Norfolk and Norwich University Hospitals NHS Foundation Trust

James Paget University Hospitals NHS Foundation Trust

The Queen Elizabeth Hospital King's Lynn NHS Foundation Trust

Joint Trust Guideline for the Use of Radioiodine in the Management of Benign Thyroid Disease

A clinical guideline recommended for use

For Use in:	Endocrine Outpatients, Nuclear Medicine
By:	Consultant endocrinologists and clinical scientists in nuclear medicine
For:	Use in adult patients with benign thyroid disease - including thyrotoxicosis and large multinodular goitres
Division responsible for document:	Medical
Key words:	Goitre, Thyrotoxicosis, Radioactive Iodine
Name and job title of document author:	Dr Ketan Dhatariya, Consultant in Diabetes, Endocrinology and General Medicine
Name and job title of document author's Line Manager:	Prof Jeremy Turner, Clinical Director, Endocrinology NNUH
Supported by:	Mr Matthew Gray,Medical Physics Expert Nuclear Medicine, NNUH Dr J Randall, Consultant Endocrinology JPUH Dr FJS Haddadin, Consultant Endocrinology QEHKL
Assessed and approved by the:	Clinical Guidelines and Assessment Group (CGAP) and Chair's Action
Date of approval:	23/11/2021
Ratified by or reported as approved to (if applicable)**:**	Clinical Safety and Effectiveness Sub-Board
To be reviewed before: This document remains current after this date but will be under review	23/11/2024
To be reviewed by:	Dr Ketan Dhatariya
Reference and / or Trust Docs ID No:	JCG0041 id 1139
Version No:	3.1
Compliance links: *(is there any NICE related to guidance)*	No
If Yes - does the strategy/policy deviate from the recommendations of NICE? If so why?	N/A

This guideline has been approved by the Trust's Clinical Guidelines Assessment Panel as an aid to the diagnosis and management of relevant patients and clinical circumstances. Not every patient or situation fits neatly into a standard guideline scenario and the guideline must be interpreted and applied in practice in the light of prevailing clinical circumstances, the diagnostic and treatment options available and the professional judgement, knowledge and expertise of relevant clinicians. It is advised that the rationale for any departure from relevant guidance should be documented in the patient's case notes.

The Trust's guidelines are made publicly available as part of the collective endeavour to continuously improve the quality of healthcare through sharing medical experience and knowledge. The Trust accepts no responsibility for any misunderstanding or misapplication of this document.

Joint Trust Guideline for the Use of Radioiodine in the Management of Benign Thyroid Disease

Version and Document Control:

Version Number	Date of Update	Change Description	Author
3.1	23/11/2021	Reviewed, no changes	Dr Ketan Dhatariya

This is a Controlled Document

Printed copies of this document may not be up to date. Please check the hospital intranet for the latest version and destroy all previous versions.

Glossary	
Abbreviation	
FNA	Fine Needle Aspiration
FNAC	Fine Needle Aspiration Cytology
RAI	Radioactive Iodine
RPA	Radiation protection Advisor
TFT	Thyroid function tests
US	Ultrasound

Joint Trust Guideline for the Use of Radioiodine in the Management of Benign Thyroid Disease

Quick reference guideline/s

Thyrotoxic patient aged over 40 and selected younger patients

Every patient should be considered eligible for RAI

Exclude women who are or might be pregnant; those who are breast-feeding, or trying to conceive

If there is ***any suggestion*** of active thyroid eye disease refer to an ophthalmologist to assess if ^{131}Iodine or radioiodine (RAI) is safe

Confirm diagnosis with TFT's

Render patient euthyroid with carbimazole or propylthiouracil ± levothyroxine

Refer to ARSAC license holders (Dr Dhatariya, Dr Swords and Dr Wallace), unless you have written permission to operate under their licenses (these are usually the consultant endocrinologists at NNUH, QEKL and JPH)

In clinic, take the patient through the RAI consent form and ask them to sign

Counsel patient about special precautions to be taken after RAI (information leaflets are available in Medical Outpatients)

Refer the patient to Nuclear Medicine for RAI therapy

If the patient has **any suggestion of active** thyroid ophthalmopathy they **MUST** be referred to a consultant ophthalmologist before requesting RAI so that protective steroid cover can be arranged

