Welcome to this October issue of Respiratory Research Review with the topics of VTE (venous thromboembolism) and pulmonary hypertension. These pulmonary vascular illnesses are among the leading causes of preventable mortality, and in 2008 in Australia, almost 15,000 cases of VTE were reported.

Our treatment regimens are well established with a good evidence base, but less certain is who to screen. The current level of suspicion is high and less than 10% of CTPA scans performed are positive for a PE (pulmonary embolism). Also less certain is when to stop anticoagulation, particularly in unprovoked VTE, which may have a recurrence rate of up to 50% in 10 years. Several of the chosen articles address issues around simplifying diagnostic algorithms in patients with suspected PE, identifying asthma as a potential risk factor for PE, which is about as strong as the oral contraceptive pill or obesity, and noticing that the rate of recurrent PE in patients with COPD is not higher than in the general population. Rivaroxaban has been shown to be superior to aspirin in preventing recurrent VTE in patients with unprovoked VTE.

"It is impossible to give a validated recommendation as to how such patients (and families) should be selected" for thrombophilia testing – that was the concluding statement of the British Committee for Standards in Haematology and has been picked up by Jean Connors in her outstanding review – "ordering thrombophilia tests is easy, determining who to test and how to use the results is not". She took this as a challenge and has written the clearest summary on when to request thrombophilia testing: i) never during the acute VTE episode; ii) possibly in patients aged less than 50 years with an unprovoked VTE; iii) in patients with a strong family history of VTE; iv) in patients with recurrent VTE, especially at a young age; and v) at VTE in usual sites like splanchic or cerebral veins. I can highly recommend glancing at this well-written, comprehensive review, which also covers topics like thrombophilia testing in provoked and unprovoked VTE, suspected antiphospholipid syndrome and special circumstances like pregnancy. If you wanted to make VTE a peer-review topic, consider utilising the paper by Rory Wallace and colleagues on the knowledge of thrombophilia testing – that was the concluding statement of the previous issue of Respiratory Research Review in September, we reviewed the effect of cancer immune screening in unprovoked VTE.

In the previous issue of Respiratory Research Review in September, we reviewed the effect of cancer immune therapy on interstitial lung disease, here we review the connection between the tyrosine kinase inhibitor dasatinib and PAH (pulmonary arterial hypertension). The field continues to move rapidly and we can only touch on a few topics; like the beneficial effects of exercise training in pulmonary hypertension, of upfront combination therapy on RV (right ventricular) volumes and selexipag on connective tissue disease-associated PAH. One of the most enjoyable and at the same time reassuring articles was the paper from the French group on clinical phenotypes and outcomes of PVOD. We hope you enjoy the selection and are looking forward to feedback and comments.

Kind regards

Professor Lutz Beckert
lutzbeckert@researchreview.co.nz

Independent commentary by Professor Lutz Beckert.
Professor Lutz Beckert is the Head of Department of Medicine of the University of Otago, Christchurch. He is also a Respiratory Physician at Canterbury District Health Board with particular clinical interests in interstitial lung disease, pulmonary vascular disease, respiratory physiology and COPD (chronic obstructive pulmonary disease). Lutz is happy to be contacted to discuss research ideas either as a sounding board or with the view of future collaborations.

Abbreviations used in this issue
6MWD = 6-minute walk distance
COPD = chronic obstructive pulmonary disease
CTPA = computed tomography of pulmonary angiogram
DVT = deep vein thrombosis
IVC = inferior vena cava
NT-proBNP = N-terminal prohormone of brain natriuretic peptide
OR = odds ratio
PAH = pulmonary arterial hypertension
PE = pulmonary embolism
PVOD = pulmonary veno-occlusive disease
RCT = randomised controlled trial
RV = right ventricular
VTE = venous thromboembolism

GSK's Ellipta portfolio of COPD and Asthma treatments is here.

For more information, please go to www.medsafe.govt.nz
Simplified diagnostic management of suspected pulmonary embolism (the YEARS study)

Authors: van der Hulle T et al., for the show YEARS study group

Summary: The prospective YEARS cohort study enrolled 3465 evaluable consecutive patients with suspected PE and managed them by simultaneous assessment of the YEARS clinical decision rule, consisting of clinical signs of DVT (deep vein thrombosis), haemoptysis and whether PE is the most likely diagnosis, and D-dimer level. PE was considered excluded when there were no YEARS items and the D-dimer level was <1000 ng/mL or when ≥1 YEARS item was present and the D-dimer level was <500 ng/mL. All other participants underwent CTPA. Among untreated participants in whom PE was excluded at baseline (n=2946), symptomatic VTE was diagnosed in 0.61% during 3 months of follow-up, with 0.20% experiencing a fatal PE. Using the YEARS algorithm, CTPA was not indicated in 48% of patients, compared with 34% of patients if the Wells’ rule and fixed D-dimer threshold of <500 ng/mL would have been applied.

