Ultra Orphan and IMD Risk Shares

NSD hosted risk sharing arrangements for medicines for very rare diseases : A Guide

June 2024

Introduction

The aim of this guide is to provide an overview of NSD hosted risk sharing arrangements for ultra orphan conditions.

This pack has been designed for NSD and NSS staff as well as finance and pharmacy colleagues in health boards that prescribe medicines that are covered by risk sharing arrangements. It would also benefit any staff within health boards interested in learning more about risk sharing arrangements for very rare conditions.

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Introduction to NSD

National Services Directorate commissions specialist health services and national networks. We also coordinate national screening programmes.

The directorate aims to ensure that patients in Scotland have access to high quality specialist healthcare services and screening services.

We are a diverse team of programme management and commissioning experts including clinical and public health professionals, all working within the governance of NHS Scotland.

We are committed to delivering a 'once for Scotland' approach that:

- Reduces variation and duplication of effort
- Drives consistency
- Ensures patients are at the centre of all decisions about their care
- Fosters a clinical focus
- Ensures equal access to specialist and highly specialist services for all residents of Scotland
- Based on collaboration with internal and external stakeholders
- Offers value for money

Risk sharing principles and overview

Risk sharing involves the pooling of funding from all territorial health boards, to manage the financial impact of any unpredictable expenditure in relation to very rare conditions, interventions or very high cost medicines.

Every board contributes a proportion of the costs based on their size and population profile for an agreed list of treatments or medicines. Without these schemes, an individual health board could face significant financial risk.

Risk sharing is sponsored by the boards. In principle, boards can decide to fund other treatments and products through risk sharing.

Currently NSD hosts the following risk sharing arrangements agreed to by the boards:

- Forensic Medium-Secure Care for patients with learning disabilities
- Inherited Bleeding Disorders
- Ultra-Orphan (UO) Drugs
- Inherited Metabolic Disorders Medicines (IMD)
- CAR-T therapies
- Lutathera Therapy for Neuroendocrine Tumours

This guide covers arrangements for UO and IMD medicines.

NSD UO Risk Sharing pre 2020

NSD has hosted risk sharing arrangement for medicines for some rare disease since 2005.

Most of them were medicines to treat Inherited Metabolic Disorders (IMD). This scheme was referred to as the Orphan Risk Share and was later renamed the Ultra Orphan Risk Share in 2014.

Risk sharing, and risk sharing for Medicines in particular, has been reviewed a number of times. They key reviews and changes are highlighted in the blue box.

Reviews and changes

2013 - general review of risk sharing

2014/15 - review of Orphan Drug Risk Share

- Response to New Drugs Fund and New Medicines Fund
- led to renaming from Orphan Drugs Risk Share to Ultra Orphan Drugs Risk Share
- decision to not add any new non-SMC approved medicines

Jan 2018 - options appraisal to address cost of risk share

April 2020 - guidance to include Ultra Orphan Pathway medicines in NSD risk sharing arrangements approved by Board Chief Executives

Scottish Government Ultra Orphan Pathway

In 2018 the Scottish Government announced a new system for the assessment of medicines for very rare diseases – the Ultra Orphan Pathway

Drugs that fulfil the pathway criteria can be made available to patient treated by the NHS in Scotland for a period of three years prior to a decision on routine use in NHS Scotland.

Operational guidance was issued by the Scottish Government in 2019 including the initial list of Ultra Orphan pathway medicines.

The policy is based on the assumption medicines for very rare diseases should be treated differently to drugs to that treat more common conditions.

Medicines for very rare diseases often involve very small trial cohorts which means that the evidence base is often weaker than for other drugs.

This, combined with usually high acquisition costs has often led to SMC not recommending these medicines for routine use.

While non SMC approved medicines can be prescribed via non-formulary process such as IPTR and PACS, but there are concerns about equity of access for all patients (see Montgomery Review).

Ultra Orphan Pathway requirements

Ultra Orphan Medicine (SMC definition)

To be considered as an ultra-orphan medicine all criteria listed should be met:

- the condition* has a prevalence of 1 in 50,000 or less in Scotland,
- the medicine has a Great Britain (GB) orphan marketing authorisation from the Medicines and Healthcare products Regulatory Agency (MHRA)
- the condition is chronic and severely disabling, and
- the condition requires highly specialised management.

