The AHSN Network

Rapid Uptake Products – Technical Note 2021/22

Contents

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1. Background

1.1 The Rapid Uptake Products (RUP) Programme

The RUP programme takes a range of late-stage innovations (post-NICE appraisal) to accelerate uptake in the NHS. It has been designed to identify and support products with NICE approval that support the NHS Long Term Plan's key clinical priorities, but have lower than expected uptake to date.

For inclusion in the 2020/21 programme, RUPs were selected via an open, staged, selection process. NICE approved products were assessed based on the extent to which they met the following requirements:

- Innovations that had a positive NICE appraisal and delivered significant benefits (>1 quality-adjusted life-year gained) or any level of cost saving. Innovations were prioritised based on clinical and patient support, levels of uptake, alignment to strategic priorities, budgetary impact, barriers to overcome, and environmental sustainability.
- Clear barriers to adoption that could feasibly be addressed through collaboration convened by the Accelerated Access Collaborative at NHS England and delivered in partnership with the Academic Health Science Networks.

A wide range of stakeholders were consulted during the RUP selection process. Organisations and individuals included:

- National Clinical Directors (in the area associated with the RUP)
- NHSE clinical and policy leads
- NHS Specialised Commissioning
- Academic Health Science Network (AHSN)
- Royal Colleges (in the area associated with the RUP)
- Academy of Medical Royal Colleges
- Association of Medical Research Charities (AMRC)

The AAC and AHSNs will work with partners from across the health service and industry to identify and remove barriers to the uptake of the products in the 2020/21 RUPs programme through a bespoke package of support to increase the adoption and spread across the NHS at pace.

1.2 Purpose of this document

These notes are to provide commissioners and providers of NHS services, patients and the public with an overview of the products that are included in the Year 2 Rapid Uptake Products (RUPs) Programme, and how they benefit improving patient outcomes and the wider healthcare system.

1.3 Key Contacts

Work area	Lead AHSN	AHSN Contacts
Lipid management	North east North Cumbria	enquiries@ahns-nenc.org.uk
Asthma Biologics	Oxford	info@oxfordahsn.org
Fractional exhaled nitric oxide (FeNO)	Wessex	enquiriesahsn@wessexahsn.net
Tamoxifen	Health Innovation Manchester	info@healthinnovationmanchester.com

2. Lipid Management: High Intensity Statins, Ezetimibe and PCSK9 inhibitors

2.1 Background

The NHS Long Term Plan states that the single biggest area where the NHS can save lives over the next ten years is in reducing the incidence of cardiovascular disease (CVD). CVD causes a quarter of all deaths in the UK and is the largest cause of premature mortality in deprived areas. In 2010, 180,000 people died from CVD – around 80,000 of these deaths were caused by coronary heart disease and 49,000 were caused by strokes. Of the 180,000 deaths, 46,000 occurred before people were aged 75 years, and 70% of those were in men. CVD has significant cost implications and was estimated to cost the NHS in England almost £6,940 million in 2003, rising to £7,880 million in 2010 [source NICE CG181].

The Rapid Uptake Product (RUP) for lipid management is a novel, NICE-approved clinical pathway. This innovation aims to improve a person's lipid profile, by reducing cholesterol concentration in blood by treating patients with the right medicine along the evidence-based pathway. The pathway includes three medicines: high intensity statins (HIST), ezetimibe and PCSK9 inhibitors (PCSK9i).

HISTs include atorvastatin and rosuvastatin, which are available as generic medicines. They are prescribed and administered in primary and secondary care. PCSK9i are a novel class of cholesterol-lowering drugs that demonstrate significant reductions in LDL and non-HDL- cholesterol levels. They are recommended by NICE in certain groups of high-risk patients, when LDL cholesterol concentrations are persistently above the thresholds specified despite maximal tolerated lipid-lowering therapy. That is, either the maximum dose has been reached, or further titration is limited by intolerance. Clinical trials have shown that PCSK9 inhibitors like alirocumab and evolocumab also reduce the risk of cardiovascular events with a favorable safety and tolerability profile. PCSK9i comes only in injection form, and is initiated and prescribed in secondary care.

