1. Introduction

This guideline summarises consensus good practice, based on NICE guidance, to standardise the management of sialorrhea in adult patients with Parkinson's Disease.

2. Scope

The guideline is of relevance to all clinicians looking after patients with Parkinson's Disease.

3. Recommendations, Standards and Procedural Statements

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Background

Sialorrhoea (or hypersalivation) is the involuntary loss of excess saliva beyond the margin of the lips and is a common non-motor problem experienced by patients with Parkinson's Disease (PD), as well as many other chronic neurological conditions. Sialorrhoea is seldom recognised as a major symptom in the natural progression of PD, yet those living with PD often rate sialorrhoea as one of the most debilitating complaints.

Sialorrhoea can result in negative psychosocial effects including embarrassment and social isolation, in addition to increasing the burden on caregivers. Other complications may include poor oral hygiene, difficulty with eating and drinking, sleep disturbance and halitosis, as well as increasing the risk of mortality associated with aspiration pneumonia. On average, up to half of those living with Parkinson's report hypersalivation, and subclinical sialorrhoea can be observed in as many as 80 - 90% of people.

There are three primary mechanisms of sialorrhoea in PD:

i) hypersecretion of saliva
ii) poor retention of saliva within the oral cavity caused by dysfunction or weakness of muscles in the mouth, tongue, and throat (hypomimia, involuntary mouth opening, declining posture or drooping of head); and
iii) reduction in salivary clearance (due to lingual bradykinesia, oropharyngeal dysphagia, upper oesophageal sphincter dysfunction).

Assessment

Symptoms of sialorrhoea can be evaluated subjectively via discussion with the patient and/or carer, and by observation – the saliva will typically be thin and watery, which can cause drooling. Patients might also experience build-up of thick and tenacious saliva in the back of the mouth, which can be caused by dehydration and open-mouthed breathing, as well as drug treatments for sialorrhoea.

The Drooling Severity and Frequency Scale (DSFS) is a validated assessment tool that can be utilised by health professionals to provide a qualitative description and documented score of the severity and frequency of sialorrhoea in PD.

Drooling severity and frequency scale (DSFS)

- Drooling severity is rated on a scale of 1 (dry) to 5 (profuse)
- Drooling frequency is rated on a scale of 1 (never) to 4 (constantly)
- The total DSFS score is a sum of both scores, and ranges from 2 to 9

Drooling severity score	
1	Dry (never drools)
2	Mild (wet lips only)
3	Moderate (wet lips and chin)
4	Severe (clothing becomes damp)
5	Profuse (clothing, hands, objects become wet)

Drooling frequency score	
1	Never
2	Occasionally
3	Frequently
4	Constantly

Generally, if the total score is < 5, then symptoms have likely not reached an accepted threshold for benefits of drug treatment to outweigh its risks of adverse effects in most people with PD. A shared decision should be made with the individual patient to meet their needs and goals.

Recommendation: Record a baseline DSFS score for all patients with PD presenting with, or alluding to symptoms of hypersalivation, and generally consider intervention if score >=5.

Other assessment tools may be used within the specialist PD services, including the Parkinson's Disease Questionnaire (**PDQ-39**), and the Non-Motor Symptoms Questionnaire (**NMSQ**) to obtain a wider understanding of impact on quality of life.

Interventions for sialorrhea

These are grouped into non-pharmacological and pharmacological. Refer to Flowchart – Appendix 2.

Non-pharmacological interventions

Non-pharmacological management options should be considered before offering drug treatment for sialorrhoea, owing to the unfavourable side effect profile of medications used in older patients and those with cognitive impairment or concurrent neurological conditions. Advice should generally be given on swallowing, diet, posture, suctioning and hydration.

a) Identify and treat potentially reversible causative factors

This may include **other drug treatments** (antipsychotics e.g. clozapine; anticholinesterase agents e.g. rivastigmine; pyridostigmine; pilocarpine). **Dehydration** may also exacerbate production of excess saliva – patients should be encouraged to improve fluid intake. **Acidic fruits and alcohol** stimulate saliva production, so avoiding these may help to minimise drooling.

b) Behavioural interventions and oromotor exercises

Behavioural therapy uses a combination of cueing, overcorrection, and both positive and negative reinforcement to help drooling. Patients can be trained to **perform regular swallows** and/or take regular sips of fluid (apps are available e.g. Swallow Prompt, which can be downloaded to personal mobile devices and Smartwatches). Other exercises are aimed at **improving orofacial muscle strength and function**, learning techniques in lip closure and tongue movements, and encouraging habitual dabbing of corners of the mouth and chin.