Official status as a UO medicine (as per SMC definition) is dependent on validation of SMC status.

Not all medicines for very rare diseases have official UO status

See appendix for further definitions and terms.

Pharmaceutical companies have to fulfil the four criteria set out below for a medicine to become available through the pathway. This involves working with three organisations: SMC, National Procurement and the Scottish Government.

- Make a submission to SMC to validate a medicine as an ultra-orphan drug. The medicine has to meet the definition set out by SMC.
- Full submission to SMC for the initial assessment stage that meets SMC requirements for assessment under the ultra-orphan process.
- Offer acceptable Patient Access Scheme (PAS) (discounted price) to the Patient Access Scheme Assessment Group (PASAG)
- Agree data collection arrangements with SG to enable evidence generation to support re-assessment under the ultra-orphan pathway

Medicines will be reviewed by SMC after 3 years of availability to make a recommendation about routine use.

Ultra Orphan Risk Sharing since 2020

The Directors of Finance agreed in principle in 2019 that a risk sharing scheme should be set up to fund medicines that become available through the ultra orphan pathway policy.

In addition, there was also a request to consider existing risk-sharing financial arrangements administered by NSD on behalf of NHS Scotland, and possible synergies between the proposed new scheme and various existing risk sharing arrangements.

In April 2020 NSD's proposal for updated ultra orphan risk sharing arrangements was approved by the Board Chief Executives.

It was agreed that medicines which completed the pathway would be funded through a new Ultra Orphan Risk Share. Medicines would be added automatically once all four conditions of the pathway are complete.

It was further decided that medicines for rare diseases which were already risk shared, should continue to be funded in this way, including for 3 medicines that require non-formulary approval. As the pre 2020 Ultra Orphan Risk Share mainly contained medicines to treat IMD, a sperate list of IMD risk shared medicines was created.

A small number of other medicines/indications were added to the new 2020 Ultra Orphan Risk Sharing list for practical reasons.

Medicines approved in April 2020. (See page 12 and 13 for most up to date lists).

2020 Ultra Orphan Risk Share List
Nusinersen (SMC1318/18) - Spinal Muscular Atrophy (SMA) Type II and III
Nusinersen (SMC1318/18) - Spinal Muscular Atrophy (SMA) Type I
Voretigene nepaparvec (SMC2228) - Inherited retinal dystrophy (IRD) caused by RPE65 mutations
Burosumab (SMC2240) - X-linked hypophosphataemia (XLH) in children and adolescents
Patisiran (SMC2157) - Hereditary tranthyretin-mediated amyloidosis with stage 1 or stage 2 polyneuropathy (hATTR)
Inotersen (SMC2188) - Stage 1 or stage 2 polyneuropathy in heriditary transthyretin amyloidosis (hATTR)
Mifamurtide (SMC621/10) - Mifamurtide (Mepact) for the treatment of high-grade resectable non-metastatic osteosarcoma in children, adolescents and young adults.

IMD Risk Share Medicines (pre 2020 Ultra Orphan Risk Share)
Agalsidase alpha (Replagal) - Fabry Disease
Agalsidase beta (Fabrazyme) - Fabry Disease
Miglustat (Zavesca/Vevesca) - Gaucher Disease
Velaglucerase (Vpriv) - Gaucher Disease
Migalastat (Galafold) - Fabry Disease
Eliglustat (Cerdelga) - Gaucher Disease
Carbaglu (N-carbamoyl-L-glutamic acid) – Hyperammonaemia
Alglucosidase alfa (Myozyme) - Pompe disease (Subject to PACS)
Laronidase (Aldurazyme) MPS 1, Hurler-Scheie or Scheie syndrome (Subject to PACS)
Idursulfase (Elaprase) MPS II, Hunters syndrome, (Subject to PACS)

Non-Ultra Orphan Pathway Medicines and Risk Sharing

Apart from the medicines for rare conditions that were risk shared prior to 2020, the new Ultra Orphan Risk Share and IMD Risk Share contain a number of medicines/indications that have not completed the UO pathway but that were added to the scheme for practical reasons.