If the patient is a smoker they must have steroid cover for their RAI

Patients should stop their anti-thyroid drugs 5 days (carbimazole) or 10 days (propylthiouracil) prior to RAI

The patient should re-sign the consent form prior to the administration on RAI

TFT's to be taken 6 weeks after RAI with thyroid teleclinic or outpatient review of results. If then:

a) Thyroid function normal – discharge to GP if off carbimazole or propylthiouracil (PTU)
b) Hypothyroid – start thyroxine replacement and discharge to GP if off carbimazole or PTU
c) Hyperthyroid – no action unless symptomatic. If it persists after 6 - 9 months, consider further RAI

Long term follow up. Advise patients to consult their GP for TFT check 3, 6, and 9 months post RAI and then annually in perpetuity

Joint Trust Guideline for the Use of Radioiodine in the Management of Benign Thyroid Disease

Objective/s

The safe and consistent management of patients presenting with thyrotoxicosis using validated, evidence based data to ensure optimal outcomes.

Rationale

^{131}Iodine or radioiodine (RAI) has been used in the treatment of hyperthyroidism (thyrotoxicosis) for over 60 years [1]. It can also be used to reduce the size of non-toxic goitres [2]. RAI is now also more commonly used to reduce the size of large retrosternal goitres.

RAI is no longer given in a dosimetric manner based on the 48 hour ^{131}I uptake. Whilst this method often worked well it was shown to be no more effective than simply giving standard doses of ^{131}I [3] and it is more expensive than the standard dosage method [4]. In view of this evidence we have now adopted a simpler protocol, which is more cost-effective and convenient for patients.

Previously RAI was not given to women over 40 years unless there was no likelihood of subsequent pregnancy e.g. sterilization. There are conflicting opinions as to the use of RAI in children and adolescents. When dealing with thyrotoxicosis in children and adolescents, the increase in thyroid cancer after the experience in Chernobyl suggests that radioactive exposure to this group should be avoided [5]. This opinion varies around the world, and recent data challenges this view [6]. RAI is occasionally given to adolescents, but this should only be done after consultation with an endocrinologist. In summary, in older patients RAI is cheaper and safer than surgery, which should be avoided if at all possible.

Indications for RAI therapy

- **Consider as first line therapy in all patients aged over 40 with thyrotoxicosis.**
- **Consider in all patients with recurrent thyrotoxicosis after previous medical therapy, radioiodine or surgery.**
- RAI is now the treatment of choice for euthyroid, moderately sized multinodular goitres including retrosternal goitres. Older data suggested that RAI may lead to a transient increase in goitre size, thus increasing the likelihood of compressive symptoms, this has been shown not to occur in newer series and is safe down to a tracheal diameter of 1cm.

Contraindications to RAI therapy

- **RAI should not be given to female patients who are, or could be, pregnant. It should not be given to breast feeding women or to women planning to conceive within 6 months.**
- RAI should not be given to patients who are unable to comply with the necessary post-therapy restrictions e.g. parents of young children

- RAI should generally not be given to patients with severe ophthalmopathy, and definitely not unless the eye disease is deemed stable by an ophthalmologist, in which case steroid cover is required.
- Patients with eye disease who have not stopped smoking before contemplating RAI.
- Patients with nodules suspicious for malignancy should have an Ultrasound Guided Fine Needle Aspiration (FNA) biopsy prior to RAI.
- In the event of the patient needing surgery whilst on the waiting list for RAI please contact either the nuclear medicine department on extension 2808 or the referring consultant endocrinologist to discuss the relative urgency of each procedure.
- Gross urinary incontinence

Out-patient management prior to RAI treatment

When the patient has been counselled on the treatment options for their thyrotoxicosis, and they have chosen to be treated with RAI, they should sign the NNUH Trust approved consent form (Appendix A). The clinician should indicate what they feel the diagnosis is, and also what dose of RAI should be administered.

Patients should be rendered euthyroid. This is usually done by using either titrating carbimazole or propylthiouracil, or using a block and replace regime. Both drugs may be used with or without propranolol 40 mgs tds until the patient is rendered euthyroid. **This treatment should be notified to the Nuclear Medicine Department because levothyroxine and propylthiouracil will need to be discontinued 10 days, and carbimazole discontinued 5 days before RAI is administered and may need to be restarted 5 days afterwards.** If the patient has a toxic nodule then antithyroid drugs may need to be discontinued for longer before the therapeutic RAI dose is administered and this should be discussed with Nuclear Medicine. A preliminary ^{99m}Tc uptake to identify those patients with hyperthyroidism due to levothyroxine administration, iodine toxicity (e.g. amiodarone), subacute thyroiditis and patients with abnormal thyroid function tests due to interfering antibodies will no longer be done unless one is explicitly requested.

