 3 times daily	100ml= £32.14 270ml =£86.78
	Hyoscine patch 1.5mg (Scopoderm®)[c]	1 patch every 72 hours	10 patches = £128.70
	Ipratropium bromide nasal spray 0.03% ('off-label')[c]	1-2 sprays twice daily	180 dose = £6.54
	Ipratropium bromide CFC free inhaler 20micrograms / actuation ('off-label')[c]	1-2 sprays 4 times daily	200 dose = £5.56
	Procyclidine 5mg tablets	5mg daily	28 tablets = £2.94
	Procyclidine 5mg/5ml oral solution sugar free	5mg daily	150ml = £21.66
	Trihexyphenidyl 5mg tablets	5mg 3 times daily	84 tablets = £17.91
	Trihexyphenidyl 5mg/5ml oral solution	5mg 3 times daily	200ml = £26.40 450ml =£59.40

[a] doses shown do not represent the full range that can be used and do not imply therapeutic equivalence
[b] Costs based on Drug Tariff, April 2019; excluding VAT
[c] Not licensed for the treatment of sialorrhoea; use would be off-label.

Other financial considerations (if relevant)	
Health economic data (if available)	

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Declaration of Interest:

Nil

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Declaration of Interest:

Nil

Date: 13th June 2019

VERSION CONTROL SHEET

Version	Date	Author	Status	Comment
v.1	*14/6/2019*	*Richard Rodgers*		*Out for consultation*
v.2				

Comments on Evidence review for Prescribing Clinical Network

Medicine and proposed indication	
Comments by	Name, designation and organisation
Comments on evidence review	
Additional evidence and references for	Include any additional evidence and references you would like to submit for inclusion in the evidence review

consideration	
Specific clinical questions	Specific questions arising from review
Other colleagues who should be contacted	Include name, designation and contact details of any other colleagues who should be consulted about this evidence