Nusinersen for SMA Type 1

While nusinersen for SMA Type II and III was approved through the Ultra Orphan pathway, nusinersen for SMA Type I has been recommended by SMC for routine use in Scotland. The company is not required to make an updated submission to SMC for this indication after 3 years.

It was recommended to BCE that this indication be included in the risk share to minimize confusion about funding streams.

Inotersen and Patisiran

Inotersen for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hereditary transthyretin amyloidosis (hATTR) was accepted by SMC in August 2019.

Although validated as an UO according to the new definition, the company chose to submit through the previous UO process just prior to it closing, which means that there is no requirement for data collection and reassessment after 3 years.

Patisiran for the same indication was also recommended by SMC in June 2019 and would also have been likely to be eligible for the new pathway.

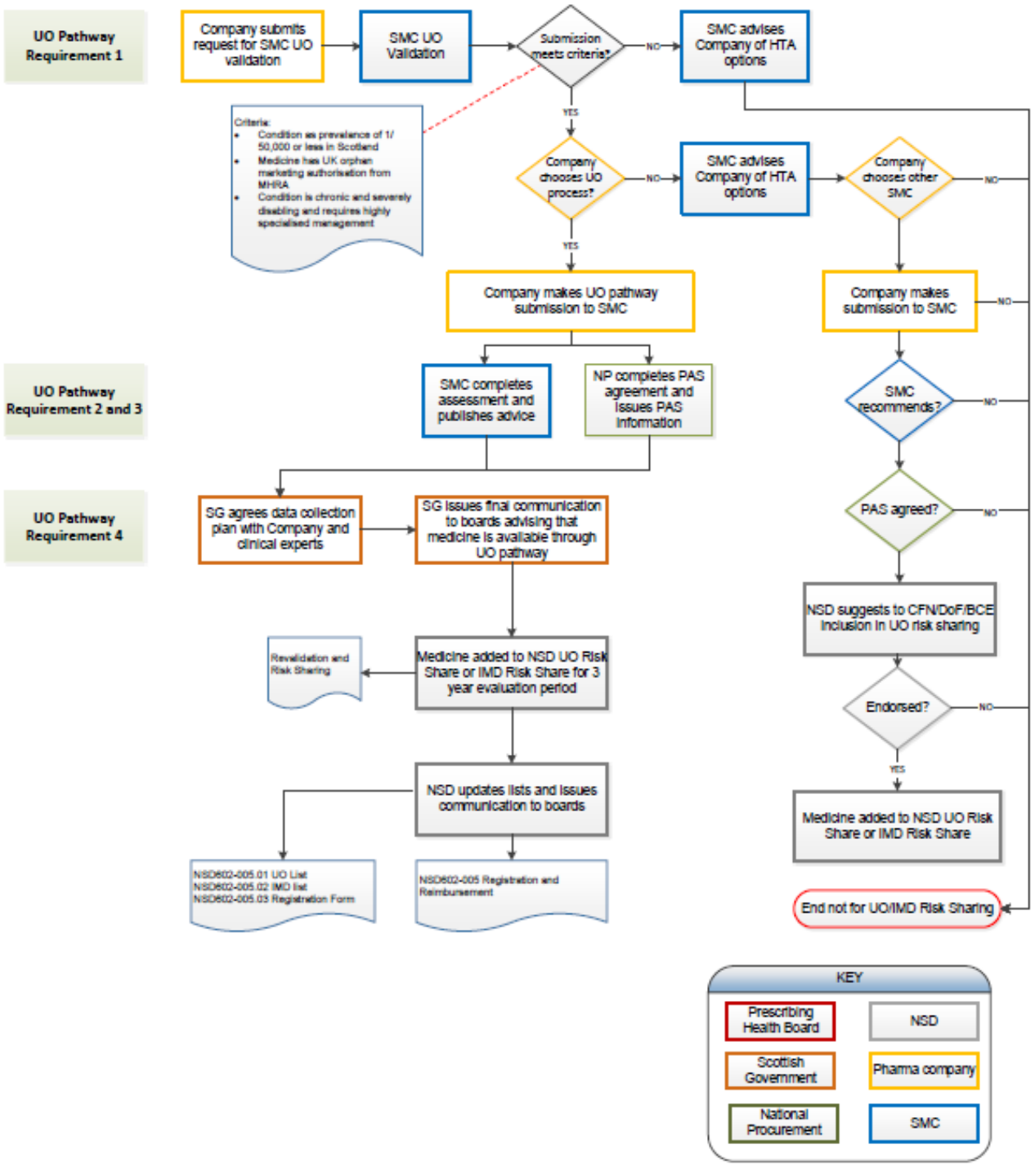
Both medicines have been approved subject to a PAS agreement.
Given that both medicines have been approved by SMC and meet the updated UO definition, it was to BCE to include both products in the UO risk sharing arrangements.