In patients with retrosternal goitres it is currently unclear which treatment option should be used. These individuals often have low uptake and may need higher doses of RAI – up to 800Mbq. Referral for radioactive iodine for these individuals needs a special referral to the ARSAC license holder (unless you have prior express written permission – these are usually the consultant endocrinologists at NNUH, QEKL and JPUH) and the department of nuclear medicine.

If the patient has any evidence of congestive ophthalmopathy then he/she must be rendered euthyroid and given steroid cover at the time of RAI treatment (see below) because of the risk of worsening ophthalmopathy [7]. In patients with severe eye complications it may be prudent to continue with medical treatment until the congestion has subsided before administering RAI under steroid cover. The management of these patients is often difficult and early referral to a specialist endocrinologist and ophthalmologist is recommended.

Treatment strategy (If Graves' Disease is suspected, see Appendix C)

a) History and examination to identify those patients with subacute thyroiditis (who usually have a painful thyroid gland and elevated ESR), iodine toxicity or thyroxine administration.

b) Confirm diagnosis by measuring free T4, free T3 and TSH, TRAb, and request thyroid antibody levels if toxic Hashimoto's suspected.

c) Counsel patients about treatment options, and if it is agreed that RAI treatment is appropriate **give the patient British Thyroid Foundation information leaflets about Thyrotoxicosis, Radioiodine and Thyroid Eye Disease (if appropriate) to take away** to read at home. (These leaflets are available in Medical Outpatients). Document that the patient has been warned re: hypothyroidism / ophthalmopathy risks.

d) Give the patient the Carbimazole and Propylthiourcil information sheet for patients Trustdocs Id: 12316

e) If the patient agrees to RAI – take them through the consent form (Appendix A) (developed from the guideline advised by the Royal College of Physicians working group [1]).

f) Render patient euthyroid with carbimazole or propylthiouracil (see above)

g) Write to Matt Gray, physicist in charge of Nuclear Medicine, NNUH requesting treatment, giving details of current treatment regime and recommended dose of RAI. **PLEASE NOTE: RAI treatment can only be prescribed by an ARSAC license holder or his/her approved nominee**. (ARSAC license holders: Dr Dhatariya, Dr Wallace, Dr Swords and the Consultant Radiotherapists), e.g. Dr Dhatariya, Dr Swords and Dr Wallace have authorised Matt Gray as their nominated deputy to prescribe and administer RAI only when the patient has being referred by a senior member of medical staff employed by NNUH, JPH, and QEKL. Even then he may only prescribe and administer RAI for patients meeting the Trust Guideline for RAI treatment of benign thyroid disease.

h) If the patient is resident in a care home or has professional carers that the information is included with the request so that the Nuclear medicine department can make appropriate arrangements with the care home staff.

i) If patient has ophthalmopathy or is a smoker arrange steroid cover (see page 7)

j) Request ^{131}I according to the following dosage schedule (may be varied on clinical grounds).

Uncomplicated Graves' disease	Guide activity – 400-600 MBq (usually 370MBq)
Uncomplicated toxic adenoma or toxic MNG /	Guide activity – 500-800 MBq (usually 600MBq)
MNG	Guide activity – 800MBq

k) Nuclear Medicine will contact the patient and arrange a suitable appointment for RAI.

l) After RAI therapy, Nuclear Medicine will contact the referring consultant's secretary to arrange follow up in Medical Outpatient's, usually 12 weeks after RAI, with a TFT done at 6 weeks after the RAI. It is the responsibility of the consultant who requested the RAI to ensure that the 6 week TFT request is given to the patient and is acted on.

Patient Restrictions

This information is for the guidance of clinicians. Each patient should be counselled individually and informed consent obtained and the consent form signed in clinic. This will normally be done by the clinician in clinic and will then be repeated in the Nuclear Medicine Department on the day of RAI administration. Advice given to patients, which is substantially different from the guidance below, will require a separate written risk assessment for the individual patient.