c) Sensory stimulation

Supporting simple techniques to increase oral stimulation and promote regular swallowing e.g. sucking on **ice cubes or lollies, sugar-free chewing gum, lozenges, or boiled sweets** to stimulate salivary flow and reduce viscosity of saliva.

d) Physiotherapy, posture, and positioning

Good posture with proper trunk and head control provides the basis for improving oral control of drooling and swallowing. Consider referral to specialist OT/PT.

e) Refer to Speech & Language Therapy (SLT)

Speech therapy should be started early to obtain good results, where specialist input is required and/or preferred.

Recommendations:

Consider non-pharmacological interventions for all patients.

Involve the Speech & Language Therapists if there are any communication or swallowing difficulties noted.

Pharmacological interventions

Consider pharmacological measures for drooling of saliva in patients with Parkinson's disease if non-drug management and SLT has not been effective, or services are not available. The DSFS score may be used as an adjunct to guide the clinical need for initiating drug treatment.

Of note, sialorrhoea in Parkinson's disease usually occurs during 'off' periods of symptom control, thus an important first step may be to optimise dopaminergic therapy to improve swallowing function.

Drug therapy is aimed at decreasing the volume of saliva, though without addressing the underlying cause of impaired orofacial functions. Salivation is primarily mediated by parasympathetic innervation of the salivary glands.
There are various drug treatments commonly used for the management of sialorrhoea in Parkinson's disease – the majority are not licensed for this indication in the UK. Non-pharmacological measures should be continued alongside drug treatment.

Appendix 1 illustrates the agreed pathway for the pharmacological management of chronic sialorrhoea in adults with Parkinson's disease at UHL

First line treatments - licensed

The only treatment currently licensed for chronic sialorrhoea in adults due to neurological disorders is Xeomin (botulinum toxin A) and is appraised by NICE as an evidence-based therapy (NICE TA605).

Local service capacity and training to deliver botulinum toxin injection clinics is expected to vary and impacts on achieving safe and timely access to this treatment. Routine off-label use of alternative non-invasive medications, as initial first-line therapy, can be considered to meet clinical needs where services for botulinum toxin injection are not available.

Patient and/or carer preference for non-invasive treatment, as well as relevant cautions or contra-indications to botulinum toxin A are also important factors to consider.

Xeomin solution is injected directly into the parotid and submandibular glands using a suitable sterile needle. Anatomic landmarks or ultrasound guidance are both possible for localisation of the involved salivary glands, though ultrasound guidance should be the preferred method because results in a better therapeutic outcome.

Xeomin must be administered by an appropriately qualified healthcare practitioner with expertise in the treatment of chronic sialorrhoea and use of the required equipment.

The recommended dose per treatment session is 100 units (30 units per side into parotid glands, 20 units per side into submandibular glands), repeated no more frequently than once every 16 weeks.

First line treatments – off-label

Drugs with potent antimuscarinic actions are typically utilised to supress hypersalivation. Blockade of cholinergic receptors effectively reduces saliva production, but a lack of selectivity often results in unwanted central and peripheral side effects, including: dizziness, drowsiness, irritability, restlessness, sinus tachycardia, blurred vision, constipation, urinary retention, confusion, and cognitive impairment.

It should be noted that excessive drooling is particularly a problem in patients with proven or suspected dementia – therefore the risk of worsening cognition and confusion is typically higher when using anticholinergic drugs in the setting of Parkinson's disease.

Available products include **glycopyrronium bromide** oral solution and chewable tablets, **hyoscine hydrobromide** transdermal patches, and **atropine sulphate** eye drops (for sublingual administration).

There are few specific, good quality head-to-head randomised controlled trials to compare efficacy of the different therapeutic options for managing sialorrhoea in adults with Parkinson's; therefore choice is based on adverse effect profile, product availability, patient preference and cost.

Prescribers would also need to review the clinical appropriateness of treatment with co-existing conditions e.g. urinary retention, arrhythmia, glaucoma, constipation etc. together with concurrent treatments that might contribute to the overall anticholinergic burden (see appendix 2). Consideration may be given to avoiding anticholinergic drugs for sialorrhoea if the anticholinergic burden is high / unacceptable (e.g. score > 3). In all cases, a shared decision should be made to meet the needs and expectations of individual patients.

