SECTION 9.1: UNLICENSED MEDICINES POLICY (ACUTE SERVICES DIVISION)

CONTENTS

1. SCOPE

This document is intended for use by all healthcare professionals employed within the acute services division of NHSGG&C engaged in the prescribing, supply and administration of unlicensed/ off label medicines. In addition, it provides guidance on continuation of supply of unlicensed medicines between healthcare sectors and is therefore also relevant to prescribers in primary care and has some relevance to community contractors.
There are separate specific policies for investigational medicinal products, which are being prescribed as part of a clinical trial.

Unlicensed medicines accessed via the Early Access to Medicines Scheme (EAMS) are not covered by this policy as they have been risk assessed by the Medicines and Healthcare Products Regulatory Agency (MHRA).

2. AIM

This policy has been put in place to

- Promote best practice when prescribing unlicensed/ off label medicines for adults and children
- Provide safe procurement and supply of unlicensed medicines (ULMs).
- Ensure continuity of supply of medicines between the acute and primary care sectors.

3. BACKGROUND

No medicine can be placed on the market in the UK without a Marketing Authorisation (formerly known as a Product Licence) granted by the MHRA (or equivalent European Authority). This Marketing Authorisation (MA) signifies that the medicine concerned meets the appropriate quality standards and is safe and efficacious for its designated use. The MA details the indications for which the product is licensed and can be marketed. It also defines the form, dose, route of administration for the medicine and the container in which it is supplied. The product information supplied with the agent will only apply to licensed indications and doses.

However, it is recognised that licensed indications for a product will not always meet the clinical needs of an individual patient in every situation. Therefore, to ensure that the patient's requirements for a medicine are met, and to preserve the prescriber's clinical freedom, the legislation provides an exemption to allow the manufacture, supply and administration of **unlicensed medicines** (i.e. medicines without a Marketing Authorisation) when necessary. In addition, provision is also made for **licensed medicines** (i.e. medicines with full Marketing Authorisation) to be prescribed for unlicensed indications or in unlicensed dosages i.e. **"off label".**

Unlicensed medicines (ULM) have not been subject to the same stringent scrutiny by the MHRA and so the same assumptions regarding product quality, safety and efficacy that accompany licensed products cannot be made. "Guidance Note 14 – the supply of unlicensed relevant medicinal products for individual patients" - issued by the MHRA provides guidance on the prescribing, procurement, manufacture and distribution of unlicensed medicines.[1]

According to MHRA guidance

- Unlicensed medicines may only be supplied to meet the special needs of an individual patient. Examples of special clinical need include an intolerance to an ingredient or inability to swallow solid oral dosage forms.[2]
- Unlicensed medicinal products may only be placed on the market (and by implication purchased) when no pharmaceutically equivalent licensed product is available for use. Products are considered pharmaceutically equivalent if they contain the same amount of the same active substance in the same dosage form and meet the same standards, when considered in the light of the clinical needs of the patient at the time of its use.

A consensus statement published by the NHS Scotland Directors of Pharmacy and Scottish Association of Medical Directors gives advice on rare circumstances where use of unlicensed and off-label medicines may be considered where a licensed alternative may be available. The use of an unlicensed medicine or off-label medicine in

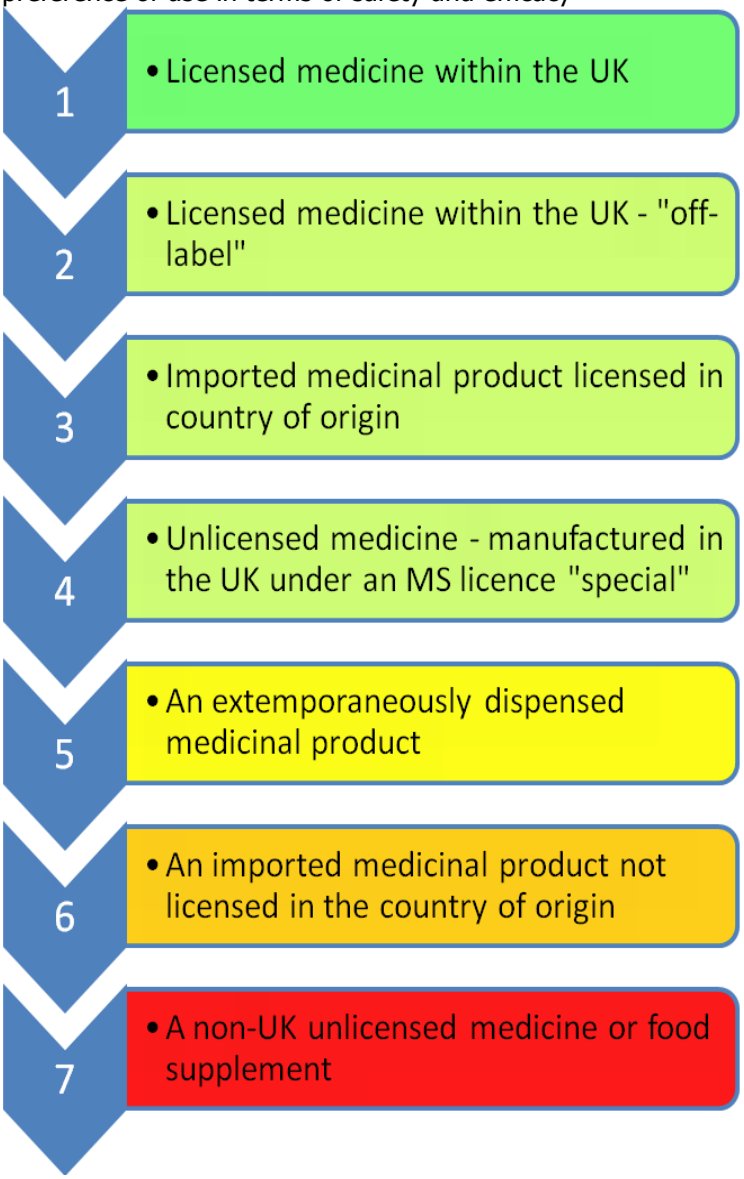
preference to a licensed alternative on the basis of improved cost effectiveness for NHSGG&C may be considered if ALL the following criteria are met, and must be approved by the Prescribing Management Group and Corporate Management Team.[3]

- Only following a robust risk assessment of the efficacy, safety, and procurement and service issues AND
- When the risk assessment suggests that the use of the off label or ULM would have no additional risks for patients AND
- Where using the licensed medicine would have a substantial financial impact potentially affecting the provision of other health services

4. POLICY STATEMENTS

4.1 WHAT IS AN UNLICENSED MEDICINE?

The following table describes the different types of unlicensed medicines and provides guidance regarding preference of use in terms of safety and efficacy



- Medicines with the appropriate Marketing Authorisation should be used to treat patients in preference to unlicensed or off label medicines whenever possible. However, use of unlicensed / off label medicines may be necessary in order to provide the optimum treatment for patients, but they should only be prescribed if their use can be clearly justified from a clinical / pharmaceutical perspective. In some specialties, such as paediatrics, many medicines are prescribed off label due to lack of MA in the paediatric setting.