Patients receiving RAI are subject to certain restrictions [8]. The table below gives an indication of the recommended approach but advice will vary according to the patient's lifestyle and the degree of understanding of risks. For instance, family members are at most risk of radiation exposure and as such, restrictions such as staying away from work can lead to increased exposure to persons in the home.

Similarly, restrictions on public transport can encourage travel in private cars with other family members when a person sitting alone on a bus or train will present little risk to the public. Contamination arising from the patients (e.g. incontinence) will greatly increase the radiation risks and must be considered separately.

If an activity of greater than 800MBq is required then the patient must be hospitalised and placed in a side room, which will become a Radiation Controlled Area. The hospital Radiation Protection Advisor (RPA) must be consulted prior to admission. The patient can be discharged when activity levels have fallen below this threshold although it may be possible to release the patient with higher activity levels under certain circumstances provided a written risk assessment is carried out by Nuclear Medicine or the ARSAC license holder. Patients may be discharged with estimated activities above the threshold as long as an estimation of dose to the patient's friends and family is recorded.

If there is any doubt about any aspect of radiation protection, then please refer to the Trust Radiation Policy document (Trust info tab on home page – Trust admin and policies – Radiation policy) or contact the nuclear medicine department.

Number of days for which patients should take special precautions, according to administered activity of ^{131}Iodine.

Precaution	**Administered Activity (MBq)**			
	200	**400**	**600**	**800**
Stay at least 1m away from children under 3	15	21	25	27
Stay at least 1m away from children under 5	11	16	20	22
Stay away from adults at home (+ children	5	11	14	16

over 5)

Avoid prolonged close contact (more than 3 hours with other adults at <1m)	-	-	4	8

- For patients travelling by private cars, journeys of up to 6 hours are permissible if the patient sits alone in the back seat.
- For public transport, journeys up to one hour are permitted sitting next to a member of the public (not family member, when table above applies).
- Most patients may return to work the next day. The exceptions are:
    1. Where the person is engaged in radiosensitive work or works with radioactive materials.
    2. Where the patient works closer than two metres from the same colleagues for a substantial part of the working day.
    3. Where the patient spends greater than 15 minutes in very close contact with an individual (particularly a child or pregnant woman).

These rules may be relaxed for persons who are carers for the patient but such persons need counselling in radiological risks and must be given written guidance on appropriate radiation protection. They must not exceed the radiation dose limit of 5mSv.

Where a patient is being discharged to a nursing home, written guidance must be provided to nursing staff on radiological protection measures and the employer must inform the local HSE office that his employees are working with radioactive substances. If the patient is resident in a care home or has professional carers that the information is included with the request so that the Nuclear medicine department can make appropriate arrangements with the care home staff.

Patients with Graves' (congestive) ophthalmopathy

Render the patient euthyroid using either block and replace or a titration regimen until the congestion (e.g. chemosis, periorbital oedema) has improved. Then treat with prednisolone starting on day 1 prior to RAI administration. Between 20 and 40% of patients respond only partially or do not respond to glucocorticoid treatment [9, 10]. Usual regimen: prednisolone 0.5mg/kg/day for a week, then gradually tailing off by 5 mg/ week. In some patients, recurrence is possible if the dose of steroid is tapered too quickly [9]. Bisphosphonate cover (alendronic acid 70mg once a week) should be considered in patients in whom a prolonged course of prednisolone is planned (>3 months) but this is **not** necessary routinely. In all cases arrange for patient to be assessed by an ophthalmologist before organising RAI treatment.

Post treatment follow up

All patients should restart their antithyroid regimen 5 days after RAI (unless otherwise advised).

Patients should be seen by their GP or in medical outpatients 12 weeks after RAI treatment, having had a TFT measured 6 weeks after their RAI. They will then

require thyroid function to be checked at 3, 6, 9 and 12 months, then annually. Early onset hypothyroidism should be treated with thyroxine replacement therapy and the patient discharged to the GP.

At 3 months if the patient is off all antithyroid drugs and is:

(a) **Still hyperthyroid** –If the patient is symptomatic restart carbimazole or propylthiouracil and reassess after a further 3 months with TFT's measured 6 weeks after restarting the. If the patient remains hyperthyroid, or continues to require carbimazole or PTU at 6 months after the administration of RAI, consider further RAI therapy.