NICE guidelines (NG71) clarify the circumstances under which use of anticholinergic agents should be avoided, given the risk of adverse effects will likely outweigh any potential benefits in Parkinson's – these include people with significant or progressive cognitive decline, who have a confirmed history of intolerance to anticholinergic side effects, or with problematic hallucinations or delusions.

Glycopyrronium bromide

Glycopyrronium is recommended as the preferred choice of anticholinergic drug by NICE guidance (NG71) on the pharmacological management of drooling in Parkinson's disease, chiefly due to its relatively lesser effect on precipitating central side effects, such as worsening of cognitive dysfunction and other important neuropsychiatric complications.

Recommended oral doses of glycopyrronium vary in the literature for treating sialorrhoea, though as with other anticholinergic drugs it is expected doses would be gradually titrated according to clinical improvement up to the maximum tolerated dose.

The only randomised controlled trial involving people with Parkinson's utilised a dose of 1mg three times daily, whereas a maximum of 2mg three times daily has been suggested for adults across several other clinical settings, including palliative care.

Recommended glycopyrronium dose:

0.5mg once or twice daily, increase by 0.5mg increments every 7 days up to max. 2mg TDS

Glycopyrronium bromide is available as an oral solution (1mg in 5ml) but can also be procured as 1mg and 2mg tablets.

During an inpatient stay, glycopyrronium may be given as the solution for injection (200micrograms in 1ml) via the oral or enteral routes of administration, as the most cost-effective formulation for those with swallowing difficulties or enteral feeding tubes in situ.

Hyoscine hydrobromide

Hyoscine hydrobromide has central and peripheral anticholinergic effects and is more potent than atropine, but less potent that glycopyrronium – whether this translates to clinically meaningful differences in efficacy is not clear from their use in practice.

Hyoscine hydrobromide is available as a transdermal patch (1mg every 72hrs), and there is more evidence for its use via this route of administration, than with oral use; but can also be procured as 150 microgram and 300 microgram tablets for oral use.

Recommended hyoscine patch dose:

1 patch (containing 1.5mg hyoscine) every 72 hour

If necessary, for more severe symptoms, a larger dose of 2 patches may be used for short periods of time, though adverse effects such as drowsiness, confusion and sinus tachycardia are more common and should be monitored closely.

Hyoscine patches should not be cut because they are developed as reservoir systems, and so cutting would cause leakage of drug – in practice, to give a lower amount of drug, the adhesive backing can be removed for only half of the patch, and then applied to the skin.

Atropine sulphate

Sublingual administration of anticholinergic medications – most commonly, atropine – has been advocated based on the presumption there is a lower probability of central adverse effects with local delivery of drug compared to systemic administration, though little good quality evidence exists to substantiate this view.

NICE guidance (NG71) nevertheless recommends the use atropine as a topical preparation to reduce the risk of adverse effects where it is necessary to use centrally acting anticholinergic drugs. It is important to consider systemic absorption can occur and atropine crosses the blood-brain barrier to produce central side effects, as well as causing cardiac effects such as tachycardia.

Atropine does not exist as a licensed preparation for sublingual administration – the 1% ophthalmic solution is utilised to deliver the appropriate number of drops of atropine under the tongue, and is available as a 10ml bottle (contains preservative) and unit dose minims (preservative-free).

Recommended dose:

1-2 drops sublingually once daily, increase by 1 drop every 2 days up to max. 2 drops QDS

Some patients may have difficulty manipulating the dropper to ensure accurate and proper dosing and carries the risk for potential accidental overdose. It should be noted that drop size might vary with the applicator type and technique used, producing a variable dose of between 200 to 500 micrograms per drop.

Recommendations:

Despite the "unlicensed" status, the NICE guidelines recommend anti-cholinergic medication for management of sialorrhea, with caution regarding anticholinergic side effects.

Anticholinergic burden estimation is an important aspect of management of sialorrhea.

Monitoring and follow-up

Botulinum toxin therapy should be reviewed every 12 - 16 weeks at the scheduled clinic appointment prior to administration by the specialist.

Effectiveness of non-injectable therapies should be reviewed every 6 - 12 months from taking a history of symptoms, assessing improvement in quality of life, and documenting changes in the DSFS score. An acceptable target for the DSFS score should be tailored to individuals, but there is no evidence-based approach to modifying treatment strategy based on the DSFS score alone.