The focus of this RUP is secondary prevention, which occurs across both primary and secondary care. When a decision is made to prescribe a statin for secondary prevention, NICE guidance CG181 recommends using a HIST (i.e achieving more than 40% reduction of non HDL-cholesterol) at the lowest acquisition cost. The guideline recommends atorvastatin at the maximum dose of 80mg daily unless there are contraindications but rosuvastatin at 20 - 40mg daily is a suitable alternative which is now available in low cost generic formulations.

To assess adequate response of a greater than 40% reduction in non-HDL-cholesterol, NICE recommends the repeated measurement of non-HDL-cholesterol

in all people started on HIST treatment after 3 months. If adequate reduction is not achieved, then the dose of HIST should be increased, where applicable, or ezetimibe should be added to achieve further reduction in non-HDL-cholesterol (NICE TA385 (2016)). Ezetimibe works by inhibiting cholesterol absorption and offers an additional LDL cholesterol reduction of 15-20%.

If statins cannot be tolerated, then ezetimibe monotherapy can be considered for in those with primary hypercholesterolaemia (heterozygous FH or non-FH).

Annual medication review for people taking lipid lowering therapies is recommended by NICE, to ensure optimal lipid management. Primary care systems, such as SystmOne or EMIS, can be used to inform these assessments.

This innovation is appropriate for use in:

- Primary care
- Secondary care

2.2 Aim and Objectives

The aim of this innovation will be to improve patient care and outcomes by effectively treating patients with hypercholesterolaemia.

Objectives:

- To reduce the risk for heart attacks and strokes occurring
- To reduce the risk of admissions and re-admissions associated with cardiovascular disease
- To reduce health inequalities by ensuring a consistent, national approach to lipid management, through the use of a NICE approved clinical pathway
- To provide more treatment options to high-risk patients who remain at risk despite maximum tolerated statin therapy.

2.3 How to access the RUP

HIST and ezetimibe are available as generic medicines and are prescribed and administered in both primary and secondary care settings, unlike PCSK9i where general practice prescribing is unavailable. HIST and ezetimibe are oral therapy/treatments, whereas PCSK9 inhibitors are injectables.

Primary prevention occurs mainly in primary care where the risk of CVD is assessed. When a decision is made to prescribe a statin, CG181 recommends using one of high-intensity (produce on average more than 40% LDL-cholesterol reduction) and

low acquisition cost. The guideline refers to atorvastatin 20-80mg daily, but rosuvastatin 10-40mg daily also now applies following a price reduction.

2.4 Clinical Standards

Sites adopting this technology must:

Follow NHS, AAC and NICE approved guidance for lipid management found here.

Inclusion criteria:

Secondary prevention adults who are at risk of or who have cardiovascular disease (CVD), such as heart disease and stroke.

Applicable NICE reviews:

- Cardiovascular disease: risk assessment and reduction, including lipid modification: Clinical guideline [CG181]
- Familial hypercholesterolaemia: identification and management: Clinical guideline [CG71]
- Ezetimibe for treating primary heterozygous-familial and non-familial hypercholesterolaemia - Technology appraisal guidance [TA385]. This guidance should be used with NICE's guidelines CG181 and CG71.
- Lipid-modifying drugs - Key therapeutic topic [KTT3]
- Cardiovascular risk assessment and lipid modification - Quality standard [QS100].
- A Summary of National Guidance for Lipid Management for Primary and Secondary Prevention of CVD, can be found here. The Statin Intolerance Pathway can be found here. Both documents are included as resources within Technology appraisal guidance [TA385].

2.5 Reporting

Reporting is conducted by prescription numbers across primary and secondary care, at both Trust and AHSN level.

3. Measuring fractional exhaled nitric oxide (FeNO) concentration in asthma: products NIOX VERO and NObreath

3.1 Background

Over 5.4 million people suffer from asthma in the UK of which 1.1 million are children (1 in 11) and 4.3 million are adults (1 in 12). The NHS spends around £1 billion a year treating and caring for people with asthma. Statistics released from Asthma UK show that over 120,000 asthma sufferers in the UK are at risk from wrongly prescribed medication. Findings from NICE demonstrate that 30% of people with asthma and NICE's findings that 30% of people with asthma are suspected to have been misdiagnosed and could potentially be on medications that they do not need. To address this in the Long Term Plan, the NHS outlined a commitment to support the diagnosis of respiratory conditions, including accurate diagnosis of asthma.