(b) **Euthyroid** – Discharge back to GP.

(c) **Hypothyroid** – Start on levothyroxine replacement (usually levothyroxine 100microgram daily), discharge to GP care and ask GP to check TFT's after 3, 6, and 9 months for dose adjustment and then annually.

G.P. follow up

Up to 82% of patients with Graves' disease and 32% with toxic multinodular goitre will eventually become hypothyroid after RAI treatment after 25 years [11]. More than 60% of these will be in the first year after treatment [12]. Therefore advise all patients to have their thyroid function checked at 3,6,9,12 months and annually for life. A rise in TSH after 3 months indicates the development of hypothyroidism and the need for levothyroxine. A subsequent fall in TSH suggests recurrent thyrotoxicosis, which if persisting beyond 6 months requires retreatment. In some patients with Graves' disease TSH remains suppressed for long periods after RAI due to the presence of stimulating antibodies, rather than recurrent thyrotoxicosis. These patients should be monitored using T_4 and T_3 levels.

Additional notes

- **Wherever possible, written advice should be given to patients to reinforce treatment compliance. This should include information about when to start/stop medication, and when to have TFT's in relation to RAI administration and out patient follow up.**
- Hypothyroidism occurs in up to 50% of RAI treated individuals at 5 years, and 80% at 25 years.
- In (compliant) patients on levothyroxine elevated TSH levels always indicates under-treatment, and the dose of levothyroxine should be increased.
- The dose of levothyroxine should be 1.6microgram/Kg and usually ranges from 75 microgram/day to 175 microgram/day, it is rarely necessary to give more than this unless the patient has thyroid hormone resistance (this is rare).
- It takes at least 6 weeks for thyroid function tests to re-equilibrate after a change in dosage of thyroxine - do not adjust the dose more frequently than this.
- Amiodarone contains free iodine which can either stimulate or suppress thyroid iodine uptake. An amiodarone-treated patient with thyrotoxicosis should be reviewed by an endocrinologist before referral for RAI therapy. A ^{99m}Tc will be needed to see if they will take up RAI.

Broad recommendations

The management pathway is laid out in the quick reference guideline

Clinical audit standards

Appropriate referrals for RAI
Consent form being signed prior to referral
Appropriate clinical monitoring

Summary of development and consultation process undertaken before registration and dissemination

This guideline was first written in the 1980s by Dr Richard Greenwood. It has been updated several times. The current guidance has been adapted and modified based on up to date publications, and comments from the chair of the thyroid cancer MDT – Dr Tom Roques, the ENT and endocrine surgeons and the ophthamlologists.
This version has been endorsed by the Clinical Guidelines Assessment Panel.

Distribution list/ dissemination method

The guideline will be on the trust Intranet. It will also be circulated to all physicians (general and MFE), general surgeons, consultants in radiotherapy / oncology, all junior medical staff and nursing sisters associated with the relevant Directorates, the Nuclear Medicine Department and relevant medical staff at James Paget Hospital.

References/ source documents

[1] Royal College of Physicians. Radioiodine in the management of benign thyroid disease - clinical guidelines. 2nd Edition. 2007. London, Royal College of Physicians.

[2] Nygaard B, Hegedus L, Hjalgrim H, Soe-Jensen P, Hansen JM. Radioiodine treatment of multinodular non-toxic goitre. *Br Med J* 1993; **307**(6908)**:**828-832.

[3] Kendall-Taylor P, Keir MJ, Ross WM. Ablative radioiodine therapy for hyperthyroidism: long term follow up study. *Br Med J* 1984; **289**(6441)**:** 361-363.

[4] Hardisty CA, Jones SJ, Hedley AJ *et al.* Clinical outcome and costs of care in radioiodine treatment of hyperthyroidism. *J R Coll Physicians Lond* 1990; **24**(1)**:**36-42.

[5] Nikiforov Y, Gnepp DR. Pediatric thyroid cancer after the Chernobyl disaster. Pathomorphologic study of 84 cases (1991-1992) from the Republic of Belarus. *Cancer* 1994; **74**(2)**:**748-766.

[6] Read CHJ, Tansey MJ, Menda Y. A 36-year retrospective analysis of the efficacy and safety of radioactive iodine in treating young graves' patients. *J Clin Endocrinol Metab* 2004; **89**(9)**:**4229-4233.