A baseline cognitive assessment (e.g. Montreal Cognitive Assessment (MoCA) or Abbreviated Mental Test Score) and assessment of anticholinergic burden (https://medichec.com, see Appendix 3) should be undertaken prior to starting an anticholinergic drug therapy, and subsequently performed at routine intervals to assess changes to cognitive function, or where decline is suspected during treatment. Clinicians should be aware of several potential problems that might result from the chronic and regular use of anticholinergic drugs for sialorrhoea, including:

- The risks of developing the sequelae of **dry mouth**, such as: oral infections, increased dental decay, and swallowing or speech difficulties.
- The risks of developing '**tolerance**', which requires escalating doses to recover previous drug effectiveness.
- The risks of '**withdrawal**' symptoms such as dizziness, nausea, vomiting, headache, vertigo – these have been reported on discontinuing treatment, and may be delayed or persist for longer than 24 hours.

References

Bavikatte, G. Lin Sit, P. Hassoon, A. 2012. Management of drooling of saliva. British Journal of Medical Practitioners. 5(1). 507-512

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Neurology Academy. Last update: Nov 2021. New treatment pathway for sialorrhea management in Parkinson's. Access from: https://neurologyacademy.org

NICE (National Institute for Health & Care Excellence). July 2017. Parkinson's Disease in Adults. NG71. Access from: https://www.nice.org.uk/guidance/ng71

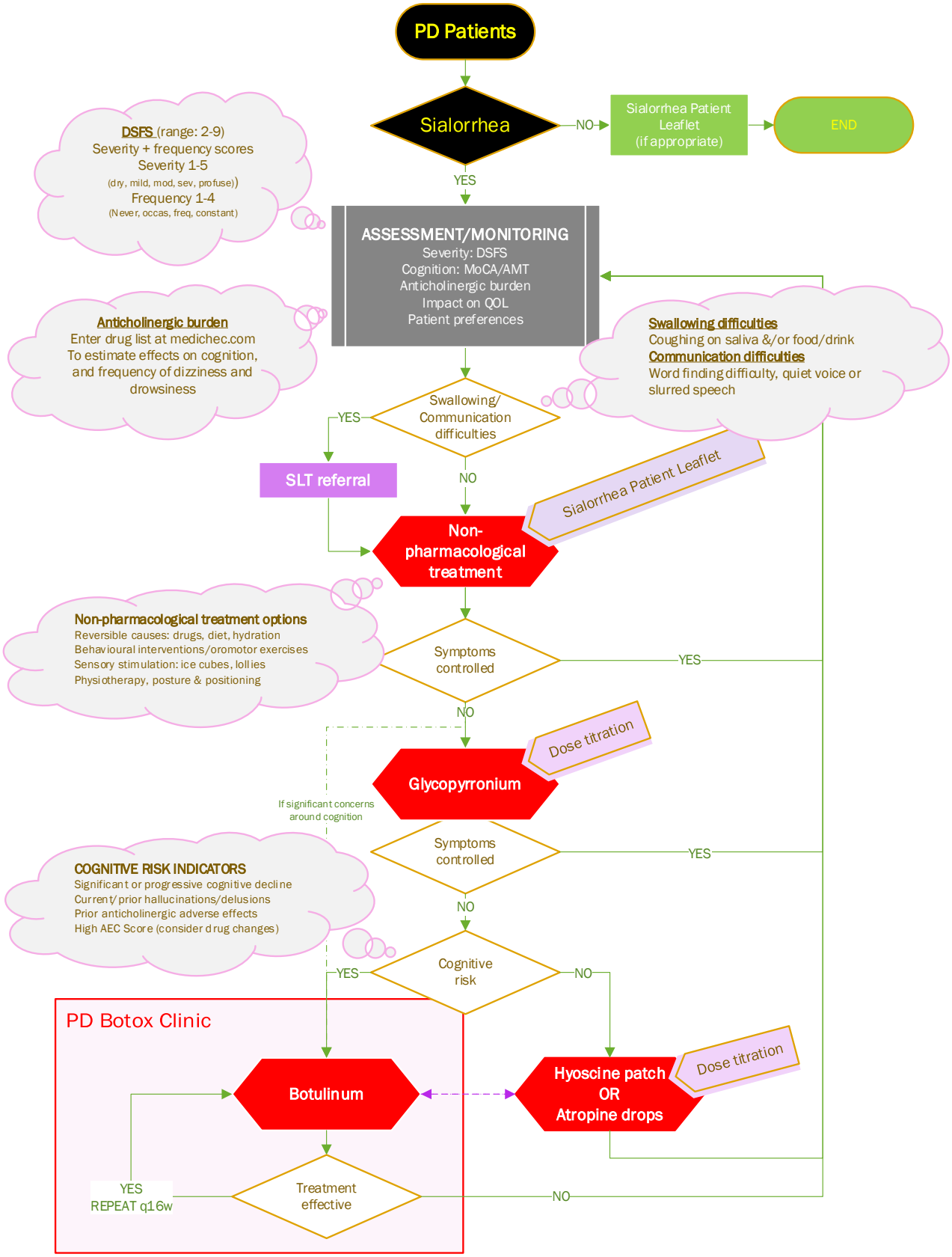
NICE (National Institute for Health & Care Excellence). Oct 2019. Xeomin (botulinum neurotoxin type A) for treating chronic sialorrhoea. TA605. Access from: https://www.nice.org.uk/guidance/ta605