Comment: CTPA scanning has established itself as the gold standard. Despite its great diagnostic accuracy, because of the nonspecific presentation of PEs, CTPA scanning is becoming clinically less useful; less than 10% of scans are positive, subsegmental emboli may be detected and patients are exposed to radiation and contrast toxicity. These Dutch researchers combined key pretest probability findings and the D-dimer result into one score: 1) signs of DVT; 2) haemoptysis; 3) clinically, PE is the most likely diagnosis; and 4) D-dimer results. Bottom line: the new score is safe and an important milestone, but not the final word in optimising investigations for PE.


Abstract

Validating the HERDOO2 rule to guide treatment duration for women with unprovoked venous thrombosis

Authors: Rodger MA et al., for the REVERSE II Study Investigators

Summary: The HERDOO2 rule was validated in a prospective cohort of women with a first unprovoked VTE treated with 5–12 months of short-term anticoagulation therapy. The study included 631 women classified as low risk of recurrent VTE (0–1 HERDOO2 criteria), 591 of whom had discontinued anticoagulants, 323 high-risk women (≥2 HERDOO2 criteria) and men who had discontinued anticoagulants, and 1802 who had continued anticoagulants according to clinician and patient discretion. Recurrent symptomatic VTE within 1 year occurred at rates of 3.0% per patient-year in low-risk women, 8.1% per patient-year in high-risk women and men who discontinued anticoagulants, and 18.9% who had continued anticoagulants of recurrent VTE (0–1 HERDOO2 criteria), 591 of whom had discontinued anticoagulants, 323 high-risk women with 5–12 months of short-term anticoagulation therapy. The study included 631 women classified as low risk

Comment: Patients with VTE with reversible risk factors need short-term anticoagulation; however, patients with unprovoked VTE should probably continue long-term anticoagulation, unless they have a risk of bleeding. This study adds to our knowledge, identifying women without hyperpigmentation, oedema, redness, D-dimer levels <250 μg/L, body mass index <30 kg/m² and age <65 years (HERDOO2). Women without risk factors or one risk factor had a 3% risk of recurrent VTE within 1 year and women with two or more risk factors had an 8% risk. Bottom line: women with their first unprovoked VTE who do not have or who have one HERDOO2 risk factor can safely discontinue anticoagulation after short-term treatment.

Reference: BMJ 2017;356:j1065

Abstract

Screening for occult cancer in patients with unprovoked venous thromboembolism

Authors: van ES N et al.

Summary: This systematic review and meta-analysis of individual patient data (n=2316) from ten studies evaluated cancer screening strategies in adults with unprovoked VTE. Extensive screening was performed in 58% of participants, and the 12-month prevalence of cancer after a VTE diagnosis was 5.2%. Participants who underwent extensive screening versus more limited screening initially had a higher point prevalence of cancer (OR 2.0 [CI 1.2, 3.4]) but this was not maintained at 12 months (1.4 [0.89, 2.1]). There was a linear increase in cancer prevalence as age increased, with patients aged ≥50 years having higher prevalence than younger patients (OR 7.1 [CI 3.1, 16]).

Comment: It was 150 years ago that Dr Armand Trousseau, physician in chief, gave his lecture about the “frequency with which cancerous patients are affected with painful oedema in the superior or inferior extremities”. As Gino Merli and Howard Wolz point out in their editorial for the last 150 years clinicians have been wondering about occult malignancies in patients with unprovoked VTE. In patients younger than 40 years the cancer risk is 0.5%, and above the age of 80 years it is 10%. Bottom line: more aggressive screening detects more cancer; however, it is unclear that this translates into improved clinical outcomes.


Abstract
Risk of pulmonary embolism and deep venous thrombosis in patients with asthma

Authors: Zöller B et al.