4.2 WHAT IS AN OFF-LABEL MEDICINE?

These are licensed medicines used outwith the parameters of their Marketing Authorisation (MA). Examples of off-label use are:

- Using a medicine for a different illness to that stated in the MA.
- Using a medicine in an age group outside the licensed range (usually children or the elderly)
- Using a medicine at a different dose than stated in the licence.

- Off label use should be managed, where appropriate, with underpinning and appropriately approved protocols. Within Paediatrics, it is recognised that the use of off label medicines is extensive but the same principles should hold true.
  It is recognised that, in some cases, the generic versions of a medicine may not have exactly the same indications as those within the MA of the original branded medicine due to patent protection issues. However, with the exception of biosimilars, bioequivalence to the branded medicine must have been demonstrated as part of the generic market authorisation process and therefore, any additional risks of prescribing and dispensing the medicine generically are considered negligible. In addition for many generic or long established medicines it is common practice to use them for well recognised off-label indication such as amitriptyline for neuropathic pain. These would be considered low-risk off-label uses of medicine.[3]
- High risk off label medicines (as defined in appendix 1) with appropriate documentation should be submitted to the clinical director for consideration and, if required, to relevant clinical governance structures.

4.3 WHAT ARE 'SPECIALS'?

A pharmaceutical 'special' as defined by law is a medicine made to satisfy the needs of an individual patient Specials are unlicensed medicines (either imported or made under a UK Specials manufacturing licence) prescribed to meet the special clinical needs of an individual patient on the direct personal responsibility of the prescriber. Specials are therefore one type of unlicensed medicine.

The term 'special' should not be used indiscriminately to describe unlicensed medicines in general. It should be noted that within community pharmacy, this term can be confused with 'special order'. a term attributed in community pharmacies to all products not held routinely by Wholesalers e.g. unusual licensed product which has to be ordered through a 'special order' process.

Use of specials should be managed, where appropriate, with underpinning and appropriately approved protocols. Within Paediatrics, it is recognised that the use of specials medicines can be frequent but the same principles should hold true.

NHS Greater Glasgow and Clyde has produced Guidance on the Use of Specials in Primary Care which describes the process for prescribing, authorisation and procurement of specials for individual patients in primary care.

4.3 WHAT ARE 'ATMPS'?

An advanced therapy medicinal product (ATMP) is

- A gene therapy medicinal product
- A somatic cell therapy medicinal product
- A tissue engineered product

The MHRA is the competent authority in the UK for clinical trial authorisation for all medicinal products, including ATMPs and for UK manufacturers or importers of ATMPs.

ATMPs may be autologous (starting material is from the intended recipient), allogeneic (starting material originates from a donor) or xenogeneic (starting material is of animal origin). ATMPS can also be classed as a combined product; this is a combination of any of the above with a medical device.

As ATMPs are medicines they are subject to the same requirements as for other medicinal products. Most current usage is in clinical trials (Advanced therapy Investigational Medicinal Products (ATIMPs), but ATMPs are also available as licensed and unlicensed medicines.

Unlicensed and investigational Gene Therapy Medicinal products are subgroup of ATMPs that fall under the Genetically Modified (GM) Organisms (Contained Use) Regulations 2014. (Licensed products only have to comply with the regulation in respect of waste pathways). These products are designed to introduce genetic material into cells. This includes direct insertion of material to compensate for abnormal genes or delivery of material to make a beneficial protein which then multiplies and exerts a positive effect. 'In vivo' gene therapy products involve direct injection of the product, eg some vaccines. 'Ex vivo' products include those where a starting raw material is taken from an individual and the gene therapy is added to the cells outside the body, before re-infusing the final product, e.g. CAR-T cells.

Gene therapy products have an activity classification and containment level applied to them under the GM regulations, which is based on the level of risk to humans and the environment. Most activities involving gene therapy products in clinical practice will be class 1 or 2.

- Class 1 – activity of no or negligible risk for which containment level 1 is appropriate to protect human health and the environment
- Class 2 – activity of low risk for which containment level 2 is appropriate to protect human health and the environment
- Class 3 – activity of moderate risk for which containment level 3 is appropriate to protect human health and the environment
- Class 4 – activity of high risk for which containment level 4 is appropriate to protect human health and the environment

There is a requirement to obtain independent competent advice on the risk assessment for GM products under the regulations. For class 1 activities competent advice can be gained from a person e.g. Biological Safety Officer (BSO) or from the local Genetically Modified Safety Committee (GMSC) – in GGC this advice can be gained from the GMSC. Class 2 activities involving GM products require the competent advice to be gained from the local GMSC. Within NHSGGC the GMSC primarily reviews risk assessments for ATIMPs, but will also review risk assessments for unlicensed ATMPs as required by the GM Regulations. The Committee is managed by the Research Governance Manager within Research & Innovation Department on behalf of the Chair of the Committee. The Lead Pharmacist for Research and Innovation must be contacted for advice, access to the risk assessment documents and process of submission, as early as possible when an unlicensed gene therapy product is being considered for use.

5. LEGAL LIABILITY AND GOOD PRACTICE POINTS

All health care professionals must be aware of their own liability and responsibilities when prescribing, supplying and administering unlicensed or off label medicines.