[7] Bartalena L, Marcocci C, Bogazzi F *et al.* Relation between therapy for hyperthyroidism and the course of Graves' ophthalmopathy. *N Eng J Med* 1998; **338**(2)**:**73-78.

[8] IPEM. Guidance notes for the protection of persons against ionising radiations arising from medical and dental use. A good practice guide on all aspects of ionising radiation protection in the clinical environment. 2002. York.

Ref Type: Pamphlet

[9] Bartalena L, Pinchera A, Marcocci C. Management of Graves' ophthalmopathy: Reality and perspectives. *Endocr Rev* 2000; **21**(2)**:**168-199.

[10] Acharya SH, Avenell A, Philip S *et al.* Radioiodine therapy (RAI) for Graves' disease (GD) and the effect on ophthalmopathy: a systematic review. *Clin Endocrinol (Oxf)* 2008; **69**(6)**:**943-950.

[11] Metso S, Jaatinen P, Huhtala H *et al.* Long-term follow-up study of radioiodine treatment of hyperthyroidism. *Clin Endocrinol (Oxf)* 2004; **61**(5)**:**641-648.

[12] Ahmad AM, Ahmad M, Young ET. Objective estimates of the probability of developing hypothyroidism following radioactive iodine treatment of thyrotoxicosis. *Eur J Endocrinol* 2002; **146**(6)**:**767-775.

Appendix A

Consent Form for Radioiodine Treatment

Statement of health professional

The intended benefits: I have explained the procedure to the patient/parent. In particular, I have explained that this treatment is being proposed to treat the thyroid gland which has become overactive and/or enlarged.

Serious or frequently occurring risks:

- The thyroid gland may stop working completely after this treatment and regular blood tests will be required to check the functioning of the gland.
- Thyroxine treatment may become necessary.
- There may be a short period of thyroid overactivity following the radioiodine treatment.
- In patients with thyroid eye disease the possible risks of radioiodine treatment have been discussed. If there is a possibility of thyroid eye disease I have sought the opinion of the local ophthalmologist prior to this radioiodine referral. If steroids have been suggested prior to radioiodine, then the patient is aware of this.
- Several radioiodine treatments may be required.
- I have satisfied myself that the patient, if female, is not pregnant and that she is aware that pregnancy must be avoided for six months after the administration of radioiodine.
- Male patients should not father children for four months after the administration of radioiodine.
- The benefits and risks of any available alternative treatments (including no treatment) have been discussed.

Signed (health professional). . . . . Date *(dd/mm/yyyy)*. . . . . .

Name (PRINT). . . . . .

Statement of patient or person with parental responsibility for patient

- **I agree** to the procedure described above.
- **I confirm** that I am/the patient is not pregnant or breast feeding.

Signed . . . . . Date *(dd/mm/yyyy)*. . . . . .

Name (PRINT) . . . . . Relationship to patient . . . .

Confirmation of consent (to be completed by a health professional before the treatment is administered)

- I have discussed what the procedure is likely to involve (including the specific written requirement to avoid contact with children and pregnant women and to take time off work), and any particular concerns of those involved.
- I have informed the patient/parent that they can withdraw their consent for treatment at any time.
- I have discussed relevant written radiation protection advice.
- I have confirmed that the patient/parent has no further questions and wishes the procedure to go ahead.

Radioiodine activity administered: . . . . . MBq 131I

Signed . . . . . .Date *(dd/mm/yyyy)*. . . . . .

Name (PRINT). . . . . Job title ... .

To be completed by physician in clinic

To be completed by nuclear medicine staff

Joint Trust Guideline for the Use of Radioiodine in the Management of Benign Thyroid Disease

One copy for the patient medicine	☐	One copy for the notes	☐	One copy for nuclear	☐

Joint Trust Guideline for the Use of Radioiodine in the Management of Benign Thyroid Disease

Referral Form for Radioactive Iodine Treatment

LARGE PATIENT ID LABEL	**Consultant:** **Date:**

Indication:

Graves' disease ☐ Toxic nodule ☐

Multinodular goitre ☐ Other _____

I-131 Activity to be prescribed:

370MBq / 600MBq / 800MBq

Eye disease present:	**Yes**	☐	**No**	☐	
Ophthalmology review requested?	**Yes**	☐	**No**	☐	**Other**
Prednisolone required?	**Yes**	☐	**No**	☐	

Medication:
Please list current thyroid medication:_____

Have standard medication instructions given to patient? Stop carbimazole for 5 days, propylthiouracil (PTU) for 10 days and levothyroxine for 10 days pre RAI treatment. Restart usual medication 5 days after RAI and continue for 6 weeks.