Summary: This study explored the association of asthma with DVT using Swedish registry data for 114,366 patients with a first hospital diagnosis of PE, 76,494 patients with DVT and 6854 patients with both PE and DVT, matched to population controls. Compared with patients without asthma, those with asthma had higher probabilities of PE (adjusted OR 1.43 [95% CI 1.37, 1.50]), DVT (1.56 [1.47, 1.65]) and PE and DVT combined (1.60 [1.32, 1.93]).

Comment: It is well documented that COPD, heart failure and pneumonia increase the risk of VTE. The risk for asthma is less well defined; however, other inflammatory conditions such as inflammatory bowel disease, rheumatoid arthritis and lupus erythematosus increase the risk of VTE. These researchers used the Swedish National Registry to assess the relationship between VTE and asthma. The authors found about a 50% increased risk for VTE within 3 months after an admission for asthma. They speculate that this may be due to airway inflammation or the antifibrinolytic effect of systemic steroids. Bottom line: the inflammatory illness, asthma, increases the risk of both DVT and PE.

Reference: Eur Respir J 2017;49(2):1601014

Abstract

Risk of recurrent venous thromboembolism in COPD patients

Authors: Le Mao R et al.

Summary: Recurrent VTE risk after stopping anticoagulation therapy was investigated in a prospective cohort of 1468 patients with a documented episode of VTE, 136 of whom also had COPD. VTE recurrence occurred in 34 patients with COPD and 272 without COPD over median follow-up of 36.5 months, giving incidence rates of 9.1% and 7.0%, respectively. The risk of VTE recurrence was not significantly greater in patients with versus without COPD (hazard ratio 1.0 [95% CI 0.7, 1.4]), nor was the risk of death.

Comment: COPD patients have an increased PE risk of 3–25%. This French group prospectively followed a cohort of about 1500 COPD patients whose treatment for VTE had been stopped to explore the risk of recurrent VTE. They found no difference in recurrence of a second VTE with a risk of 9% for COPD patients and 7% for non-COPD patients. Laurent Bertolletti wonders in his editorial whether both groups studied had an increased VTE risk, and how to investigate a COPD patient who re-presents with shortness of breath. Bottom line: the risk of recurrent VTE is about 8%; this does not differ between patients with COPD and without.


Abstract

Inferior vena cava filters to prevent pulmonary embolism

Authors: Bikdeli B et al.

Summary: This was a systematic review and meta-analysis of six RCTs and five prospective observational studies investigating the use of IVC (inferior vena cava) filters in patients at risk of PE; the quality of evidence for the RCTs was graded low to moderate. Compared with no IVC filter use, IVC filter use decreased the risk for subsequent PE (OR 0.50 [95% CI 0.33, 0.75]), increased the risk for DVT (1.70 [1.17, 2.48]), nonsignificantly reduced the risk of PE-related mortality (0.51 [0.25, 1.05]) and had no effect on all-cause mortality (0.91 [0.70, 1.19]); the findings were similar when only RCT data were analysed and also across a range of sensitivity analyses.

Comment: IVC filters play an important role in patients with PE with absolute contraindications to anticoagulation and possibly in patients with haemodynamic compromise. However, in the US about 100,000 IVC filters are inserted each year. Reviewing data from the available RCTs was complex because of the lack of adjudicated outcomes, the large heterogeneity in study design and devices and possible under-reporting of complications. Still, the authors’ bottom line is solid: IVC filters reduce the risk of subsequent PE, but increase the risk of further DVTs and don’t improve PE-related mortality or all-cause mortality.

Reference: J Am Coll Cardiol 2017;70(13):1587–97

Abstract

Disclaimer:

Privacy Policy: Research Review will record your email details on a secure database and will not release them to anyone without your prior approval. Research Review and you have the right to inspect, update or delete your details at any time.

Blindline: This publication is not intended as a replacement for regular medical education but to assist in the process. The reviews are a summarised interpretation of the published study and reflect the opinion of the reviewer rather than those of the research group or scientific journal. It is suggested readers review the full trial data before forming a final conclusion on its merits. Research Review publications are intended for New Zealand health professionals.

For more information, please go to www.medsafe.govt.nz
Freedom to breathe.

Fully funded inhalers without special authority.