5.1 HEALTH BOARD

It is the responsibility of the Health Board to ensure that medicines are prepared and administered correctly. "NHS Boards carry a liability for the actions of their employees and may accept liability for the prescription of unlicensed or off-label medicines, where such use has been authorised and agreed, provided that local policies and procedures are adhered to. The NHS Board's "vicarious liability" does not extend to independent contractors such as General Practitioners and Community Pharmacists. Independent contractors prescribing or supplying unlicensed or off-label medicines have a **personal liability** for their actions which cannot be transferred to the manufacturer or the importer of the medicine."[3]

While any liability associated with the use of unlicensed or off label medicines will be accepted by the employing authority, healthcare professionals must operate within agreed policies and guidances.

5.2 PRESCRIBER

The prescriber is always responsible for the use of a medicine and the patient's welfare and in the event of adverse reactions may be called upon to justify the decisions that they have made. They need to ensure that prescribing unlicensed and/or off label medicines falls within their regulatory framework, their own clinical competency and scope of practice.

The person who first prescribes a ULM or off label medicine in the acute services division **should** be the clinician in charge of the patient's care, usually this will be the patient's consultant. Ongoing prescribing can be delegated to a registered medical practitioner or independent non-medical prescriber as appropriate.
The clinician, including non-medical prescribers, initiating the use of the medicine must comply with the following:

Before prescribing an unlicensed/ off label medicine:
- Aware of its unlicensed / off label status
- Be satisfied that an alternative, licensed medicine would not meet the patient's needs
- Be satisfied that there is sufficient evidence base and/or experience of using the medicine to show its safety and efficacy
- Risk assess the use of ULMs/ off label medicines (see section 6.1 and appendix 1).
- Provide detailed written information to support the decision taken regarding the selection of the particular medicine. This should include benefit to the patient, evidence of efficacy, side-effects and why any alternative licensed medicine is inappropriate in this situation. In the case of unlicensed medicines, this will ALWAYS be required prior to medicine procurement.
- Discuss with the relevant pharmacist where to obtain the medicine, what formulation and dose is required and duration of administration.
- Complete the relevant request form where appropriate (see section 6.3 and appendices 2 and 3)
- Discuss with the patient/ carer the status of the medicine, side- effects, continuation of supply and document discussions.
- Ensure any adverse event related to the ULM/ off label medicine is documented via the Yellow Card system and/or the clinical incident reporting system e.g. Datix.
- Ensure the ULM / off label medicine continues to be appropriate for that patient.

Before administration of a ULM/ off label medicine:
- Ensure that all staff are aware the medicine is being used is unlicensed/ off label
- Ensure that all relevant staff are aware of side effects/ dosing/ monitoring etc. that may be different from its licensed indications.
- Provide, in conjunction with pharmacy, information to staff regarding handling and administration that may be different from its licensed indications.

Before transferring patient care into another sector:
- Provide written information about rationale for use, dosage, side-effects, monitoring requirements etc. at the time of discharge for primary care if the medicine is to be taken by the patient in the community setting.
- Ensure continuity of supply on patient discharge, if this is required either via primary care or hospital out patients. Liaise with the relevant acute sector pharmacy, if required.
- Where a GP is being asked to prescribe in primary care, sufficient information should be provided to reassure the prescriber (see 9.2 Primary Care).

5.3 PHARMACIST

In the role of purchaser of the medicine a pharmacist assumes professional responsibility, particularly if this involves specifying an unlicensed medicine to be purchased (see Royal Pharmaceutical Society website).

It is a requirement of Guidance Note 14 (MHRA) that all patients receiving ULM can be identified and that the use of that medicine can be accounted for.[1] Adequate records must be kept regarding the requisition, procurement and supply of ULMs. Principles described in NHSGG&C "Safe and Secure Handling of Medicines" policy will apply to ULMs.
Many pharmacy staff may be involved in the process of ULM procurement and prescribing. Therefore, all members of the staff should be aware of relevant professional standards, this ULM policy and the role they need to fulfil in order to comply with these requirements.

Pharmacy staff working at ward level or in clinical areas:
- Highlight ULM/ off label status of medicine to prescribers and clinical staff
- Provide information on how to access local ULM prescribing policy

Lead Clinical Pharmacists:
- Assist with the completion of the required paperwork including information on medicine procurement costs, product risk assessment and professional opinion on the request presented.
- If in the professional opinion of a pharmacist, the use of a ULM/ off label would be unsafe for a given patient, it is their responsibility not to support the request and to inform the prescriber of their reasons. Such cases should be referred to the clinical director for the specialty for review / arbitration.

Pharmacy staff working in procurement/ dispensing areas:
- Responsibilities of pharmacy staff are described in detail in the GGC Pharmacy procedures.
- Provide information on available products, lead times, procurement costs
- Keep adequate records regarding the requisition, procurement and supply of ULMs.
- Follow safe and secure handling of medicines policies and practice

5.4 STAFF ADMINISTERING ULM

Nursing staff, or other health care professionals, administering ULMs/ off label medicines must be made aware of the medicine's status. It is the responsibility of the prescriber and pharmacist to inform them of this.

Nursing staff should:
- Be aware of its unlicensed / off label status
- Ensure that they have information on the safe use of a ULM/ off label medicine before administration
- Be informed about any adverse drug reactions, clinical risks and how to deal with them.
- Follow safe and secure handling of medicines policies and practice
- Keep adequate records of the administration of an unlicensed medicine
- Inform pharmacy staff when transferring a patient to a different ward / department to allow appropriate redirection of future supplies
- Inform staff in the new ward /department of the status of the medicine and ensure that stocks are sent with the patient.

For ULMs held as stock items on the ward / in department it is the responsibility of the nurse in charge to ensure additional records are kept regarding administration e.g. stock control records. These MUST include drug batch numbers and each patient's name and CHI number

5.5 MANUFACTURER

If an untoward incident occurs with:

- **a licensed medicine** prescribed and administered according to the Marketing Authorisation, liability rests with the manufacturer.
- **off label use of a licensed medicine** i.e. prescribed or administered out with Marketing Authorisation then the manufacturer is **unlikely** to be found liable for any harm caused by that medicine, unless harm is directly attributable to a defect in it, rather than the way it was prescribed.

- **an unlicensed medicine** with no Marketing Authorisation within the UK then the manufacturer is not liable (unless the medicine is shown to be defective).

N.B It should be noted in the event of an adverse event the manufacturer has no right to be supplied with the patient name. Indeed the divulgence of any information which can identify the patient would be a breach of confidentiality.

5.6 AREA DRUG AND THERAPEUTICS COMMITTEE

The ADTC is responsible for the development of policy and ongoing review of the use of unlicensed and off label medicines within NHSGGC.