Onasemnogene abeparvovec (Zolgensma) for treatment of patients with SMA was approved by SMC for restricted use in 2021. The gene therapy was included on cost grounds and to ensure equity of funding streams for high cost medicines for SMA.

Risdiplam (Evrysdi) for the treatment of SMA was accepted for use by SMC in 2022. The medicine was included on cost grounds and to ensure equitable funding streams for high cos medicines for SMA.

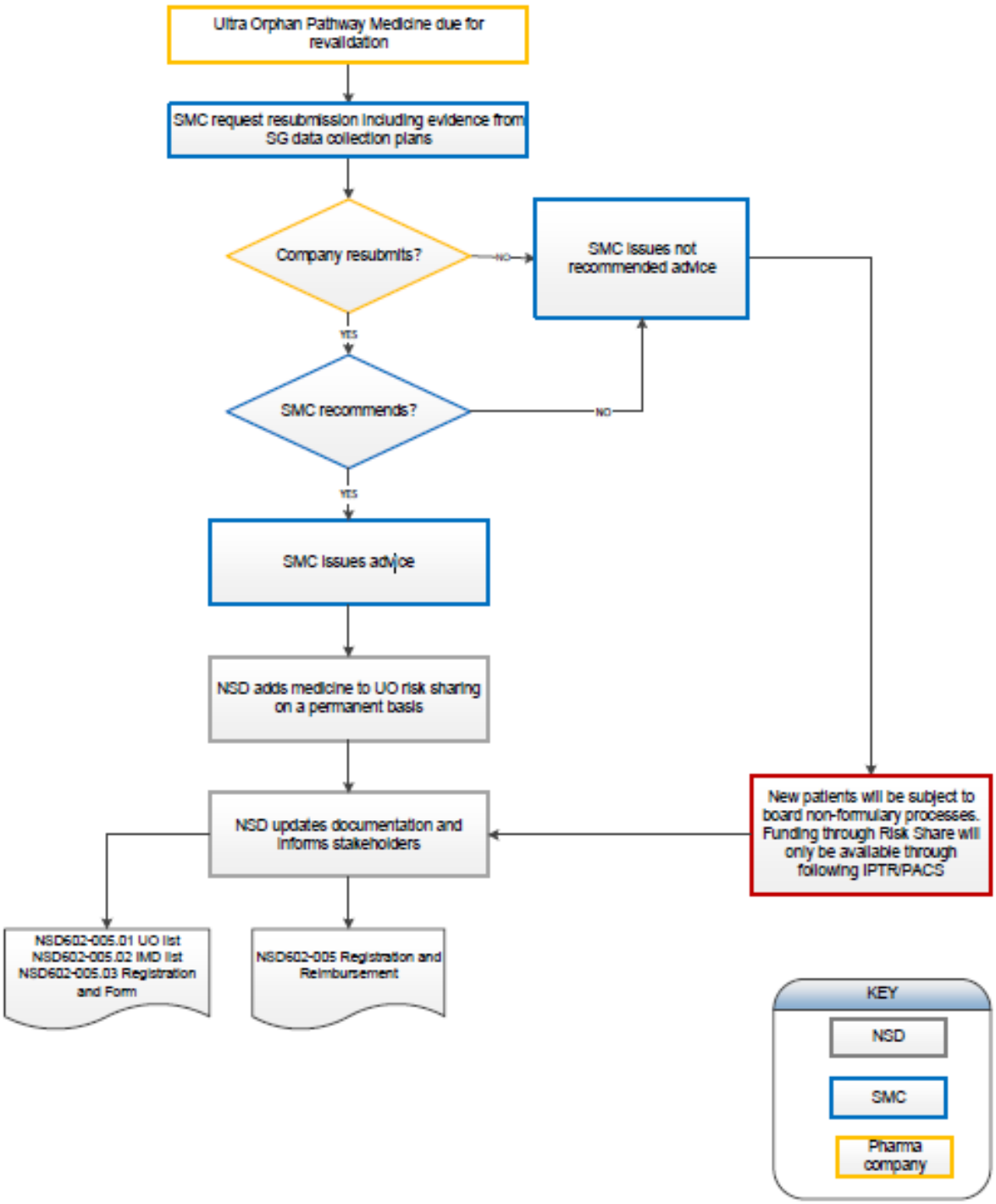
Avalglucosidase alfa (Nexviadyme) for the treatment of Pompe disease was approved by SMC in 2023. The medicine was added to the IMD Risk Share as it is a therapeutic alternative to the medicine Alglucosidase alfa (Myozyme), which is already risk shared.