Appendices

Appendix 1: Summary of non-injectable drug therapies

Drug name	Glycopyrronium bromide	Hyoscine hydrobromide	Atropine sulphate
Licensed for sialorrhoea?	Yes (paediatric only)	No	No
NICE recommendation	First line	If risk of cognitive adverse effects minimal	If risk of cognitive adverse effects minimal
Available product(s)	1mg in 5ml oral solution 1mg and 2mg tablets	1.5mg patch (1mg per 72 hr)	1% ophthalmic solution
Route(s) of administration	Oral / NG / PEG	Transdermal	Sublingual
Initial dose & titration	0.5mg once or twice daily, increase by 0.5mg every 7 days	1 patch, change every 72 hours	1-2 drops once daily, increase by 1 drop every 2 days
Maximum dose	2mg three times daily	2 patches, change every 72 hours	2 drops four times daily
Drug cost per annum	+ + +	+	+ +
Key advantages	Long duration of action; limited ability to cross BBB, lower incidence of central side effects	Useful in limited oral access or adherence issues; Convenient to administer; Achieves steady state drug levels	Fewer systemic side effects due to local application; fast onset of action and reversibility of side effects on cessation
Key disadvantages	Alternative drug formulations difficult to procure	Dose adjustment is limited; support required in limited dexterity	Short duration of action; greater risk of overdose; short shelf-life; support required in limited dexterity
Anticholinergic burden (ACB) rating	Not published	3	3

Appendix 2: Flowchart for management of sialorrhea in patients with PD



For full details, please refer to
UHL Guideline on the management of sialorrhea in adult patients with Parkinson's disease

Appendix 3: Anticholinergic Burden estimation

Medications with varying degrees of anticholinergic activity are thought to contribute to the incidence of adverse events including accelerating cognitive decline, injurious falls, confusion, hallucinations, as well as a greater risk for developing dementia/delirium. There is also an increased risk of mortality related to cardiovascular events.

There are various toolkits available to evaluate and address the impact of anticholinergic agents especially when used in combination. We propose the use of the online tool available at https://medichec.com, which provides an estimate of effect on cognition (Anticholinergic Effect on Cognition) and reported frequency of dizziness and drowsiness (Figure 1).