Rivaroxaban or aspirin for extended treatment of venous thromboembolism

Authors: Weitz JI et al., for the EINSTEIN CHOICE Investigators

Summary: These researchers randomised 3365 patients with VTE to receive rivaroxaban 20mg or 10mg or aspirin 100mg once daily for ≥12 months (median 351 days) in this phase 3 trial; all study participants had completed 6–12 months of anticoagulation therapy and were in equipoise regarding the need for continued anticoagulation. Compared with aspirin, rivaroxaban at the 20mg and 10mg doses was associated with significantly lower rates of symptomatic recurrent fatal or nonfatal VTE (primary efficacy outcome; 1.3% and 1.2%, respectively, vs. 4.4%, respective hazard ratios 0.34 [95% CI 0.20, 0.59] and 0.26 [0.14, 0.47]) and similar rates of major bleeding (0.5% and 0.4% vs. 0.3%), clinically relevant nonmajor bleeding (2.7% and 2.0% vs. 1.8%) and any adverse event.

Comment: These Canadian investigators report data on the risk of recurrent VTE within 1 year comparing rivaroxaban with aspirin. All patients had a previous VTE and completed 6–12 months of warfarin or direct oral anticoagulant therapy. Following 1 year of treatment, the risk of recurrent VTE was documented as 1.2% with rivaroxaban 10mg, 1.5% (two fatal) with rivaroxaban 20mg, and 4.4% (two fatal) with aspirin 100mg. The incidences of bleeding and other adverse events were similar. The accompanying editorial raised the question of whether it is time to consider long-term anticoagulation for all patients with VTE. Bottom line: the risk of recurrent VTE after 1 year was reduced with rivaroxaban.


Abstract

Venous thromboembolism management practices and knowledge of guidelines: a survey of Australian haematologists and respiratory physicians

Authors: Wallace R et al.

Summary: Australian doctors (71 haematologists and 110 respiratory physicians) were surveyed on their VTE management practices in this cross-sectional research; most respondents were aged 31–50 years and worked in teaching hospitals or acute-care settings. Undertreatment of high-risk PE was reported by 32% of respondents, 83% reported inadequate duration of anticoagulation for first-episode unprovoked PE, and 16% and 41% reported overtreatment for thrombolysis for intermediate-risk PE and duration of anticoagulation respectively. The research also uncovered uncertainty and variations in the respondents’ management approaches.

Comment: Currently we don’t have any Australian/NZ guidelines and clinicians will choose to follow the UK NICE (National Institute of Health and Care Excellence), ESC (European Society of Cardiology) or ACCP (American College of Chest Physicians) guidelines. In preparation for a possible regional document, our colleagues from Melbourne conducted a survey of approaches to managing VTE among haematologists and respiratory physicians. It makes interesting reading and could be used as a discussion document for an in-service or peer-group session. Bottom line: although we are aware of guidelines, our practice is variable, leading to both undertreatment and overtreatment.


Abstract
The benefit of exercise training in pulmonary hypertension

Authors: Chia KSW et al.

Summary: This clinical review discusses the pathophysiology of exercise impairment in pulmonary hypertension. It also includes sections discussing 18 studies investigating exercise training in adults with pulmonary hypertension, 15 of which reported improvements in 6MWD and seven reported improvements in quality of life. Mechanisms by which exercise provides benefits in pulmonary hypertension were discussed, including improvements in peak oxygen consumption, cardiac function and haemodynamics, and changes in skeletal muscle fibre type. The authors went on to discuss the evidence base for prescribing exercise including intensity, duration and frequency, types of exercise, safety/supervision and barriers to exercise.

Comment: Pulmonary hypertension, regardless of the aetiology, leads to RV remodelling, right heart failure and eventually to death. Specific therapy for idiopathic pulmonary hypertension has probably improved the median survival from 2.4 to 7.0 years. In comparison with pharmacotherapy, exercise training is of low cost and it has a low risk of side effects. This excellent review acknowledges earlier safety concerns, reviews the evidence of improving 6MWD and quality of life, and even gives examples of typical outpatient-based and home-based programmes. Bottom line: exercise training in patients with pulmonary hypertension improves 6MWD similar to that seen with pharmacotherapy.


Abstract

Upright combination therapy reduces right ventricular volumes in pulmonary arterial hypertension

Authors: van de Veerdonk MC et al.