FeNO testing is a method of diagnosing asthma by measuring fractional exhaled nitric oxide in the breath of patients suspected of having asthma. This produces a FeNO score which is indicative of active inflammation in the airway of asthma patients and can therefore be used to accurately diagnose asthma, in conjunction with other objective tests. The FeNO score can indicate how well a patient is responding to a particular treatment, which could then be adjusted accordingly.

FeNO testing would occur within primary care where the risk of COVID-19 would be assessed. According to the Association of Respiratory Technology and Physiology, FeNO testing is regarded as low risk of being an aerosol-generating procedure and is therefore low risk of spreading COVID-19.

FeNO testing has been recommended by NICE to help diagnose asthma. This innovation aims to improve patient care by providing rapid and accurate diagnosis of asthma.

3.2 Aim and Objectives

The aim of this innovation will be to improve patient care and outcomes by more effective diagnosis of patients suspected of having asthma. FeNO monitoring also has the potential to improve management of asthma patients by using the test to inform further adjust dosing of steroids or guide biological agent treatment.

Aims:

- Improve patient care and outcomes by more effective diagnosis of patients suspected of having asthma

Objectives

- Be able to measure fractional exhaled nitric oxide (FeNO) concentration in the patient's breath
- Improve management of asthma patients by using FeNO monitoring to adjust dosing of steroids or guide biological agent treatment
- Reduced referral to secondary care clinics
- Reduced use of Salbutamol (associated risk with >12 inhalers per year)
- Reduction in Prednisolone rescue steroid prescribing
- Reduction in emergency hospital admissions
- Reduction in A&E attendances

3.3 How to access the RUP

NIOX VERO, manufactured by Circassia, and NObreath, manufactured by Bedfont Scientific, have both been recommended by NICE for the diagnosis of asthma. Both devices measure fractional exhaled nitric oxide as a biomarker for Type 2 inflammation in the lungs of asthma patients and produce a FeNO score in parts per billion (ppb).

FeNO testing could be offered by a clinician in any of the following settings;

- GP practices
- Specialist respiratory clinics/diagnostic hubs
- Lung function departments
- Respiratory wards

3.4 Clinical Standards

Applicable NICE guidelines:

- Measuring fractional exhaled nitric oxide concentration in asthma: NIOX MINO, NIOX VERO and NObreath. Diagnostics guidance [DG12]
- Asthma: diagnosis, monitoring and chronic asthma management. NICE guideline [NG80]

Sites adopting this technology must:

- Follow the NICE approved guidance by performing FeNO as an objective test for asthma

- Offer a FeNO test to adults (aged 17 and over) where clinically indicated, if a diagnosis of asthma is being considered, regarding a FeNO level of 40 parts per billion (ppb) or more as a positive test
- Consider a FeNO test in children and young people (aged 5 to 16) if there is diagnostic uncertainty after initial assessment and they have either normal spirometry or obstructive spirometry with a negative bronchodilator reversibility (BDR) test. A FeNO score of 35 ppb or more can be considered a positive test

Exclusion criteria:

- FeNO testing is not suitable for children of 4 years of age or younger

3.5 Reporting

Uptake will be monitored through the national sales data of devices and mouthpieces on a monthly basis. The data collected will act as a proxy for the following measures:

- Device Sales – Represent increasing access
- Mouthpiece Sales – Representing increasing impact

The sales data will be provided by the suppliers of Niox Vero and NObreath who are supporting with the FeNO Rapid Uptake Product programme. In addition, we will also receive postcodes of areas suppliers have sold to so we can infer geographical impact of the programme and spread of adoption.

4. Biologics for treating severe asthma: Reslizumab, Benralizumab, Mepolizumab and Omalizumab

4.1 Background

Severe asthma (in particular eosinophilic severe asthma) does not respond to standard treatment alone and requires more intensive therapies to control symptoms to prevent asthma attacks, hospitalisations and deaths.

The precise population of those with severe asthma in the UK is currently unknown. The proportion is often estimated to be 5% of the total asthma population, and the most recent publicly available data shows 2,397 patients (November 2019) on the UK Severe Asthma Registry. Asthma UK estimate that there are up to 200,000 undiagnosed severe asthma patients (*Slipping through the net*, Asthma UK, 2018, and, *Living in limbo,* Asthma UK, 2019).