Yes ☐ **No** ☐

If other instructions have been given please list below, with any special precautions / preferred date for treatment

_____

Follow up clinic Time (weeks) ☐ Via GP ☐

Referrer's signature_____

Nuc Med Use:

Date/Time of appointment _____

Name of Practitioner	☐	Authoriser	☐
Patient ID/LMP/Consent Confirmed	☐	^{99m}Tc Activity	☐
Injected by	☐	Scanned by	☐
Name of RAI dispenser	☐	Activity dispensed	☐

Appendix B

Carbimazole/propylthiouracil (PTU): information for health care professionals

Rash

This patient is taking carbimazole/propylthiouracil (PTU) for their thyroid condition. If they have developed a rash, please consider switching to an alternative agent. If they are taking carbimazole, please prescribe PTU in its place. The dose of PTU is 10 times the dose of carbimazole (for example 20mg carbimazole = 200mg PTU). PTU doses should be divided and given two or three times a day (for example 100mg bd). Antihistamines may be given for associated pruritus if necessary. If the patient has had both carbimazole and PTU, or you are concerned about the patient or require further information, please contact the endocrinology doctor on call via the hospital switchboard 01603 286286.

Sore throat, fever, jaundice or mouth ulcers

If the patient attends with a fever, flu like symptoms, mouth ulcers or a sore throat, this may indicate the development of neutropaenia. Please ensure that they have stopped their medication, and check their full blood count urgently. If the patient develops any features of liver disease eg jaundice, please also ensure they have stopped their medication and check their liver function test. If their blood tests are normal, the patient can continue the drug. If the white cell count is low, or liver function is abnormal please contact the endocrine team immediately.

Re: Prednisolone cover for radioactive iodine

This patient with thyrotoxicosis due to Graves' disease has been referred for radioactive iodine therapy. Since they have signs of Graves' ophthalmopathy, they will require steroid cover for this procedure to protect them from a possible flare up of their eye disease.

Please prescribe prednisolone to start one day before radioactive iodine is administered.

The usual starting dose is 0.3mg/kg/day prednisolone for one week, with the dose gradually reduced over a 6 week course.

Typical prescription:
25mg prednisolone daily 1st week
20mg 2nd week
15mg 3rd week
10mg 4th week
5mg 5th week
2.5mg 6th week and stop

Bisphosphonate cover (alendronic acid 70mg once a week) should be considered in patients in whom a prolonged course of prednisolone is planned (>3 months) but this is **not** necessary routinely.

Proton pump inhibitors should also be considered in patients at high risk of gastrointestinal bleeding (omeprazole 20mg in patients with a previous ulcer, or taking concomitant aspirin, clopidogrel, warfarin, oral bisphosphonate or SSRI therapy), but again is **not** necessary routinely for this short course of therapy.