6. RISK MANAGEMENT AND CLINICAL GOVERNANCE ARRANGEMENTS

All medicines have side-effects which can vary dependent on the indication being treated and this should be considered when prescribing off label. If there is little data for use in a particular setting adverse events may occur which have not been previously described with possibly unforeseen consequences. In the case of ULMs, the level of knowledge about product quality, efficacy and side-effects will frequently be lower than for medicines used within a MA and knowledge may be minimal if the medicine is used early on in its development.

It is important that systems are in place to show that when prescribing an unlicensed/ high risk off label medicine this was the most appropriate therapy for the patient.
A risk management programme with associated controls has been developed and implemented within NHSGG&C.

There are two aspects to risk management.
- Prescribing / requesting supply– clinical risk management (unlicensed and off label medicines)
- Procurement / receipt – product risk management (unlicensed medicines; separate pharmacy procedures)

6.1 CLINICAL RISK MANAGEMENT

Prior to initiating therapy with an ULM / off label medicine, the clinician should:
- Assess suitability of licensed alternative agents for the patient
- Be aware of current peer group opinion of treatment options for the patient
- Consider the evidence base for the ULM/ off label medicine
- Consider the risks of the ULM/ off label medicine including route of administration, possible side-effects, contraindications and precautions which may be required when using the medicine e.g. intrathecal and epidural routes are, by their very nature, higher risk and side-effects are more likely to be severely disabling / life threatening (see appendix 1).
- Weigh up the risk / benefit to the patient or patient group in the proposed setting

Unlicensed Medicine (requires approval documentation)
From a **clinical** perspective **all unlicensed medicines**, including ATMPs, should be considered as "**high risk"** and treated accordingly. Products, which have had their marketing authorisation revoked due to concerns over product quality and/or safety must be considered as **"very high"** risk. An extensive assessment will be required in each individual case to weigh up risk versus patient benefit before use of the product.

Off label medicines and 'specials'
For medicines falling within the **intermediate risk** category where regular use is anticipated, it is **highly recommended** that an approved guideline or protocol be put in place that describes in detail the prescribing and monitoring requirements of the medicine. This is particularly important for those medicines that may be continued in primary care (see section 9). The presence of an approved protocol would negate the requirement to complete individual ULM forms.

6.2 PRODUCT RISK MANAGEMENT

The medicine must be deemed to meet minimum standards of safety. This aspect of risk management is primarily an assessment of product quality and includes knowledge and confidence in the manufacturer / supplier, certificate of analysis information and whether or not the product is licensed within its country of origin. This will be carried out by pharmacy.

The pharmacy department has produced a series of standard operating procedures which guide staff through the procurement and receipt process. A number of controls have been established to ensure that products sourced meet the required standard.

Particular attention is given to the safe and secure handling of products sourced from outside the UK which may not have packaging or product information in English. Specific instructions are provided to control this issue.

In case of ATMPs, the process risk assessment is as above for any medicine. Depending on the type of ATMP, there are Pharmacy SOPs and guidelines for either research or licensed ATMP products that must be used to ensure the safe and secure handling of the product.

6.3 COMPLETION OF REQUEST FORM

The decision to prescribe unlicensed and off label medicines is the responsibility of the clinician in charge of the patient's care, usually this will be the patient's consultant.

An unlicensed medicine request must be completed in the following circumstances:
- All medicines with no Marketing Authorisation for any formulation or indication in the UK
- Off label medicines that fall into the high risk category (see appendix 1)
- Off-label medicines that fall into other risk categories, but which have an associated cost of over £3,000 per annum or per patient treatment period.

The submission MUST include:
- Published evidence supporting use of the particular product
- Rationale for prescribing for this patient compared with alternative products, particularly if a licensed product is available

Appropriate documentation for requests (ULM eform 1) can be found on www.ggcmedicines.org.uk under the 'ULM' tab or use the hyperlink in appendix 3.

The request for use of an unlicensed medicine or off label medicine should be signed and approved by the appropriate clinical director. Where the cost of the medicine is over £3,000 per annum or per patient treatment period , the supply should be approved by the Chief of Medicine. See appendices 2 and 3 for an overview of the request process.

If an advanced therapy medicinal product (ATMP) is being requested which is the subtype of gene therapy product that requires assessment by the GM Safety Committee (GMSC), the required risk assessment may be submitted in parallel with the ULM form for assessment. If the ATMP (gene therapy subtype) is approved after its clinical risk assessment the approval should be communicated to the GMSC via the Lead Pharmacist for Research & Innovation. In turn the GMSC acceptance of the Risk Assessment should be communicated to the Clinical Director/Chief of Medicine via the Lead Pharmacist for Research & Innovation/ Clinical Pharmacist involved in the ULM request submission. Treatment must not proceed until both applications have been completed and any identified risks mitigated.

The following do NOT require a request form
- Extemporaneously prepared medicines e.g. suspensions, ointments, creams
- Off label use of established, low or intermediate risk medicines if they are under the £3,000 cost threshold (see appendix 1)

- Unlicensed/ high risk off label medicines where approved protocols for the medicines are in place (see section 6.1)

6.4 SUBMISSION AND APPROVAL OF UNLICENSED/ OFF LABEL MEDICINES REQUEST

The clinical director will consider, in a timely fashion, the use of an unlicensed or a high risk off label medicine following receipt of the fully completed request form. High cost medicines (over £3000 per annum or per patient treatment period) must be submitted for consideration to the Chief of Medicine. Refer to appendix 3 (flow chart for approval process)

The use of an unlicensed medicine in preference to a licensed alternative on the basis of improved cost effectiveness for NHSGGC must be approved by the Prescribing Management Group and Corporate Management Team. A copy of the eform ULM1, detailing the decision, should be filed in the patient's clinical portal records under correspondence.

6.5 SUBMISSION AND APPROVAL OF UNLICENSED/ OFF LABEL MEDICINE REQUESTS FOR PATIENTS FROM OTHER HEALTH BOARDS MANAGED WITHIN NHSGGC

The West of Scotland Health Boards have a general agreement on the management of patients within each others' boards. The host board is the one to which the patient has been referred from a home board. The host board (in this case NHSGGC) and the host board's clinician assume responsibility for the patient's care. Two separate mechanisms will be applied, dependent on the cost per patient treatment or cost per patient per annum for continuing treatment:

- < £25,000
  The standard NHSGGC procedures will apply, with notification of the decision to the Chief of Medicine/ Medical Director of the home board (or their nominee) at the conclusion of the approval process.
- ≥ £25,000
  An invitation will be extended to the Medical Director of the home Board (or their nominee) to participate as a panel Member with full voting rights. The decision of the NHS GG&C Panel will be final and will not be subject to a further review at home board level.