From Ultra Orphan Pathway (or other SMC approval) to UO or IMD Risk Share (NSD602-005.06)



Funding for Ultra Orphan Pathway Medicines following revalidation by SMC

The below approach was agreed by the BCE in April 2020. A review of these arrangements may be prudent now that the scheme has been in operation for 3 years.



Registration and reimbursement

NSD reimburses boards for the cost of the medicines that are included on the Ultra Orphan or IMD Risk Share Lists from the date that they have been added to either scheme.

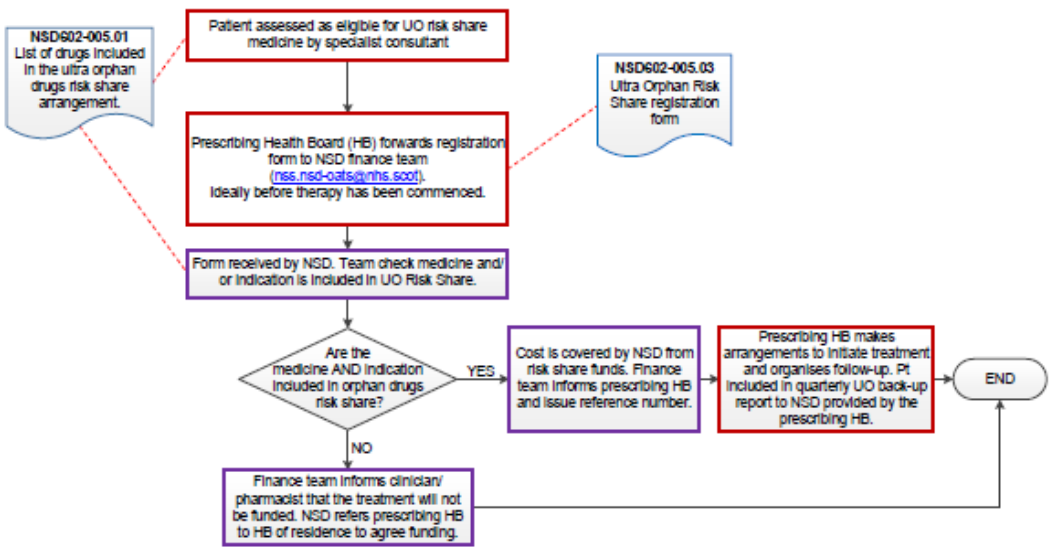
Prescribing boards are asked to complete a registration for each new patient that they wish to commence on a medicine that is included in the Ultra Orphan Risk Share List. This enables NSD to forecast and plan. It also supports the reconciliation of invoices.

As the medicines on the IMD risk share list are prescribed through the IMD service commissioned by NSD, a registration form is only required for medicines that have been added to the list via the ultra orphan pathway to ensure the use of these medicines is tracked.