In the UK, the average asthma death rate is almost 50% higher than the EU average. In 2014 (the most recent data), 1,216 people died from asthma in the UK.

As well as patient outcomes, this has a severe impact on the NHS, patients and services:

- Cost: the NHS spends around £1billion a year on asthma patients
- Hospitalisations: asthma attacks hospitalise someone every 8 minutes; a child is admitted to hospital every 20 minutes due to an asthma attack
- Overburdened services: almost two thirds (65%) of people with asthma are not receiving the basic care from healthcare professionals
- Access: 57% of people who died from asthma were not recorded as being under specialist supervision during the 12 months prior to death. 43% were managed in secondary care (SC) or tertiary Care (TC), which is the most appropriate setting for care

People with difficult or severe asthma should be managed differently to those with mild or moderate asthma. Biologic therapies provide an effective treatment option for those with severe asthma and reduces reliance on oral corticosteroids (OCS) which are known to have debilitating side effects (such as weight gain, bone weakening and mood changes).

These biological agents can transform patient lives by reducing long-term side effects of other treatments and can also reduce the number of exacerbations and life-threatening asthma attacks. Large numbers of patients who would qualify for

these drugs are not currently able to access them, as highlighted in Asthma UK's report *Do no harm.*

The objectives will be to:

- To improve awareness and access to biologics for appropriate patients
- To increase appropriate referrals to severe asthma centres
- To reduce the reliance on oral corticosteroid therapy where an asthma biologic may be appropriate
- To increase the number of appropriate patients on Homecare

4.2 How to access the RUP

Reslizumab is currently supplied to the NHS under a Simple Patient Access Scheme (PAS) that was outlined in the NICE guidance which includes a discount from the list price.

Benralizumab is associated with a confidential net price agreement. It is available through NHS Supply Chain's direct to pharmacy model. Service Level Agreements are in place for provision through Astra Zeneca's (AZ) funded Homecare services.

Mepolizumab has a confidential Patient Access Scheme in operation that provides a straight discount on price. It is available directly from GlaxoSmithKline's (GSK) approved wholesaler to NHS Trusts or supplied to patients via the GSK-funded homecare service.

Omalizumab is supplied direct to pharmacies, who order it direct from Novartis.

These products can only currently be accessed after appropriate assessment by a multi-disciplinary team under the oversight of severe asthma centres.

4.3 Clinical Standards

This innovation must be appropriate for use in the following settings:

- Prescribed by severe asthma centres (specialist centres or satellite centres)
- Administration in severe asthma centres or home settings with increasing uptake of self-administration

Sites adopting this technology must:

- Follow NICE approved guidance and the licensed product literature (for dosing and administration instructions)

- Support home monitoring and encourage patients to self-administer where appropriate .

Exclusion criteria:

- Use in children and/or adolescents for some of the biologic products is not licensed
- Hypersensitivity to active substances or any excipients
- These biologics are not to be used to treat the acute phase of the condition (i.e. during asthma exacerbations/attacks)

Applicable NICE reviews:

- Reslizumab for treating severe eosinophilic asthma: Technology appraisal guidance (TA479)
- Benralizumab for treating severe eosinophilic asthma: Technology appraisal guidance [TA565]
- Mepolizumab for treating severe refractory eosinophilic asthma: Technology appraisal guidance [TA431]
- Mepolizumab for treating severe eosinophilic asthma [ID3750]. In development [GID-TA10622] Expected publication date: 03 February 2021
- Omalizumab for treating severe persistent allergic asthma: Technology appraisal guidance [TA278]

4.4 Reporting

Uptake will be monitored nationally through the review of new patient initiations on a monthly basis.

In addition to the current uptake data, we will seek to understand how the programme impacts the following proxy measures:

- Use/prescribing of steroids (inhaled and oral)
- Proportion of patients on home/self-administration

5. Licensed repurposed therapies for use in managing breast cancer risk in people with a family history: Tamoxifen

5.1 Background

Approximately 3.7% of England's female population aged 35–74 were previously found to have moderate or high risk of breast cancer by application of NICE criteria (up to 500,000 women may be eligible for chemoprevention). Tamoxifen has been shown to reduce the risk of breast cancer by 30-50% seven years after taking them for five years. It is the first licensed repurposed medicine for chemoprevention in women at risk of developing breast cancer (this includes those with known BRCA1, BRCA2 and TP53 mutations).