6.6 EMERGENCY REQUESTS

Timescales for the decision-making process will be established in accordance with the patient's clinical needs and be communicated to the patient by the clinician responsible for the patient's care. In an emergency, in order to request a supply the prescriber must complete the eform ULM1. However, interim approval will be available via virtual routes to allow timely process of the medicines request

6.7 APPEALS PROCESS IN THE EVENT THAT A REQUEST TO PRESCRIBE AN UNLICENSED OR OFF LABEL MEDICINE IS DECLINED

It is anticipated that this will be a rare occurrence for ULMs or high risk off label medicines. In the first instance any appeal will be heard by the chief of medicine.

7. PATIENT INFORMATION AND CONSENT

Patients and, where appropriate, carers have the right to participate in the making of properly informed decisions about their health care.

Unlicensed medicine - Prescribers MUST advise patients/ carers that they are being treated with an unlicensed medicine. Written consent MUST ALWAYS be obtained in this setting.

Off label medicines – It is good practice when starting a patient on any new form of therapy that benefits and significant side effects are discussed. In the 'high risk' setting this discussion should be documented and consent (verbal/ written) obtained.

The MHRA recommends that prescribers should provide patients/ carers with the following[1]

- Sufficient information about the proposed treatment, including known serious or common adverse reactions, to enable them to make an informed decision
- Where current practice supports the use of a medicine outside the terms of its licence, it may not be necessary to draw attention to the licence when seeking consent. However, it is good practice to give as much information as patients or carers require or which they may see as relevant
- Explain the reasons for prescribing a medicine off-label or prescribing an unlicensed medicine where there is little evidence to support its use, or where the use of a medicine is innovative

Patient/carer information sheets for the adult and paediatric settings can be found in appendixes 5 and 6.

8. INCLUSION OF OFF LABEL MEDICINES IN THE NHS GG&C FORMULARY

Where the use of an off label medicine has become established practice within a defined patient group, who have been shown to benefit from the medicine, it may be appropriate for the Area Drugs and Therapeutics Committee and the Paediatric Drug and Therapeutic Committee to consider this medicine for inclusion in the NHSGG&C Adult Formulary and/or the NHSGGC Paediatric Formulary for this use (appendix 7).

NB This process will **not** be available for off label medicines given "not recommended for use in NHS Scotland" advice by the Scottish Medicines Consortium (SMC) for a licensed indication.

9. PRIMARY CARE

Medicines are frequently used off label in all specialties in the acute services division and there are a large number of unlicensed medicines also in common usage. The dosage, side-effects, monitoring etc. of these medicines for each indication will be well known to hospital staff and be documented in the patient's notes. However, the primary care team may not be familiar with the use of the agent at all, or not be aware of the indication for which it is used. Unless adequate information is supplied to the primary care team errors in dosing, response assessment etc can be made, particularly where drugs are used off label as, although information will be readily available from sources such as the BNF, it may not be applicable to the indication in question.

GPs can be asked to continue to prescribe off label medicines i.e. used out with their licence indications e.g. amitriptyline for neuropathic pain. However, within the intermediate and high risk categories, off label prescribing is best done where there is a written protocol for use. These instances are best discussed with the GP on a case by case basis. The development of a Shared Care Agreement may be considered in accordance with local processes for off label use of medicines considered low-medium risk.[4]

Where it is intended that either unlicensed or off label treatment will be commenced in out patient setting or continued after patient discharge, the unlicensed/ off-label status of the medicine MUST be highlighted and clear arrangements MUST be agreed between primary and secondary care regarding sourcing, prescribing, clinical monitoring and dispensing responsibilities. A decision on final responsibility should depend primarily on the best interests of the patient in terms of safety and convenience.

It should be noted that GPs are not obliged to prescribe ULMs as defined by this policy if this is outwith their expertise or they feel they have not been given sufficient information to prescribe safely. Unlike hospital doctors, independent contractors such as GPs and Community Pharmacists prescribing or supplying unlicensed or off-label

medicines are not covered by the Health-board's "vicarious liability" and have a **personal liability** for their actions which cannot be transferred to the manufacturer or importer of the medicine.

Where initiation of treatment with an off label medicine/ ULM occurs in hospital or an outpatient setting, the consultant, in conjunction with the acute sector pharmacy where applicable, is responsible for ensuring that relevant information is passed on to community pharmacists.

For unlicensed medicines Community Pharmacists will require an authorisation code from the Health Board before proceeding to order the medicine according to the NHSGGC Guidance on Use of Specials in Primary Care. As part of the authorisation process the community pharmacist will be asked to ensure the prescriber is aware that the medicine is unlicensed and has taken reasonable steps to ensure that there is no suitable licensed equivalent for the individual patient. They will also be expected to procure the medicine at an acceptable cost to the Health Board.[5]

9.1 INFORMATION REQUIRED BEFORE PATIENT TRANSFER TO PRIMARY CARE

The consultant who has initiated treatment with the unlicensed / off label medicine is responsible for ensuring that the relevant GP is given sufficient information about the product.

The following information should be provided:

- Name of Drug
- Dose and formulation
- Licensed status of drug
- Reason for prescribing
- Monitoring requirements, if any
- Duration of treatment
- Common side effects
- How to source the product in primary care, if possible

9.2 MONITORING

In situations where there is expected to be a high incidence of side-effects, or special monitoring is required, the appropriate arrangements must be put in place for this.

This is the responsibility of the consultant and acute division unless it falls within pre-existing agreements between primary care and the acute division i.e. in line with the 'near patient testing local enhanced service'. For some individuals it may be possible to transfer monitoring to primary care but this requires the agreement of the patient's GP.