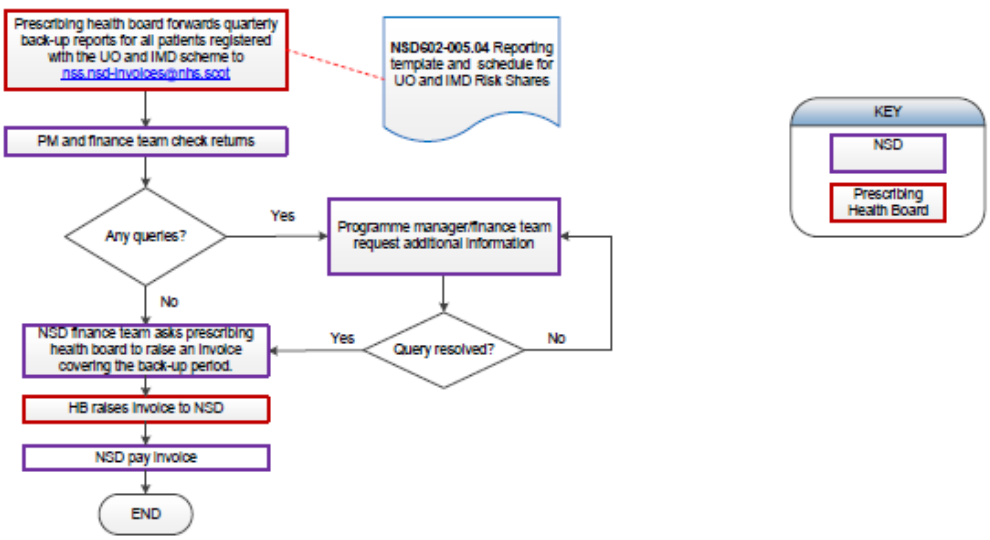
Boards must submit quarterly usage reports and invoices to NSD for IMD and UO risk share medicines. Prescribing boards are also required to inform NSD of any changes (dosage, therapy stopped) as soon as possible.

below: **(NSD602-005)**

Patient Registration Process



UO (and IMD) Risk Share Reimbursement Process



Summary and useful information

The Ultra Orphan Pathway and the Ultra Orphan Risk Share are not one and the same. The Ultra Orphan Pathway is a Scottish Government Policy. The other is a financial mechanism endorsed by the boards for funding ultra orphan pathway medicines in addition to other high cost drugs for rare diseases.

- Ultra Orphan Pathway medicines are added to the Ultra Orphan or IMD Risk Shares automatically once all four pathway requirements are in place
- Other SMC recommended medicines can be added if supported by the boards
- In recent years, this has mainly happened in the case of SMC approved medicines that are a clinical alternative to products that are already covered by either scheme
- Prescribing boards must register new patients and submit quarterly usage reports (including any changes) and invoices to NSD within the specified deadlines

- **Scottish Government Guidance**

  https://www.gov.scot/publications/ultra-orphan-medicine-pathways-guidance/
- **SMC guidance**

  https://www.scottishmedicines.org.uk/how-we-decide/ultra-orphan-medicines-for-extremely-rare-conditions/
- The up to date Ultra Orphan and IMD Risk Share lists are available online
- **Ultra Orphan Risk Share**

  https://www.nss.nhs.scot/specialist-healthcare/financial-risk-share/ultra-orphan-medicines/
- **IMD Risk Share**

  https://www.nss.nhs.scot/specialist-healthcare/financial-risk-share/ultra-orphan-medicines/
- For queries about the Ultra Orphan and IMD Risk Shares and to get a registration form email: nss.nsd-oats@nhs.scot

Ultra Orphan Risk Share Medicines

Afamelanotide (Scenesse®) for prevention of photoxicity in adult patients with erythropoietic protoporphyria (EPP).

Ataluren (Translarna®) for the treatment of Duchenne muscular dystrophy (DMD) resulting from a nonsense mutation in the dystrophin gene, in ambulatory patients aged 2 years and older.