Many thanks for your help,

CC patient in all cases

Appendix C

Pathway of care for patients with Graves' thyrotoxicosis

Graves' disease

- On receipt of GP letter, advise carbimazole 20mg BD to start immediately unless the patient is pregnant, breast feeding or planning a pregnancy. In cases of mild biochemical abnormality eg T4 level <30pmol/L, isolated T3 toxicosis, or with minimal symptoms lower doses may be chosen (e.g. 20mg).
- At start of treatment issue patient with Patient Information leaflet Carbimazole and Propylthiourcil information sheet for patients Trustdocs Id: 12316 and see written instructions for staff Appendix B above.
- **Visit 1:** See patient with result of pre clinic bloods for full assessment of thyroid status, other autoimmune diseases, eye disease, smoking cessation advice, pregnancy and contraception plans, and discussion of standard precautions and long term treatment options. Recommend selenium 200mcg od if mild to moderate eye disease is present, and refer to ophthalmology if eye disease is present or suspected using the standard letter.
- Give patient two NNUHFT ICE request forms to have their TSH and T4 levels checked at 6 and 12 weeks (from the start of treatment not post clinic).
- On receipt of the results of this test, issue a standard written advice letter on dose titration, to the patient with a copy sent to the GP. This letter will typically advise cutting the dose to 20mg.
- **Visit 2: 3 months:** See patient with results of their 12 week blood test = 3 months post first clinic. Advise dose titration as appropriate (typically to 10-15mg). Consider radioactive iodine treatment now if euthryoid and clinically appropriate. In the presence of eye disease, only consider radioactive iodine after ophthalmology assessment.
- Continue blood tests every 6 weeks with written advice to the patient and copied to the GP on dose titration using the standard letter. Dose will typically be reduced by 5mg every 6 weeks to a usual maintenance dose of 5mg.
- **Visit 3: 6 months:** Reassess and consider radioactive iodine treatment at that visit if euthyroid and if clinically appropriate, and if not already referred at 3 months.
- If not for radioiodine, set date to stop treatment at this visit – typically 12-18 months total treatment duration, or 12 months of euthyroid state.
- Discharge at that visit with a defined date for treatment end documented in the GP letter. Ask GP to please undertake 3 monthly blood tests from this point until end of treatment, and for 12 months after stopping treatment, unless otherwise indicated by earlier symptom recurrence.
- Warn patients about the possibility of relapse post future pregnancies.
- Ask GP to re-refer if patient relapses post treatment course, to reconsider RAI, a repeat course of treatment, surgery or long term treatment.

Radioactive iodine

- Render euthyroid medically before making the decision on radioactive iodine (e.g. at 3 or 6 month visit).
- In the case of suspected eye disease, refer patient to ophthalmology before considering radioactive iodine.
- Unless ophthalmologists have expressly stated that no steroid cover is required, in all cases of suspected eye disease referred for radioactive iodine, send patient and GP a copy of the standard steroid cover for radioactive iodine letter at the time of referral.
- Use standard radioactive iodine referral and consent form to arrange radioactive iodine therapy (Appendix A). Give the patient NNUHFT ICE request forms to have blood tests performed at 6 and 12 weeks post iodine treatment.
- Standard advice is to stop carbimazole 5 days before and resume 5 days after RAI. In cases with very mild toxicosis or those already on very low doses e.g. 5mg only, advice may be to stay off treatment. Conversely, in patients currently taking very large doses of carbimazole e.g. 40mg, advice may be to restart on half previous dose.
- Advise patient to continue this treatment until 6 weeks after their iodine therapy (5 weeks and 2 days post restarting their tablets), then have a blood test.
- Review results and send standard post iodine letter to patient with copy to GP, with advice on whether to stop treatment at this stage.
- Advise patient to have another blood test 6 weeks later (12 weeks post iodine).
- Review patient 3 months post RAI with the result of their 12 week blood test. The patient should typically be off treatment by now, and should be informed whether they need to start thyroxine at that stage.
- Discharge patient at that 3 months post RAI visit, unless the patient is still thyrotoxic.
- Advise GP to repeat blood tests 3 monthly for the first year, then annually thereafter to seek emerging hypothyroidism or recurrent thyrotoxicosis.
- Ask GP to refer back if recurrent thyrotoxicosis occurs after 6 months for consideration of repeat RAI.

Block and Replace therapy

- Consider use of block and replace in selected patients, eg some cases of severe eye disease, cases of poor adherence or difficulty with regular blood tests, difficult control medically with fluctuating levels. Block and replace should not generally be used in young women in whom pregnancy is a possibility.

- **Visit 1:** Start carbimazole 20mg BD at diagnosis and issue the standard carbimazole warning sheet.
- Arrange 6 weekly blood tests and write with instructions. Carbimazole dose is fixed. Levothyroxine 75-100mcg should be added once the fT4 level is within the normal range. T4 dose may then need adjustment to achieve normal TSH.
- **Visit 2:** Review at 3 months with result of repeat blood test at 12 weeks, and advise on levothyroxine requirement as above. Once the patient is euthyroid, consider RAI as for patients on standard dose titration therapy above.
- Continue 6 weekly blood tests and write with dose instructions using standard letter (appendix 6).
- **Visit 3:** Review at 6 months, titrate T4 dose to achieve normal TSH and symptoms, consider RAI again, advise all patients of date to stop treatment (total treatment course typically 12 months), and advise GP to perform 3 monthly blood tests for rest of the treatment course, then stop treatment and continue 3 monthly blood tests for next 12 months or if symptoms recur as above.