Summary: The impact of upfront combination endothelin-receptor antagonist plus phosphodiesterase-5 inhibitor therapy (n=35) versus monotherapy (n=45) for PAH on RV volumes was explored in this retrospective research. The study patients were New York Heart Association class II or III and had undergone right-sided heart catheterisation and cardiac MRI at baseline and again at 1 year. Compared with monotherapy, combination therapy was associated with reductions in pulmonary vascular resistance and pulmonary pressures that were of greater significance, and a greater decrease in NT-proBNP level (−77% vs. −51% [p<0.001]). Combination therapy was also associated with improvements in RV volumes and calculated RV wall stress (p<0.001 for both), whereas these parameters remained unchanged after monotherapy. There was also a greater improvement in RV ejection fraction with combination therapy compared with monotherapy (p<0.001).

Comment: Upright combination therapy with ambrisentan and tadalafil has been shown to improve 6MWD by 25m in comparison with sequential therapy (Respiratory Research Review, Issue 117). The difference in 6MWD distance achieved was significant, albeit small. These Dutch authors investigated NT-proBNP levels and RV volumes to calculate RV wall stress to explore the physiological background of the effect of upfront combination therapy versus monotherapy. The therapy mode was decided on by the treating physician. Bottom line: in comparison with monotherapy, upfront combination therapy achieved significant reductions in NT-proBNP level, pulmonary vascular resistance and RV volume and improved RV function.

Reference: Eur Respir J 2017;49(6):1700007

Abstract

Clinical phenotypes and outcomes of heritable and sporadic pulmonary veno-occlusive disease

Authors: Montani D et al.

Summary: This population-based study explored the impact of EIF2AK4 mutations on the clinical phenotypes and outcomes of 94 registry patients with sporadic or heritable PVOD and/or pulmonary capillary haemangiomatosis. The proportion of patients with bi-allelic EIF2AK4 mutations was 29%. Patients with PVOD or pulmonary capillary haemangiomatosis due to EIF2AK4 mutations presented between birth and age 50 years, and they were of younger median age at presentation than noncarriers (26.0 vs. 60.0 years [p<0.0001]). Precapillary pulmonary hypertension and functional impairment were similarly severe at diagnosis in EIF2AK4 mutation carriers and noncarriers. PAH-approved therapy was received by 81% and 94% of EIF2AK4 mutation carriers and noncarriers, respectively, with 23% and 21% developing drug-induced pulmonary oedema. Only three patients achieved a satisfactory clinical response. The respective 1-year and 3-year event-free survival rates were 63% and 32% in EIF2AK4 mutation carriers and 75% and 34% in noncarriers, with no significant between-group difference. Among patients who underwent lung transplantation (n=33), the respective estimated post-transplant 1-year, 2-year and 5-year survival rates were 84%, 81% and 73%.

Comment: This may well become a seminal paper for patients with this rare but devastating illness. The authors use data from the French registry and carefully define venous occlusive disease as the underlying cause for PAH based on: i) consistent right heart catheter results; ii) centrilobar ground-glass opacities, interlobular septal lines or lymph node enlargement; and iii) low diffusing capacity. Of their 94 cases, about one-third had the EIF2AK4 gene mutation. Patients with the gene mutation were younger at diagnosis; however, both groups had a similar relentless illness progression. Bottom line: about 20% of patients develop drug-induced oedema to PAH drugs, and lung transplantation remains the treatment of choice.


Abstract

Idiopathic pulmonary fibrosis (IPF) treatment now funded

Before prescribing Esbriet® please review the data sheet for information on dosage, contraindications, precautions, interactions and adverse effects. The data sheet is available at www.medsafe.govt.nz


For more information, please go to www.medsafe.govt.nz
Long-term outcomes of dasatinib-induced pulmonary arterial hypertension

Authors: Weatherald J et al.

Summary: Long-term outcomes were reported for 21 cases of incidental dasatinib-induced PAH identified from the French Pulmonary Hypertension Registry. The patients’ median age was 52 years and 71% were female. Dasatinib was administered for a median of 42 months before PAH diagnosis in 19 patients with chronic myelogenous leukemia. Among ten patients tested, no BMPR2 mutations were detected. Dasatinib was discontinued in all patients, and eleven received medications for PAH. There were four deaths during median follow-up of 24 months. Improvements were seen in New York Heart Association functional class (from 76% in class IV to 90% in class I II [p<0.01]), median 6MWD (from 306 to 430m [p<0.01]), median mean pulmonary arterial pressure (from 45 to 26mm Hg [p<0.01]) and pulmonary vascular resistance (from 6.1 to 2.6 Wood units [p<0.01]). Compared with untreated patients, those who received PAH medications had worse baseline haemodynamics but similar long-term outcomes. PAH persistence was recorded for 37% of the patients.