Atidarsagene autotemcel (Libmeldy®) for the treatment of metachromatic leukodystrophy.

Burosumab (Crysvita®) for the treatment of X-linked hypophosphataemia (XLH) with radiographic evidence of bone disease in children 1 year of age and older and adolescents with growing skeletons.

Burosumab (Crysvita®) for the treatment of X-linked hypophosphataemia (XLH) in adults.

Inotersen (Tegsedi®) for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hereditary transthyretin amyloidosis (hATTR).

Metreleptin (Myalepta®) an adjunct to diet as a replacement therapy to treat the complications of leptin deficiency in lipodystrophy (LD) patients.

Mifamurtide (Mepact®) for the treatment of high-grade resectable non-metastatic osteosarcoma in children, adolescents and young adults.

Nusinersen (Spinraza®) for Spinal Muscular Atrophy (SMA) Type I.

Nusinersen (Spinraza®) for SMA Type II and III.

Odevixibat (Bilvay®) for treatment of progressive familial intrahepatic cholestasis (PFIC) in patients aged 6 months or older.

Onasemnogene abeparvovec (Zolgensma®) treatment of patients with 5q spinal muscular atrophy (SMA) with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of SMA type 1, or patients with 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene.

Patisiran (Onpattro®) for the treatment of hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis) in adult patients with stage 1 or stage 2 polyneuropathy.

Risdiplam (Evrysdi®) for the treatment of 5q spinal muscular atrophy (SMA) in patients 2 months of age and older, with a clinical diagnosis of SMA type 1, type 2 or type 3 or with one to four SMN2 [survival of motor neuron 2] copies.

Voretigene neparvovec (Luxturna®) for the treatment of adult and paediatric patients with vision loss due to inherited retinal dystrophy caused by confirmed biallelic RPE65 mutations and who have sufficient viable retinal cells.

IMD Risk Share Medicines

Medicines included in NSD risk sharig arrangements prior to establishment of Scottish Medicines Consortium (SMC):

- Agalsidase alpha (Replagal) for the treatment of Fabry Disease
- Agalsidase beta (Fabrase/Fabrazyme) for the treatment of FabryDisease
- Imiglucerase (Cerezyme) for the treatment of Type 1 Gaucher Disease

Medicines accepted for use by SMC:

- Miglustat (Zavesca/Vevesca) for the treatment of Type 1 Gaucher Disease.
- Velaglucerase (Vpriv) for the treatment of Type 1 Gaucher Disease.
- Migalastat (Galafold) is indicated for the long-term treatment of adults and adolescents aged 16 years and older with a confirmed diagnosis of Fabry disease (α-galactosidase A deficiency) and who have an amenable mutation
- Eliglustat (Cerdelga) for the long-term treatment of adult patients with Gaucher disease type 1 (GD1) who are CYP2D6 poor metabolisers, intermediate metabolisers or extensive metabolisers
- Volanesorsen sodium (Waylivra) for genetically confirmed familial chylomicronaemia syndrome (FCS) and at high risk for pancreatitis, in whom response to diet and triglyceride lowering therapy has been inadequate (approved via SMC ultra-orphan pathway).
- Velmanase alfa (Lamzede®) enzyme replacement therapy for the treatment of non-neurological manifestations in patients with mild to moderate alpha-mannosidosis (approved via SMC ultra-orphan pathway)
- Avalglucosidase alfa (Nexviadyme®) for the treatment of Pompe disease

Medicines accepted for restricted use by SMC:

- Carbaglu (N-carbamoyl-L-glutamic acid) for the treatment of hyperammonaemia due to N-acetylglutamate synthase deficiency.

Medicines not recommended by SMC but included in the risk share if there has been a recommendation following Individual Patient Treatment Request (IPTR)/Peer Approved Clinical System (PACS) within the NHS Board of residence of the patient:

- Alglucosidase alfa (Myozyme) for the treatment of Pompe disease (acid maltase deficiency).
- Laronidase (Aldurazyme) for the treatment of MPS 1, Hurler-Scheie or Scheie syndrome.
- Idursulfase (Elaprase) for the treatment of MPS II (Hunters syndrome).