10. REFERENCES

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APPENDIX 1: SUGGESTED CRITERIA FOR CLINICAL RISK ASSESSMENT OF OFF-LABEL MEDICINES OR SPECIALS

Established Practice	Low Risk	Medium Risk	High Risk
▪ Established generally e.g. BNF, nationally recognised guidelines ▪ BNF for Children	▪ Established use in speciality e.g. Specialist published guidelines ▪ Phase III / IV clinical trial data published in established Journals	Phase II clinical trial data, abstracts of phase III/IV	▪ Phase I clinical trials or case reports
▪ Few significant side effects		▪ Teratogenic ▪ Carcinogenic ▪ Cytotoxic ▪ Biological Agent	
▪ Oral / external ▪ Subcutaneous / respiratory / nasal		▪ Intravenous or installation into cavity or bone	▪ Intrathecal ▪ epidural

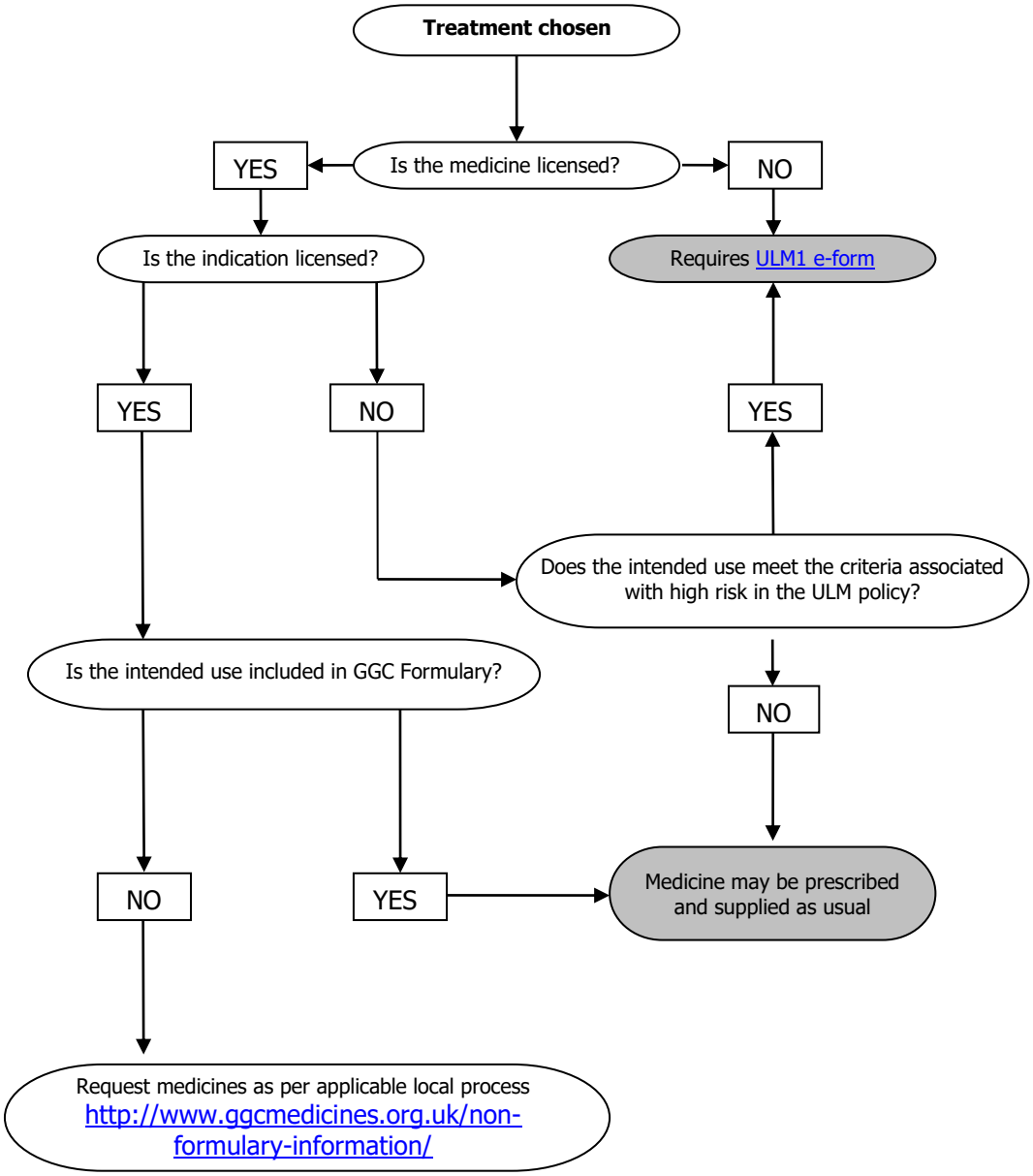
Any off label medicine fulfilling any of the criteria in the high risk column automatically requires an unlicensed medicines form.

Note – there is an element of subjectivity in assigning clinical risk category. The above table provides guidance only and should not be considered as an exhaustive list.