Comment: Dasatinib is a second-generation oral tyrosine kinase inhibitor that is currently funded for the treatment of chronic myelogenous leukemia. Dasatinib is associated with pleural and pericardial effusions, and in 0.5% of cases with PAH. The authors used the French Pulmonary Hypertension Registry to identify 21 patients with dasatinib-related PAH. Dasatinib was discontinued in all patients, and in two-thirds the pulmonary artery pressure improved with significant improvements in shortness of breath and 6MWD. Bottom line: in about one-third of patients with dasatinib-related PAH, the pressure didn’t normalise and they needed PAH-specific drug therapy.

Abstract

Mortality in pulmonary arterial hypertension: prediction by the 2015 European pulmonary hypertension guidelines risk stratification model

Authors: Hooper MM et al.

Summary: An abbreviated version of the risk stratification strategy for patients with PAH proposed in the 2015 European pulmonary hypertension guidelines was assessed in 1588 European registry patients with newly diagnosed PAH. The strategy defines low-, intermediate- and high-risk strata according to estimated 1-year mortality risks of <5%, 5–10% and >10%, respectively. There were significant differences in mortality rates across the three risk groups (p<0.001 for all). The respective 1-year postdiagnosis mortality rates were 2.8%, 9.9% and 21.2% in the low-, intermediate- and high-risk cohorts. Validity of the risk assessment strategy was confirmed at follow-up and in major PAH subgroups.

Comment: Eur Respir J published two articles on risk assessment in PAH, this one from a European consortium and one based on the French registry. Both articles are clinically relevant, sensible and present simplified risk assessment tools for the management of PAH. Still, maybe the editorial by Raymond Benza and colleagues should be the correct citation for these articles. He and his colleagues have published the original REVEAL score and they remind us that these tools are based on expert opinion. So we’ll use his bottom line: collective, collegial and prospective collaboration is needed to make progress in managing PAH.

Abstract

Time spent reading this publication has been approved for CME by Royal New Zealand College of General Practitioners (RNZCGP) General Practice Educational Programme Stage 2 (GPEP2) and the Maintenance of Professional Standards (MOPS) purposes, provided that a Learning Reflection Form is completed. Please CLICK HERE to download your CPD MOPS Learning Reflection Form. One form per review read would be required.

Time spent reading this publication has been approved for CNE by The College of Nurses Aotearoa (NZ) for RNs and NPs. For more information on how to claim CNE hours please CLICK HERE.

RACP MyCPD Program participants can claim one credit per hour (maximum of 50 credits per year) for reading and evaluating Research Reviews.

FOR MORE INFORMATION CLICK HERE

Support your patients with Asthma and COPD booklets including Management Plans for your practice. Order online here

Asthma + Respiratory FOUNDATION NZ

Esbriet® Abridged Prescribing Information (API)

Esbriet (pirfenidone) 267 mg oral capsule is a Prescription Medicine indicated for the treatment of idiopathic pulmonary fibrosis (IPF). Dosage and Administration: Please see Esbriet Data Sheet for information. Contraindications: Contraindicated in patients with a hypersensitivity to pirfenidone or any of the excipients; Patients taking fluvoxamine and patients with a history of angioedema with pirfenidone. Precautions: Hepatic Function: Elevations in ALT and AST ≥3 x ULN have been reported. Liver function tests should be conducted prior to and during treatment. If significant elevations occur the dose of Esbriet should be adjusted, refer to dosage guidelines in Data Sheet. Caution when used in patients with mild or moderate hepatic impairment. Photosensitivity reaction/rash: exposure to direct sunlight should be minimised during treatment and patients instructed to wear sunblock and protective clothing. Dosage adjustment or temporary discontinuation may be required, refer to dosage guidelines in Data Sheet. Angioedema: patients who develop signs or symptoms of angioedema, Esbriet should be withdrawn. Other known ADRs are cough, rash, dyspepsia, arthralgia, somnolence and non-cardiac chest pain.

ESBRIET is a funded medicine for patients with IPF who meet pre-defined criteria. Prescription and doctors’ fees may apply. Before prescribing, please review the ESBRRIET Data Sheet available at www.medsafe.govt.nz. API based on Data Sheet [26-09-2016]. Roche Products (New Zealand) Limited, Auckland. Ph 0800 656 464. www.roche.co.nz All trademarks mentioned herein are protected by law.

For more information, please go to www.medsafe.govt.nz