Uptake of prophylaxis tamoxifen may be low in clinical practice (roughly 10% in England) due to factors such as access to a prescriber after women have been identified as at high risk, GP confidence in prescribing these treatments, and patient information.

5.2 Aim and Objectives

The aim of this innovation is to improve patient care and outcomes by effectively providing chemoprevention in women at risk of developing breast cancer.

The objectives of this Rapid Uptake Product are to:

- Increase prescribing of Tamoxifen for prophylaxis
- Reduce the number of women developing breast cancer
- Reduce the number of women ceasing treatment early

This will have downstream benefits in terms of:

- Reducing risk of avoidable illness for patients
- Delivering care cost effectively through preventative medicine
- Reduction of demand for NHS oncology services
- Personalised care improves patient experience ensuring confidence to seek healthcare when needed.

5.3 How to access the RUP

Healthcare professionals within secondary care or specialist genetic clinics should discuss the absolute benefits and risks of options for chemoprevention with women at high or moderate risk of breast cancer. If appropriate, they can be prescribed Tamoxifen for breast cancer prevention. Repeat prescriptions can be issued by a GP practice.

Prescriptions for chemoprevention can be issued in primary care following recommendation (in some regions following initiation) by a specialist. These prescriptions are then dispensed by community pharmacies:

Tamoxifen is listed in Part VIIIA of the NHS Drug Tariff. All drugs listed in this Part have a pack size and price which has been determined by the Secretary of State for Health as respects England and the Welsh Ministers as respects Wales.

Tamoxifen is listed in Part VIIIA of the NHS Drug Tariff. All drugs listed in this Part have a pack size and price which has been determined by the Secretary of State for Health as respects England and the Welsh Ministers as respects Wales.

Tamoxifen 10mg are Category A: Drugs which are readily available. The prices listed in this Part of the Drug Tariff are indicative of the prices determined by the Secretary of State for Health. (The price is based on a weighted average of the List Prices from 2 wholesalers and 2 generic manufacturers).

Tamoxifen 20mg are Category M: Drugs which are readily available. The Secretary of State determines the price based on information obtained under the Health Service Products (Provision and Disclosure of Information) Regulations 2018 (i.e. the Department of Health and Social Care calculates the reimbursement price based on information submitted by manufacturers)

Prices therefore are not static. Category M drugs in particular change on a quarterly basis.

Tamoxifen is a generic drug and we have identified 6 suppliers through consultation with NICE and the British Generic Manufacturers Association. There may be additional unidentified suppliers.

10mg

- Teva UK
- Wockhardt UK
- Rosemont Pharmaceuticals (10mg/5ml oral solution)

20mg

- Wockhardt UK
- Genesis
- Mylan

Tillomed Labs are a UK Marketing authorisation Holder for both 10mg and 20mg.

5.4 Clinical Standards

This innovation must be appropriate for use in:

- Primary Care
- Outpatient Clinic
- Breast Screening Centres

For women at **high risk** of breast cancer, tamoxifen can be offered for 5 years unless the patient has a past history or may be at increased risk of thromboembolic disease or endometrial cancer.

For premenopausal women at **moderate risk** of breast cancer, tamoxifen can be offered for 5 years, unless they have a past history or may be at increased risk of thromboembolic disease or endometrial cancer.

For postmenopausal women at **moderate risk** of breast cancer who have severe osteoporosis or do not wish to take anastrozole, tamoxifen can also be considered for 5 years if they have no history or increased risk of thromboembolic disease or endometrial cancer.

Sites adopting this technology must:

- For Tamoxifen Rosemont 10mg/5ml Oral Solution 150ml an additional step to identify that a patient has a need or requirement for a liquid over an oral solid dose. Understanding the importance of a multidisciplinary team in treating a patient experiencing difficulties with swallowing i.e. Pharmacists & SaLT.

Exclusion criteria:

- Non-NHS patients

Applicable NICE reviews:

Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer [CG164]

5.5 Reporting

Reporting methodology is still in development but will look at the increase in the total / cumulative number of women receiving Tamoxifen (including new initiations and women who have been receiving the drug for a period of time). It is anticipated that data will be drawn from Public Health England and/or NHS Business Services Authority.