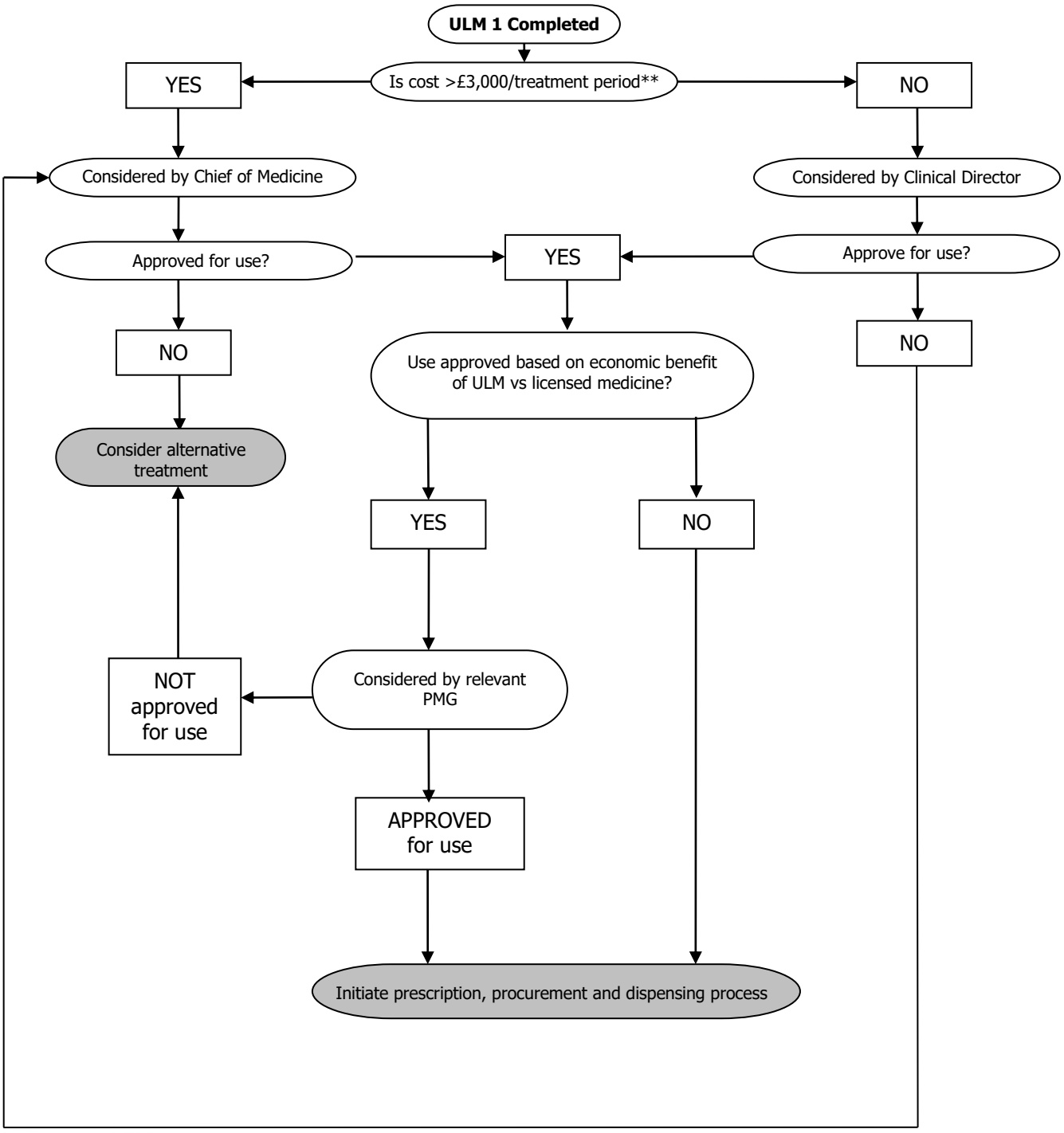
Discussion should take place with clinical peers, Medicines Information and clinical pharmacists as required to assign the risk

If you require further assistance please contact Medicines Information 0141 211 4407 or via medinfo@ggc.scot.nhs.uk

APPENDIX 2: WHEN IS AN ULM REQUEST FORM REQUIRED?

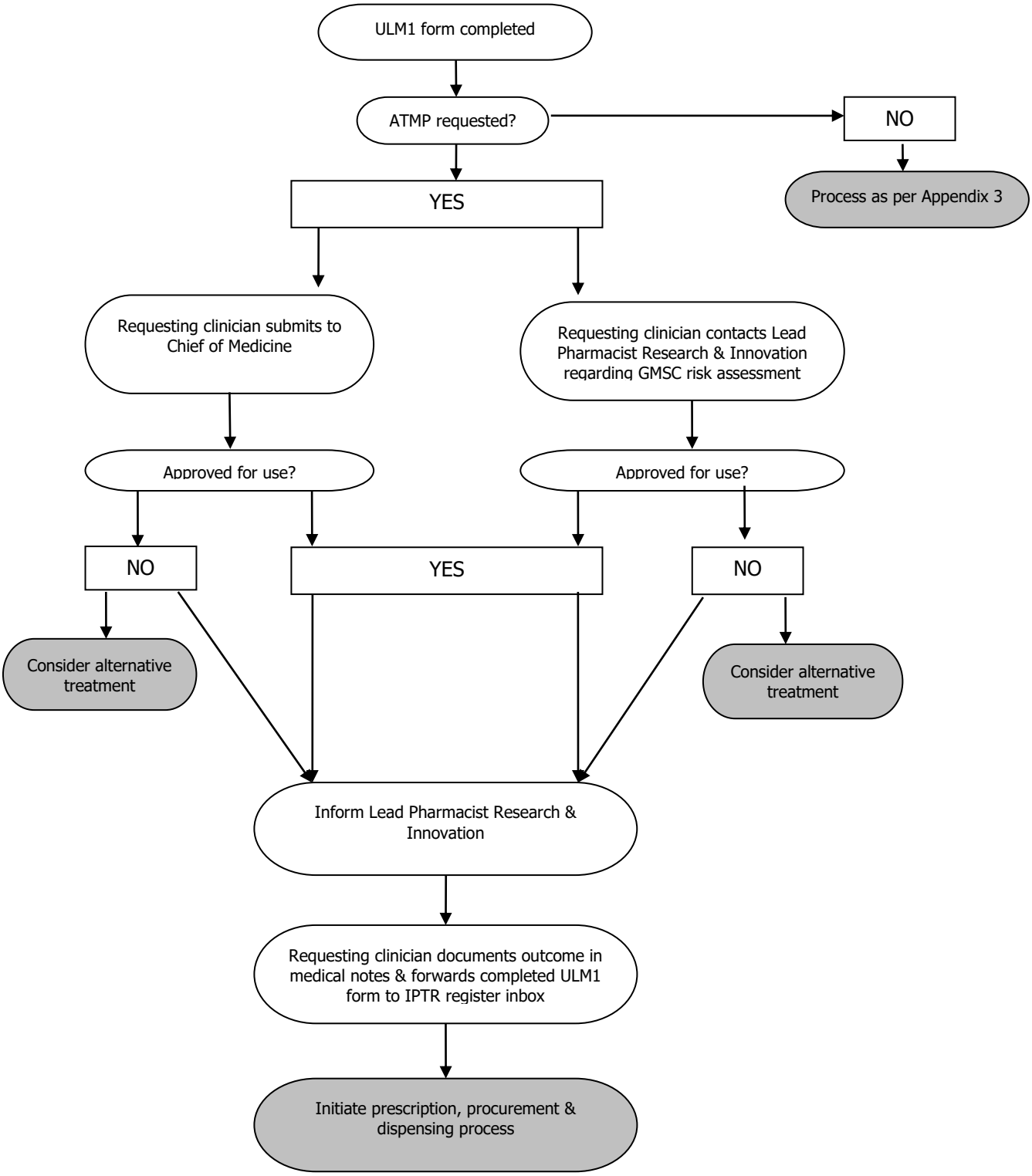


APPENDIX 3: HOW AN ULM REQUEST IS PROCESSED



** for patients from other health boards managed within NHSGGC, please see section 6.5 in the policy document

APPENDIX 4: HOW AN ATMP REQUEST IS PROCESSED



APPENDIX 5: PARENT & CARER LEAFLET – USE OF UNLICENSED MEDICINES IN PAEDIATRIC PATIENTS

Please refer to the information leaflet produced by Medicines for Children which can be accessed via