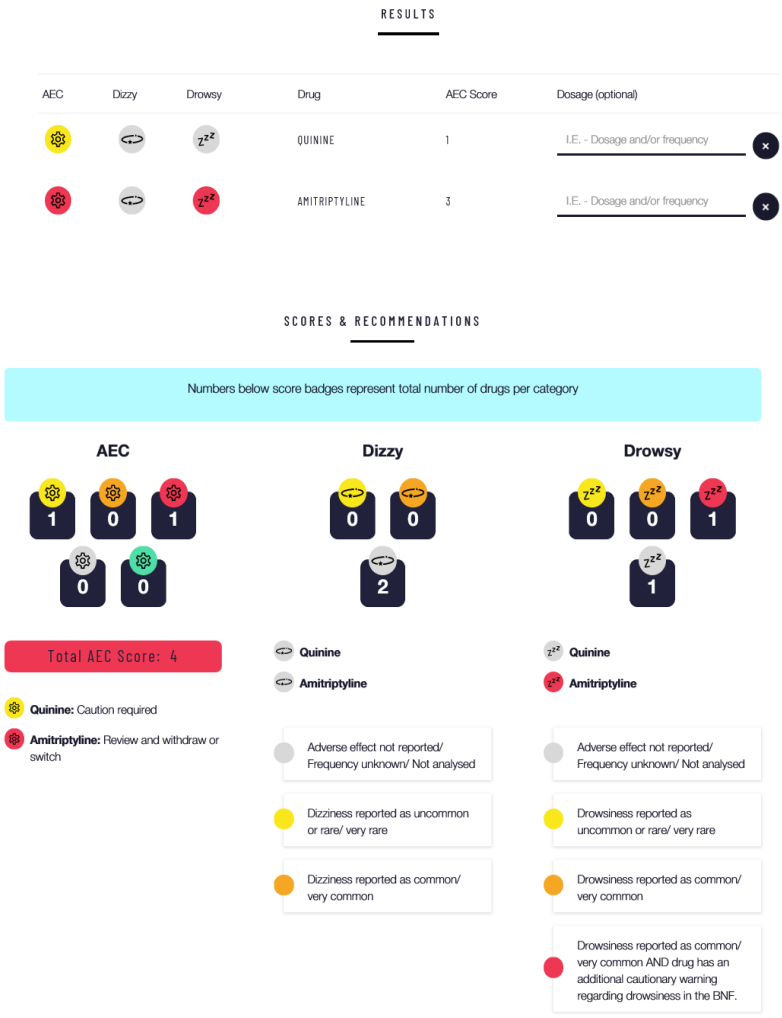


Figure 1. Snapshot from medichec.com (example using quinine and amitriptyline)

The Calculator is proposed as an aid for clinicians in shared decision-making during a medication review or when adding new drug therapies. This calculator does not include an exhaustive list of medications.

Glycopyrronium may be considered as low risk for precipitating central anticholinergic side effects, but of similar risk to hyoscine and atropine for causing peripheral side effects e.g. constipation, urinary retention, blurred vision, sinus tachycardia.

This section contains the information / guidance that staff are expected to follow. It should be set out in a logical order and bullet points, tables (such as the example below) and flow diagrams are easier to read than lots of text.

The Guideline / Procedure / Process / Protocol should be simple, succinct and easy to read. If there is lots of information within the body of the document it may be better to have an overarching policy and have the Guideline / Procedure / Process / Protocol appendices. These must then be clearly referenced within the main Guideline as associated documents.

The footer must also be completed as detailed in the footer of this template and Section 6.2.3 of the UHL Policy for Polices

Procedure / Process for xxxxxxxxxxxxx	
No.	**Action**

4. Education and Training

Are there any new skills required to implement the guideline? Is a training programme being provided to support implementation or is it more a case of 'awareness raising'

If training is being considered as 'mandatory' this must be taken through the Training, Education and Development (TED) group before the policy is approved

Awareness raising only – email shot to all clinicians intended on approval.

5. Monitoring and Audit Criteria

All guidelines should include key performance indicators or audit criteria for auditing compliance,

if this template is being used for associated documents (such as procedures or processes) that support a Policy then this section is not required as all audit and monitoring arrangements will be documented in section 8 of the Policy.

Key Performance Indicator	Method of Assessment	Frequency	Lead
Incidents related to Sialorrhea management	Ad hoc	Annual	Kate O'Kelly

6. Legal Liability Guideline Statement

See section 6.4 of the UHL Policy for Policies for details of the Trust Legal Liability statement for Guidance documents

7. Supporting Documents and Key References

If applicable

8. Key Words

List of words, phrases that may be used by staff searching for the Policy on SharePoint

Sialorrhea, Parkinson's, hypersalivation, excess salivation, glycopyrronium, hyoscine, atropine, botulinum, botox

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This table is used to track the development and approval and dissemination of the document and any changes made on revised / reviewed versions

DEVELOPMENT AND APPROVAL RECORD FOR THIS DOCUMENT		
Author / Lead Officer:	Kate O'Kelly	**Job Title:** Consultant, Lead for PD Services
Reviewed by:	ESM Q&S	
Approved by:	**Policy and Guideline Committee**	**Date Approved: 29.7.22**

REVIEW RECORD			
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**
20/07/22	1	PD Group	New guideline document

DISTRIBUTION RECORD:			
Date	**Name**	**Dept**	**Received**