1. Medicines for Children website
https://www.medicinesforchildren.org.uk/sites/default/files/content-type/leaflet/pdf/MfC_Unlicensed_medicines.pdf

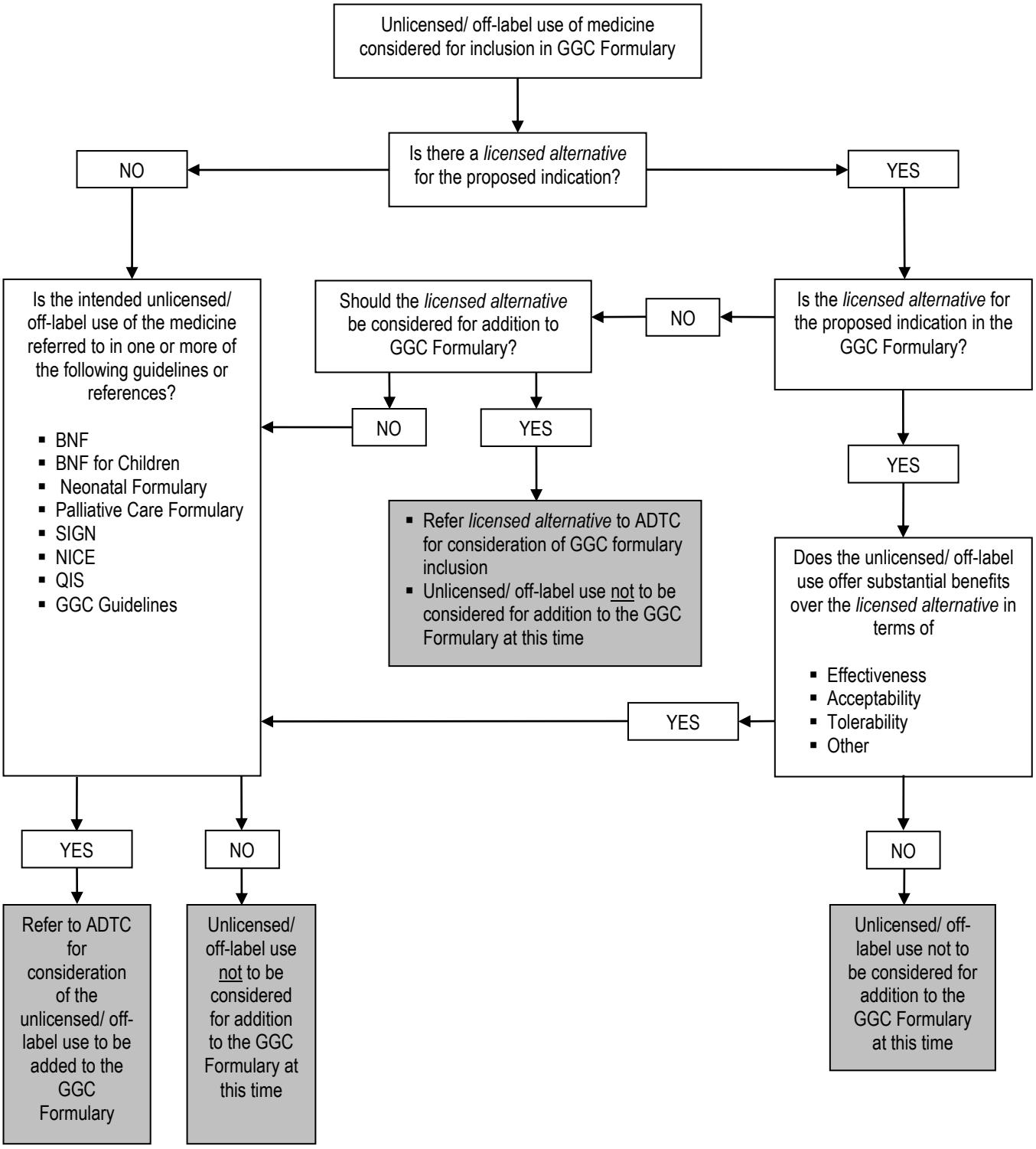
2. GGC Medicines website, Patient Information, Unlicensed Medicines https://ggcmedicines.org.uk/information-for-patients/unlicensed-or-off-label-medicines/

APPENDIX 6: PATIENT & CARER LEAFLET - USE OF UNLICENSED MEDICINES IN ADULT PATIENTS

Please refer to the information leaflet produced by NHSGGC which can be accessed via

GGC Medicines website, Patient Information, Unlicensed Medicines https://ggcmedicines.org.uk/information-for-patients/unlicensed-or-off-label-medicines/

APPENDIX 7: TEMPLATE FOR ASSESSING MEDICINES USE FOR INDICATIONS OUT WITH THE MARKETING AUTHORISATION FOR INCLUSION INTO THE FORMULARY



APPENDIX 8: UNLICENSED MEDICINES POLICY SHORT-LIFE WORKING GROUP

Acute Services Representatives
Rosemary Anderson, Lead Pharmacist Dispensing Services Clyde
Collette Byrne, Lead Pharmacist Medicines Governance Dr David Dodds, Chief of Medicine, Regional Services
David Dodds, Chief of medicine, Regional Services
Jackie Dunlop, Lead Nurse Burns, Plastics and CIC
Carla Forte, Lead Clinical Pharmacist Cancer Care
Dr Rachel Green, Chief of Medicine, Diagnostic Services
Kathrin Greschner, Pharmacist Medicines Policy and Guidance (chair)
Lynn Morrison, Regional QA Pharmacist
Steve Bowhay, Lead Clinical Pharmacist, Royal Hospital for Children
Samantha Carmichael, Lead Pharmacist Clinical Trials/ R&D (ATMPs)

Primary Care Representatives
Karen Liddell, Prescribing Support Pharmacist